US010898709B2

(12) **United States Patent**
Wagner et al.

(10) **Patent No.: US 10,898,709 B2**
(45) **Date of Patent: Jan. 26, 2021**

(54) **STIMULATION FOR TREATING SLEEP DISORDERED BREATHING**

(71) Applicant: **INSPIRE MEDICAL SYSTEMS, INC.**, Golden Valley, MN (US)

(72) Inventors: **Darrell Wagner**, Ham Lake, MN (US); **Quan Ni**, Golden Valley, MN (US); **John Rondoni**, Plymouth, MN (US); **David Dieken**, Minneapolis, MN (US)

(73) Assignee: **Inspire Medical Systems, Inc.**, Golden Valley, MN (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **15/562,714**

(22) PCT Filed: **Mar. 16, 2016**

(86) PCT No.: **PCT/US2016/022611**
§ 371 (c)(1),
(2) Date: **Sep. 28, 2017**

(87) PCT Pub. No.: **WO2016/149344**
PCT Pub. Date: **Sep. 22, 2016**

(65) **Prior Publication Data**

US 2018/0117316 A1 May 3, 2018

Related U.S. Application Data

(60) Provisional application No. 62/135,305, filed on Mar. 19, 2015.

(51) **Int. Cl.**
A61N 1/00 (2006.01)
A61N 1/36 (2006.01)
(Continued)

(52) **U.S. Cl.**
CPC ***A61N 1/3601*** (2013.01); ***A61B 5/0816*** (2013.01); ***A61B 5/0826*** (2013.01);
(Continued)

(58) **Field of Classification Search**
CPC ... A61B 5/3601; A61B 5/0816; A61B 5/0826; A61B 5/113; A61B 5/4818;
(Continued)

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,379,462 A 4/1983 Borkan et al.
4,567,892 A 2/1986 Plicchi et al.
(Continued)

FOREIGN PATENT DOCUMENTS

CN 102548610 A 7/2012
JP H11514557 12/1999
(Continued)

OTHER PUBLICATIONS

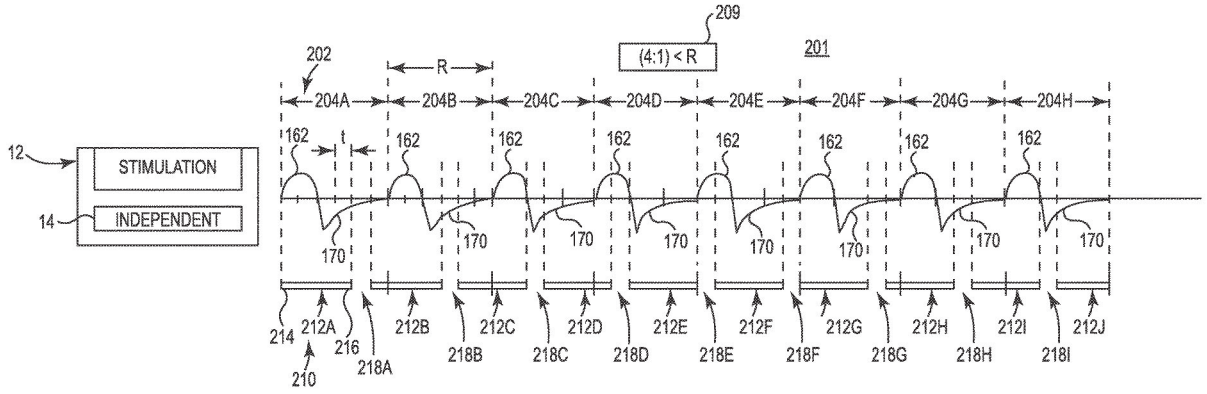
Eisele Article—David W. Eisele, MD et al., "Tongue neuromuscular and direct hypoglossal nerve stimulation for obstructive sleep apnea," Otolaryngologic Clinics of North America, Otolayngol Clin N Am 36 (2003) 501-510 (10 pages).
(Continued)

Primary Examiner — Carl H Layno
Assistant Examiner — Michael J Lau
(74) *Attorney, Agent, or Firm* — Dicke, Billig & Czaja, PLLC

(57) **ABSTRACT**

A device for treating sleep disordered breathing includes a stimulation element to stimulate an airway-patency-related nerve.

15 Claims, 13 Drawing Sheets



(51) **Int. Cl.**

A61B 5/08	(2006.01)
A61B 5/00	(2006.01)
A61B 5/113	(2006.01)
G06F 19/00	(2018.01)
A61B 5/0205	(2006.01)

(52) **U.S. Cl.**

CPC ***A61B 5/113*** (2013.01); ***A61B 5/4818*** (2013.01); ***A61B 5/4848*** (2013.01); ***A61B 5/686*** (2013.01); ***A61N 1/3611*** (2013.01); *A61B 5/0205* (2013.01); *A61N 1/3614* (2017.08); *A61N 1/36146* (2013.01); *A61N 1/36171* (2013.01); *G06F 19/3481* (2013.01)

(58) **Field of Classification Search**

CPC ... A61B 5/4848; A61B 5/686; A61B 1/36135; A61N 1/3611; A61N 1/36135; A61N 1/36146; A61N 1/36171; G06F 19/3481

USPC 607/42, 72, 73

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,630,614	A		12/1986	Atlas
4,813,431	A		3/1989	Brown
4,830,008	A		5/1989	Meer
5,123,425	A		6/1992	Shannon, Jr. et al.
5,133,354	A		7/1992	Kallok
5,134,995	A		8/1992	Gruenke et al.
5,148,802	A		9/1992	Sanders et al.
5,158,080	A		10/1992	Kallok
5,167,229	A		12/1992	Peckham et al.
5,174,287	A		12/1992	Kallok et al.
5,178,156	A		1/1993	Takishima et al.
5,190,053	A		3/1993	Meer
5,203,343	A		4/1993	Axe et al.
5,211,173	A		5/1993	Kallok et al.
5,215,082	A		6/1993	Kallok et al.
5,233,983	A		8/1993	Markowitz
5,239,995	A		8/1993	Estes et al.
5,245,995	A		9/1993	Sullivan et al.
5,265,624	A		11/1993	Bowman
5,281,219	A		1/1994	Kallok
5,300,094	A		4/1994	Kallok et al.
5,335,657	A		8/1994	Terry, Jr. et al.
5,344,438	A		9/1994	Testerman et al.
5,351,394	A		10/1994	Weinberg
5,385,144	A		1/1995	Yamanishi et al.
5,388,578	A		2/1995	Yomtov et al.
5,398,682	A		3/1995	Lynn
5,458,137	A		10/1995	Axe et al.
5,483,969	A		1/1996	Testerman et al.
5,485,851	A		1/1996	Erickson
5,522,862	A		6/1996	Testerman et al.
5,524,632	A		6/1996	Stein et al.
5,540,731	A		7/1996	Testerman
5,540,732	A		7/1996	Testerman
5,540,733	A		7/1996	Testerman et al.
5,540,734	A		7/1996	Zabara
5,546,952	A		8/1996	Erickson
5,549,655	A		8/1996	Erickson
5,588,439	A		12/1996	Hollub
5,591,216	A		1/1997	Testerman et al.
5,605,151	A		2/1997	Lynn
5,645,053	A		7/1997	Remmers et al.
5,671,733	A		9/1997	Raviv et al.
5,797,852	A		8/1998	Karakasoglu et al.
5,823,187	A		10/1998	Estes et al.
5,843,135	A		12/1998	Weijand et al.
5,895,360	A		4/1999	Christopherson et al.
5,904,141	A		5/1999	Estes et al.
5,919,221	A		7/1999	Miesel
5,944,680	A	*	8/1999	Christopherson A61B 5/03 128/897
5,999,846	A		12/1999	Pardey et al.
6,015,389	A		1/2000	Brown
6,021,352	A		2/2000	Christopherson et al.
6,025,624	A		2/2000	Figura
6,041,780	A		3/2000	Richard et al.
6,099,479	A		8/2000	Christopherson et al.
6,120,441	A		9/2000	Griebel
6,125,290	A		9/2000	Miesel
6,125,291	A		9/2000	Miesel et al.
6,126,611	A		10/2000	Bourgeouis et al.
6,132,384	A		10/2000	Christopherson et al.
6,134,459	A		10/2000	Roberts et al.
6,144,866	A		11/2000	Miesel et al.
6,175,767	B1		1/2001	Doyle, Sr.
6,181,961	B1		1/2001	Prass
6,198,952	B1		3/2001	Miesel
6,223,064	B1		4/2001	Lynn et al.
6,240,316	B1		5/2001	Richmond et al.
6,248,080	B1		6/2001	Miesel et al.
6,249,703	B1		6/2001	Stanton et al.
6,251,126	B1		6/2001	Ottenhoff et al.
6,269,269	B1		7/2001	Ottenhoff et al.
6,307,481	B1		10/2001	Lehrman et al.
6,309,350	B1		10/2001	Van Tassel et al.
6,314,324	B1		11/2001	Lattner et al.
6,342,039	B1		1/2002	Lynn et al.
6,345,202	B2		2/2002	Richmond et al.
6,361,494	B1		3/2002	Lindenthaler
6,393,325	B1		5/2002	Mann et al.
6,449,507	B1		9/2002	Hill et al.
6,450,957	B1		9/2002	Yoshimi et al.
6,456,866	B1		9/2002	Tyler et al.
6,509,164	B1		1/2003	Guirguis
6,522,928	B2		2/2003	Whitehurst et al.
6,532,388	B1		3/2003	Hill et al.
6,572,543	B1		6/2003	Christopherson et al.
6,574,507	B1		6/2003	Bonnet
6,587,725	B1		7/2003	Durand et al.
6,609,016	B1		8/2003	Lynn
6,609,032	B1		8/2003	Woods et al.
6,629,527	B1		10/2003	Estes et al.
6,641,542	B2		11/2003	Cho et al.
6,645,143	B2		11/2003	Van Tassel et al.
6,647,289	B2		11/2003	Prutchi
6,651,652	B1		11/2003	Ward
6,654,634	B1		11/2003	Prass
6,665,560	B2		12/2003	Becker et al.
6,666,830	B1		12/2003	Lehrman et al.
6,689,068	B2		2/2004	Hale et al.
6,703,939	B2		3/2004	Lehrman et al.
6,718,208	B2		4/2004	Hill et al.
6,719,708	B1		4/2004	Jansen
6,731,976	B2		5/2004	Penn et al.
6,731,984	B2		5/2004	Cho et al.
6,735,471	B2		5/2004	Hill et al.
6,752,765	B1		6/2004	Jensen et al.
6,770,022	B2		8/2004	Mechlenburg et al.
6,773,404	B2		8/2004	Poezevera et al.
6,805,667	B2		10/2004	Christopherson et al.
6,811,538	B2		11/2004	Westbrook et al.
6,842,647	B1		1/2005	Griffith et al.
6,881,192	B1		4/2005	Park
6,890,306	B2		5/2005	Poezevera
6,893,405	B2		5/2005	Kumar et al.
6,904,320	B2		6/2005	Park et al.
6,907,293	B2		6/2005	Grill et al.
6,928,324	B2		8/2005	Park et al.
6,935,335	B1		8/2005	Lehrman et al.
6,936,011	B2		8/2005	Sheldon
6,964,641	B2		11/2005	Cho et al.
6,978,171	B2		12/2005	Goetz et al.
6,988,498	B2		1/2006	Berthon-Jones et al.
7,025,730	B2		4/2006	Cho et al.
7,041,049	B1		5/2006	Raniere
7,054,692	B1		5/2006	Whitehurst et al.
7,077,810	B2		7/2006	Lange et al.
7,081,095	B2		7/2006	Lynn et al.
7,082,331	B1		7/2006	Park et al.
7,082,336	B2		7/2006	Ransbury et al.

(56) **References Cited**

U.S. PATENT DOCUMENTS

7,087,053	B2	8/2006	Vanney	
7,117,036	B2	10/2006	Florio	
7,128,717	B1	10/2006	Thach et al.	
7,145,461	B2	12/2006	Lehrman et al.	
7,149,573	B2	12/2006	Wang	
7,155,278	B2	12/2006	King et al.	
7,160,252	B2	1/2007	Cho et al.	
7,160,255	B2	1/2007	Saadat	
7,167,743	B2	1/2007	Heruth et al.	
7,174,215	B2	2/2007	Bradley	
7,186,220	B2	3/2007	Stahmann et al.	
7,187,978	B2	3/2007	Malek et al.	
7,189,204	B2	3/2007	Ni et al.	
7,195,594	B2	3/2007	Eigler et al.	
7,200,440	B2	4/2007	Kim et al.	
7,206,635	B2	4/2007	Cho et al.	
7,212,862	B2	5/2007	Park et al.	
7,214,197	B2	5/2007	Prass	
7,252,640	B2	8/2007	Ni et al.	
7,269,457	B2	9/2007	Shafer et al.	
7,269,459	B1	9/2007	Koh	
7,277,749	B2	10/2007	Gordon et al.	
7,330,760	B2	2/2008	Heruth et al.	
7,336,996	B2	2/2008	Hartley et al.	
7,340,302	B1 *	3/2008	Falkenberg	A61N 1/3611 607/9
7,351,208	B2	4/2008	Brodnick et al.	
7,366,572	B2	4/2008	Heruth et al.	
7,371,220	B1	5/2008	Koh et al.	
7,387,608	B2	6/2008	Dunlop et al.	
7,395,113	B2	7/2008	Heruth et al.	
7,396,333	B2	7/2008	Stahmann et al.	
7,398,115	B2	7/2008	Lynn	
7,422,015	B2	9/2008	Delisle et al.	
7,438,686	B2	10/2008	Cho et al.	
7,447,545	B2	11/2008	Heruth et al.	
7,454,250	B1	11/2008	Bjorling et al.	
7,453,928	B2	12/2008	Lee et al.	
7,468,040	B2	12/2008	Hartley et al.	
7,469,697	B2	12/2008	Lee et al.	
7,473,227	B2	1/2009	Hsu et al.	
7,491,181	B2	2/2009	Heruth et al.	
7,510,531	B2	3/2009	Lee et al.	
7,526,341	B2	4/2009	Goetz et al.	
7,542,803	B2	6/2009	Heruth et al.	
7,572,225	B2	8/2009	Stahmann et al.	
7,590,455	B2	9/2009	Heruth et al.	
7,591,265	B2	9/2009	Lee et al.	
7,596,413	B2	9/2009	Libbus et al.	
7,603,170	B2	10/2009	Hatlestad et al.	
7,610,094	B2	10/2009	Stahmann et al.	
7,634,315	B2	12/2009	Cholette	
7,644,714	B2	1/2010	Atkinson et al.	
7,662,105	B2	2/2010	Hatlestad	
7,672,728	B2	3/2010	Libbus et al.	
7,678,061	B2	3/2010	Lee et al.	
7,680,538	B2	3/2010	Durand et al.	
7,702,385	B2	4/2010	Moffitt et al.	
7,717,848	B2	5/2010	Heruth et al.	
7,720,541	B2	5/2010	Stahmann et al.	
7,725,195	B2	5/2010	Lima et al.	
7,734,340	B2	6/2010	De Ridder	
7,734,350	B2	6/2010	Dubnov et al.	
7,742,819	B2	6/2010	Moffitt	
7,747,323	B2	6/2010	Libbus et al.	
7,751,880	B1	7/2010	Cholette	
7,775,993	B2	8/2010	Heruth et al.	
7,783,353	B2	8/2010	Libbus et al.	
7,792,583	B2	9/2010	Miesel et al.	
7,809,442	B2 *	10/2010	Bolea	A61N 1/0558 607/42
7,818,063	B2	10/2010	Wallace et al.	
7,853,322	B2	12/2010	Bourget et al.	
7,881,798	B2	2/2011	Miesel et al.	
7,908,013	B2	3/2011	Miesel et al.	
7,917,230	B2	3/2011	Bly	
7,942,822	B1	5/2011	Koh	
7,957,797	B2	6/2011	Bourget et al.	
7,957,809	B2	6/2011	Bourget et al.	
7,979,128	B2	7/2011	Tehrani et al.	
8,016,776	B2	9/2011	Bourget et al.	
8,021,299	B2	9/2011	Miesel et al.	
8,150,531	B2	4/2012	Skelton	
8,160,711	B2	4/2012	Tehrani et al.	
8,160,712	B1	4/2012	Freed	
8,175,720	B2	5/2012	Skelton et al.	
8,233,987	B2 *	7/2012	Gelfand	A61N 1/36171 607/42
8,265,759	B2 *	9/2012	Tehrani	A61N 1/3627 607/42
8,280,513	B2 *	10/2012	Tehrani	A61N 1/3601 607/42
8,718,776	B2	5/2014	Mashiach et al.	
8,781,587	B2	7/2014	Alt et al.	
9,895,540	B2	2/2018	Mashiach	
2001/0010010	A1	7/2001	Richmond et al.	
2002/0010495	A1	1/2002	Freed et al.	
2002/0049479	A1	4/2002	Pitts	
2002/0156507	A1	10/2002	Lindenthaler	
2003/0093128	A1	5/2003	Freed et al.	
2003/0114905	A1	6/2003	Kuzma	
2003/0224895	A1	6/2003	Gordon et al.	
2003/0163059	A1	8/2003	Poezevera et al.	
2003/0195571	A1	10/2003	Burnes et al.	
2003/0216789	A1	11/2003	Deem et al.	
2004/0015204	A1	1/2004	Whitehurst et al.	
2004/0073272	A1	4/2004	Knudson et al.	
2004/0111139	A1	6/2004	McCreery	
2004/0215288	A1	10/2004	Lee et al.	
2004/0230278	A1	11/2004	Dahl et al.	
2004/0254612	A1	12/2004	Ezra	
2005/0004628	A1	1/2005	Goetz et al.	
2005/0010265	A1	1/2005	Baru Fassio et al.	
2005/0042589	A1	2/2005	Hatlestad et al.	
2005/0043765	A1	2/2005	Williams et al.	
2005/0043772	A1	2/2005	Stahmann et al.	
2005/0074741	A1	4/2005	Lee et al.	
2005/0076908	A1	4/2005	Lee et al.	
2005/0080348	A1	4/2005	Stahmann et al.	
2005/0080461	A1	4/2005	Stahmann et al.	
2005/0081847	A1	4/2005	Lee et al.	
2005/0085865	A1	4/2005	Tehrani	
2005/0085866	A1	4/2005	Tehrani	
2005/0085868	A1	4/2005	Tehrani et al.	
2005/0085869	A1	4/2005	Tehrani et al.	
2005/0085874	A1	4/2005	Davis et al.	
2005/0101833	A1	5/2005	Hsu et al.	
2005/0113710	A1	5/2005	Stahmann et al.	
2005/0115561	A1	6/2005	Stahmann et al.	
2005/0145246	A1	7/2005	Hartley et al.	
2005/0148897	A1	7/2005	Cho et al.	
2005/0165457	A1	7/2005	Benser et al.	
2005/0182457	A1	8/2005	Thrope et al.	
2005/0209513	A1	9/2005	Heruth et al.	
2005/0209643	A1	9/2005	Heruth et al.	
2005/0222503	A1	10/2005	Dunlop et al.	
2005/0234523	A1	10/2005	Levin et al.	
2005/0251216	A1	11/2005	Hill et al.	
2005/0261747	A1	11/2005	Schuler et al.	
2005/0267380	A1	12/2005	Poezevera	
2005/0277844	A1	12/2005	Strother et al.	
2005/0277999	A1	12/2005	Strother et al.	
2005/0278000	A1	12/2005	Strother et al.	
2006/0052836	A1	3/2006	Kim et al.	
2006/0058852	A1	3/2006	Koh et al.	
2006/0064029	A1	3/2006	Arad (Abboud)	
2006/0079802	A1	4/2006	Jensen et al.	
2006/0095088	A1	5/2006	De Ridder	
2006/0103407	A1	5/2006	Kakizawa et al.	
2006/0135886	A1	6/2006	Lippert et al.	
2006/0155341	A1	7/2006	Tehrani et al.	
2006/0167523	A1 *	7/2006	Tehrani	A61N 1/3601 607/42
2006/0142815	A1	9/2006	Tehrani et al.	

(56) **References Cited**

U.S. PATENT DOCUMENTS

2006/0212096	A1	9/2006	Stevenson	
2006/0224209	A1	10/2006	Meyer	
2006/0241708	A1	10/2006	Boute	
2006/0247729	A1*	11/2006	Tehrani	A61N 1/3601 607/42
2006/0259079	A1	11/2006	King	
2006/0264777	A1	11/2006	Drew	
2006/0266369	A1	11/2006	Atkinson et al.	
2006/0271137	A1	11/2006	Stanton-Hicks	
2006/0276701	A1	12/2006	Ray	
2006/0293720	A1	12/2006	DiLorenzo	
2006/0293723	A1	12/2006	Whitehurst et al.	
2007/0021785	A1	1/2007	Inman et al.	
2007/0027482	A1	2/2007	Parnis et al.	
2007/0038265	A1	2/2007	Tcheng et al.	
2007/0150022	A1	6/2007	Ujhazy et al.	
2007/0233204	A1	10/2007	Lima et al.	
2007/0255379	A1	11/2007	Williams et al.	
2008/0009685	A1	1/2008	Kim et al.	
2008/0039904	A1	2/2008	Bulkes et al.	
2008/0046055	A1	2/2008	Durand et al.	
2008/0064977	A1	3/2008	Kelleher et al.	
2008/0103545	A1	5/2008	Bolea et al.	
2008/0103570	A1	5/2008	Gerber	
2008/0109046	A1	5/2008	Lima et al.	
2008/0109048	A1	5/2008	Moffitt	
2008/0132802	A1	6/2008	Ni et al.	
2008/0154330	A1*	6/2008	Tehrani	A61N 1/3601 607/42
2008/0161878	A1*	7/2008	Tehrani	A61N 1/3601 607/42
2008/0294060	A1	11/2008	Haro et al.	
2009/0024047	A1	1/2009	Shipley et al.	
2009/0062882	A1*	3/2009	Zhang	A61N 1/3601 607/42
2009/0112116	A1	4/2009	Lee et al.	
2009/0118787	A1	5/2009	Moffitt et al.	
2009/0216293	A1	8/2009	Sasaki et al.	
2009/0234427	A1	9/2009	Chinn et al.	
2009/0287279	A1	11/2009	Parramon et al.	
2009/0308395	A1	12/2009	Lee et al.	
2009/0326408	A1	12/2009	Moon	
2010/0010566	A1	1/2010	Thacker et al.	
2010/0016749	A1	1/2010	Atsma et al.	
2010/0094379	A1	4/2010	Meadows	
2010/0125310	A1	5/2010	Wilson et al.	
2010/0125314	A1	5/2010	Bradley et al.	
2010/0125315	A1	5/2010	Parramon et al.	
2010/0137931	A1	6/2010	Hopper et al.	
2010/0152553	A1	6/2010	Ujhazy et al.	
2010/0174341	A1*	7/2010	Bolea	A61N 1/0556 607/42
2010/0198103	A1	8/2010	Meadows et al.	
2010/0198289	A1*	8/2010	Kameli	G06F 19/3481 607/14
2010/0228133	A1	9/2010	Averina et al.	
2010/0228310	A1	9/2010	Shuros et al.	
2010/0228317	A1	9/2010	Libbus et al.	
2010/0241195	A1	9/2010	Meadows et al.	
2010/0262210	A1	10/2010	Parramon et al.	
2011/0060380	A1	3/2011	Gelfand et al.	
2011/0093032	A1*	4/2011	Boggs, II	A61N 1/3611 607/42
2011/0093036	A1	4/2011	Mashiach	
2011/0112601	A1	5/2011	Meadows et al.	
2011/0152706	A1	6/2011	Christopherson et al.	
2011/0152965	A1	6/2011	Mashiach et al.	
2011/0160794	A1	6/2011	Bolea et al.	
2011/0172733	A1	7/2011	Lima et al.	
2011/0264164	A1	10/2011	Christopherson et al.	
2011/0288609	A1*	11/2011	Tehrani	A61N 1/36031 607/42
2012/0192874	A1*	8/2012	Bolea	A61N 1/3601 128/848
2012/0253249	A1*	10/2012	Wilson	A61N 1/3611 601/154
2012/0290036	A1*	11/2012	Karamanoglu	A61B 5/686 607/42
2013/0253627	A1	9/2013	Meadows et al.	
2014/0135868	A1*	5/2014	Bashyam	A61N 1/3601 607/42
2014/0228905	A1*	8/2014	Bolea	A61F 5/56 607/42
2014/0364919	A1*	12/2014	Doan	A61N 1/36164 607/46
2015/0039045	A1	2/2015	Ni et al.	
2015/0328451	A1*	11/2015	Kobayashi	A61N 1/0492 607/42
2016/0022204	A1*	1/2016	Mostov	A61B 5/0002 600/301
2016/0193468	A1	7/2016	Rondoni et al.	
2016/0354602	A1	12/2016	Keenan	
2016/0354603	A1	12/2016	Keenan	
2016/0354608	A1*	12/2016	Keenan	A61N 1/3611
2017/0368337	A1	12/2017	Steier	

FOREIGN PATENT DOCUMENTS

JP	4960704 B2	8/2008	
JP	2010502276	1/2010	
JP	2011520526	7/2011	
JP	2013509943	3/2013	
JP	5636129 B2	12/2015	
WO	199750049	12/1997	
WO	WO-9750049 A1 *	12/1997	A61B 5/03
WO	WO199749455	12/1997	
WO	2006047264	5/2006	
WO	2006057734	6/2006	
WO	2006102591	9/2006	
WO	2007068284	6/2007	
WO	2008048471	4/2008	
WO	2009048580	4/2009	
WO	2009048581	4/2009	
WO	2009135138	11/2009	
WO	2009135140	11/2009	
WO	2009140636	11/2009	
WO	2010039853	4/2010	
WO	2010057286	5/2010	
WO	2010059839	5/2010	
WO	WO-2010059839 A2 *	5/2010	A61B 5/0803
WO	2010117810	10/2010	
WO	WO2013023218	2/2013	

OTHER PUBLICATIONS

Goodall Article—Eleanor V. Goodhall et al., "Position-Selective Activation of Peripheral Nerve Fibers with a Cuff Electrode," IEEE Transaction on Biomedical Engineering, vol. 43, No. 8, Aug. 1996, pp. 851-856.

Naples Article—Gregory G. Naples et al., "A Spiral Nerve Cuff Electrode for Peripheral Nerve Stimulation," 8088 IEEE Transactions on Biomedical Engineering, 35. Nov. 1988, No. 11, New York, NY, pp. 905-915.

Oliven Article—Arie Oliven et al., "Upper airway response to electrical stimulation of the genioglossus in obstructive sleep apnea," Journal of Applied Physiology, vol. 95, pp. 2023-2029, Nov. 2003, www.jap.physiology.org on Sep. 18, 2006. (8 pages).

Schwartz Article—Alan R. Schwartz MD et al., Theraputic Electrical Stimulation of the Hypoglossal Nerve in Obstructive Sleep Apnea, Arch Otolaryngol HeadAnd Neck Surg., vol. 127, Oct. 2001, pp. 1216-1223. Copyright 2001 American Medical Association. (8 pages).

Park, "Preoperative Percutaneous Cranial Nerve Mapping in Head and Neck Surgery," Arch Facial Plast Surg/vol. 5, Jan./Feb. 2003, www.archfacial.com pp. 86-91.

Stanescu, "Expiratory flow limitation during sleep in heavy snorers" European Respiratory Journal, 1996, 9, 2116-2121.

J Sleep Res., "Hypoglossal nerve stimulation improves obstructive sleep apnea: 12-month outcomes" Journal, 2014, 23, 77-83.

(56) **References Cited**

OTHER PUBLICATIONS

The Laryngoscope, "Implanted Upper Airway Stimulation Device for Obstructive Sleep Apnea" Journal, 2012, 122, 1626-1633.

* cited by examiner

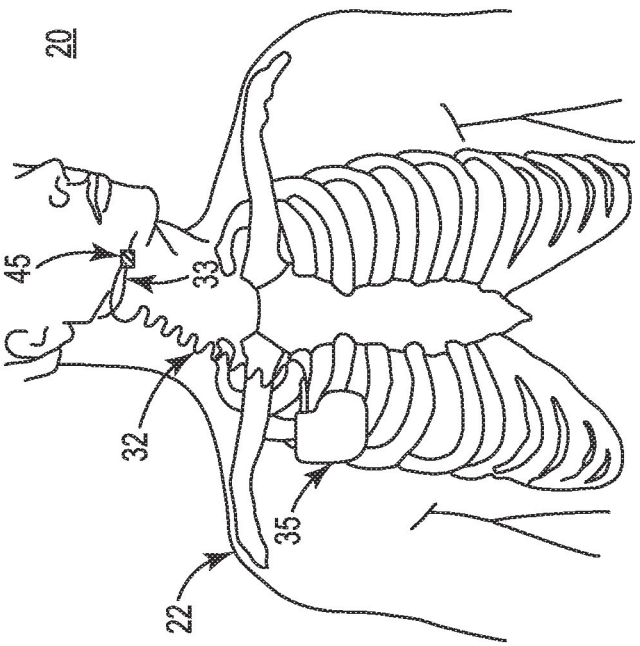


Fig. 2A

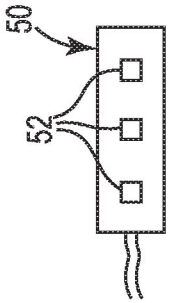


Fig. 2E

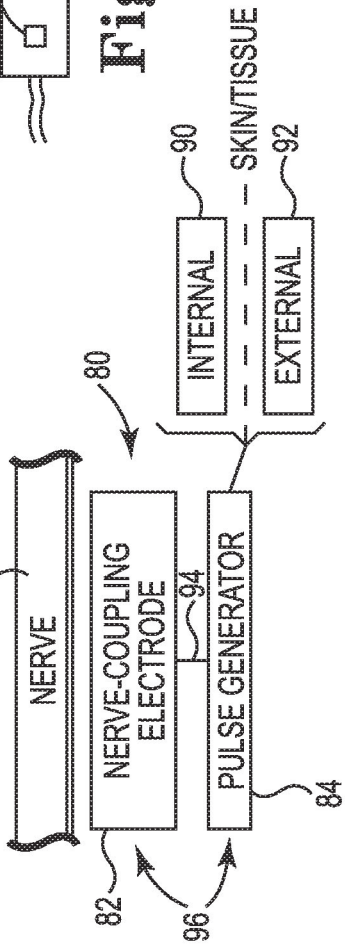


Fig. 2D

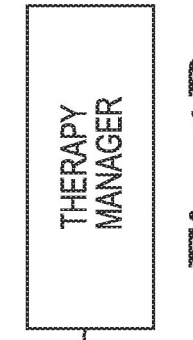


Fig. 1B

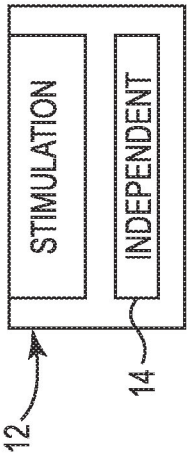


Fig. 1A

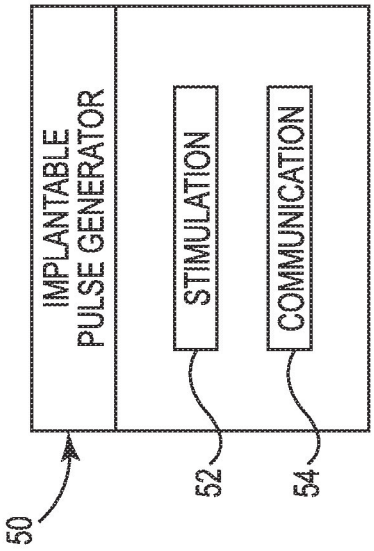


Fig. 2B

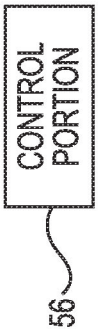


Fig. 2C

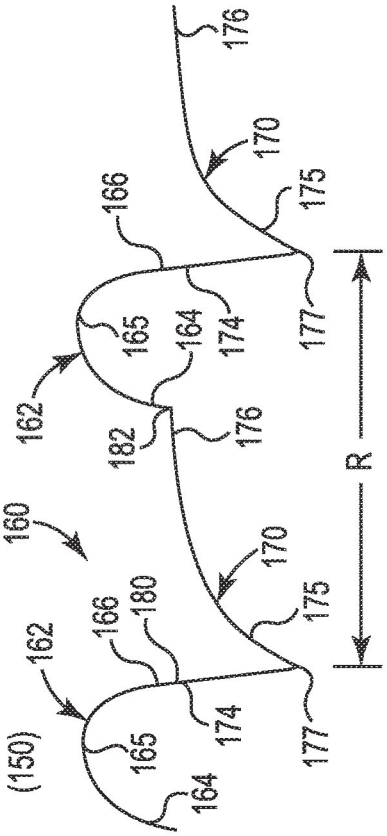

160
162
166
180
165
164
174
177
175
170
176
182
R
(150)

Fig. 3A

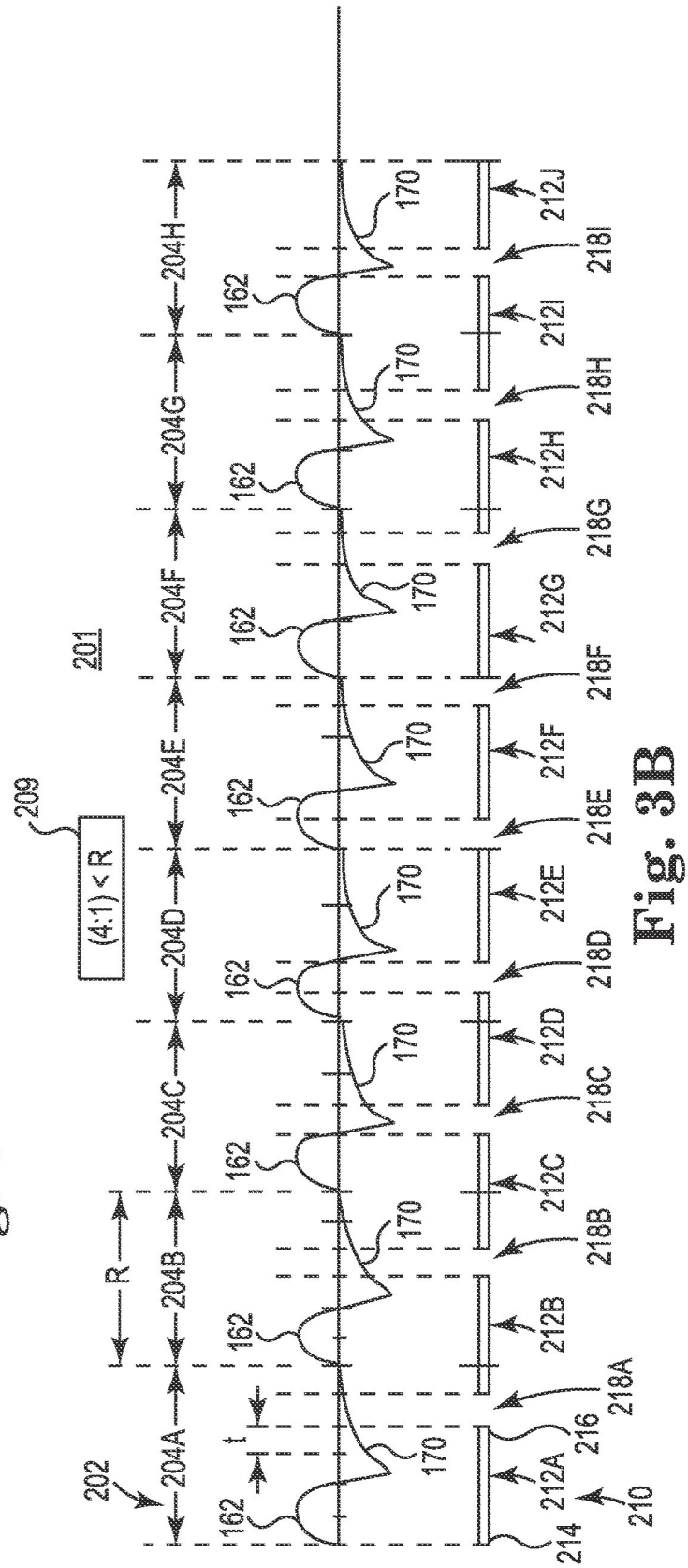

201
209
(4:1) < R
R
t
202
204A
204B
204C
204D
204E
204F
204G
204H
162
170
212A
212B
212C
212D
212E
212F
212G
212H
212I
212J
214
216
218A
218B
218C
218D
218E
218F
218G
218H
218I
210

Fig. 3B

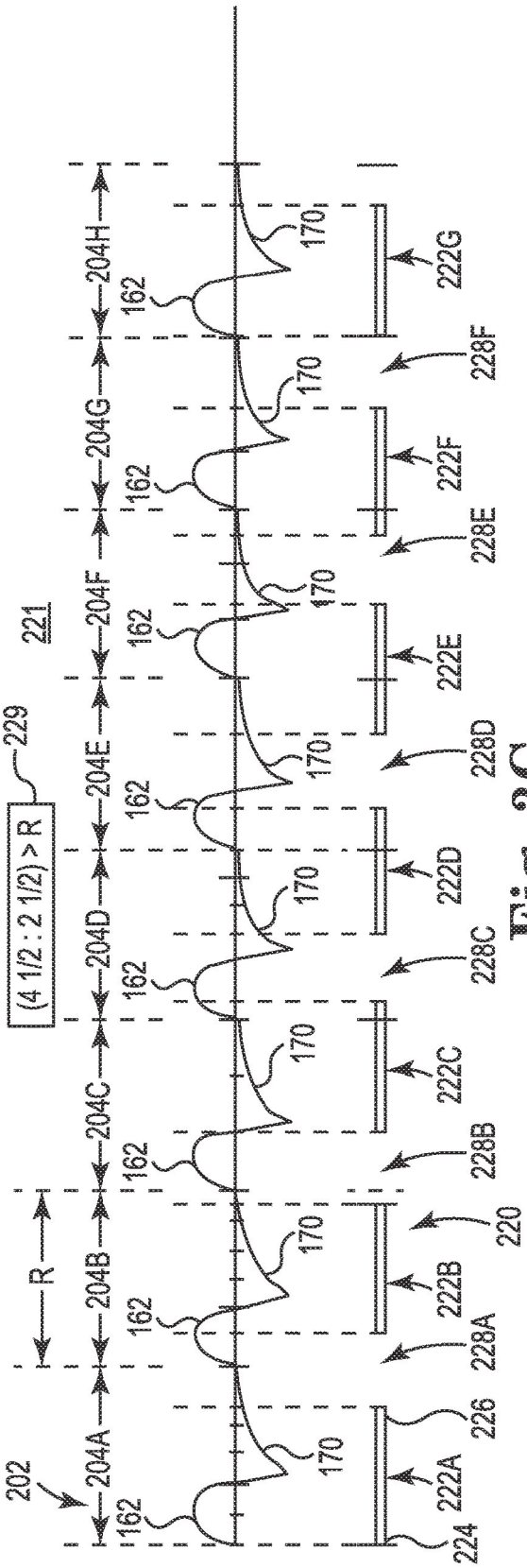

202
R
204A
204B
204C
204D
204E
204F
204G
204H
(4 1/2 : 2 1/2) > R
229
221
220
162
170
222A
222B
222C
222D
222E
222F
222G
224
226
228A
228B
228C
228D
228E
228F

Fig. 3C

202
R
204A
204B
204C
204D
204E
204F
204G
(7 1/2 : 2 1/2) > R
239
231
162
170
205
t
230
232A
232B
232C
232D
234
236
238A
238B
238C
238D

Fig. 3D

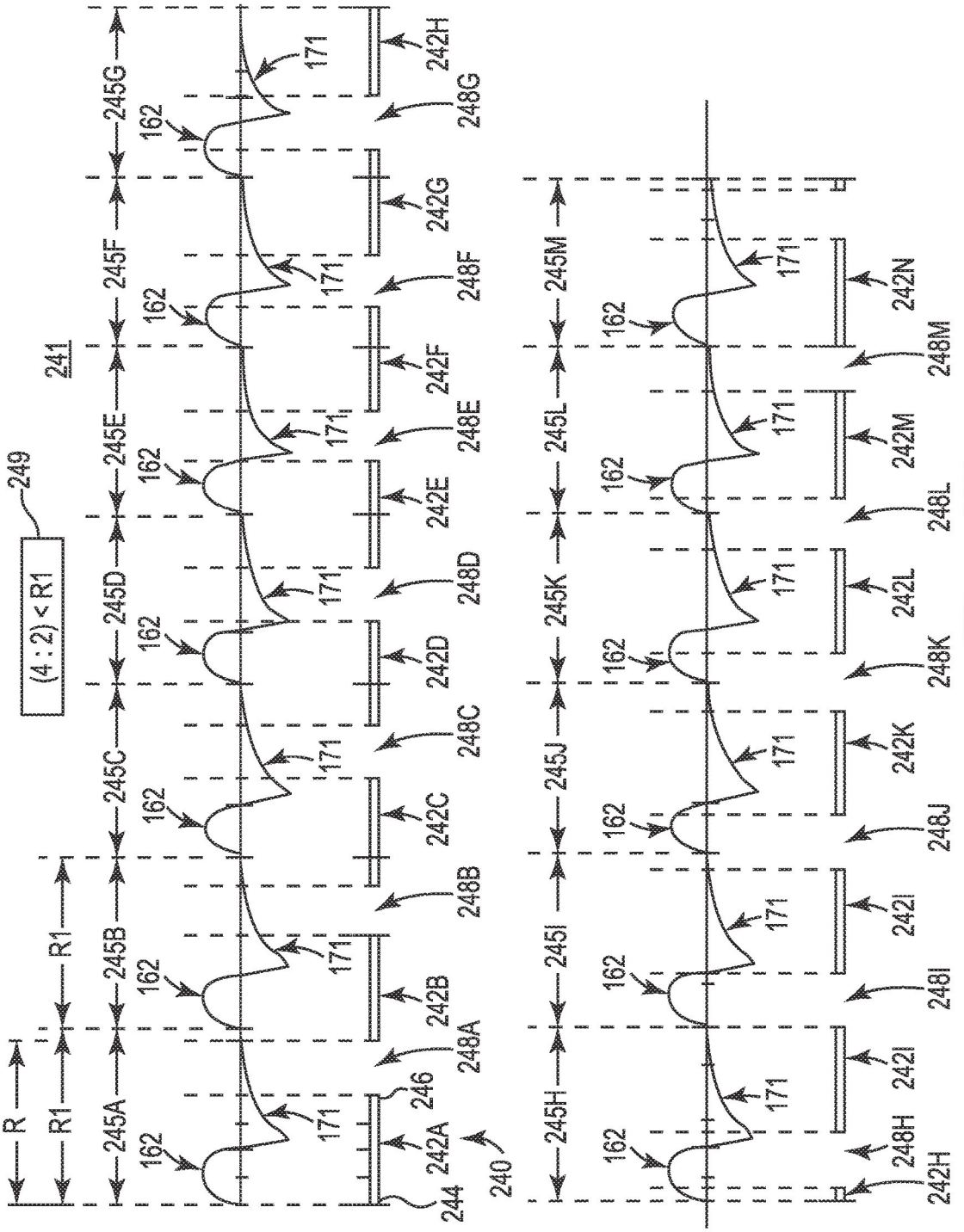

R
R1
R1
245A
245B
245C
245D
245E
245F
245G
245H
245I
245J
245K
245L
245M
241
249
(4 : 2) < R1
162
171
242A
242B
242C
242D
242E
242F
242G
242H
242I
242K
242L
242M
242N
244
246
240
248A
248B
248C
248D
248E
248F
248G
248H
248I
248J
248K
248L
248M

Fig. 3E

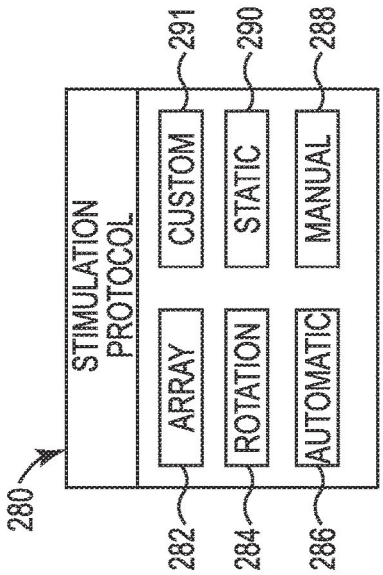


Fig. 5

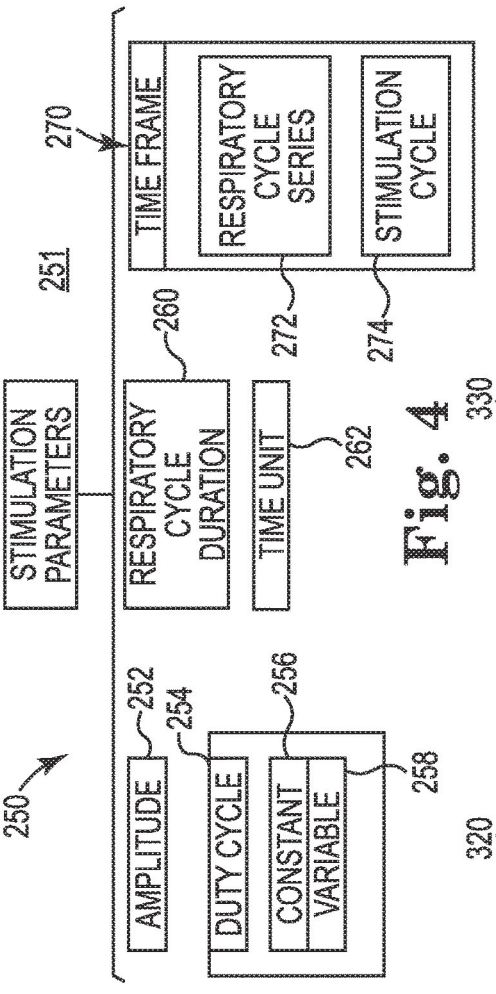


Fig. 4

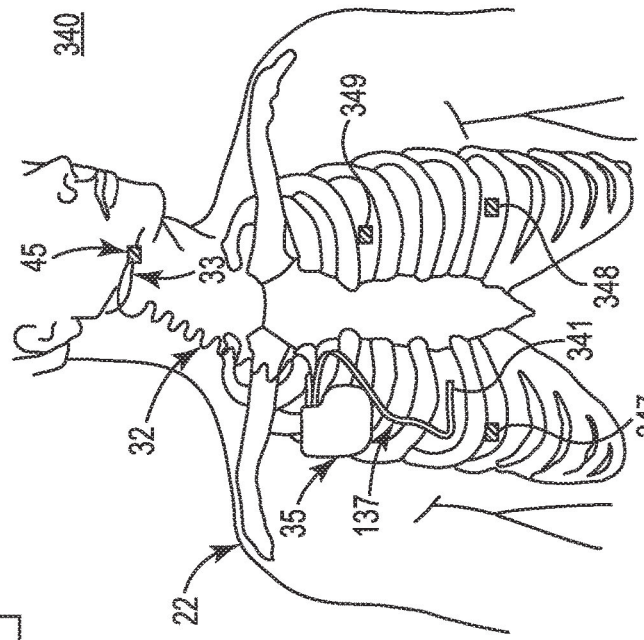


Fig. 7B

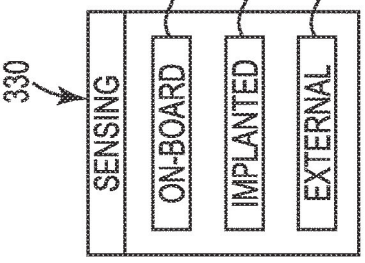


Fig. 7A

Fig. 6

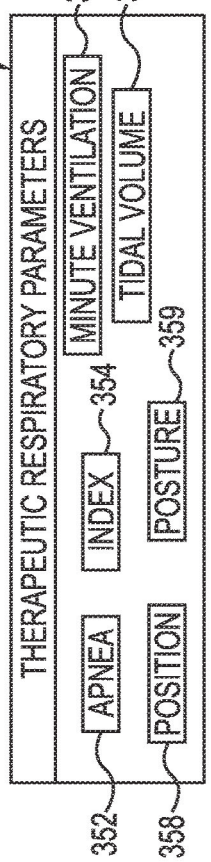


Fig. 8

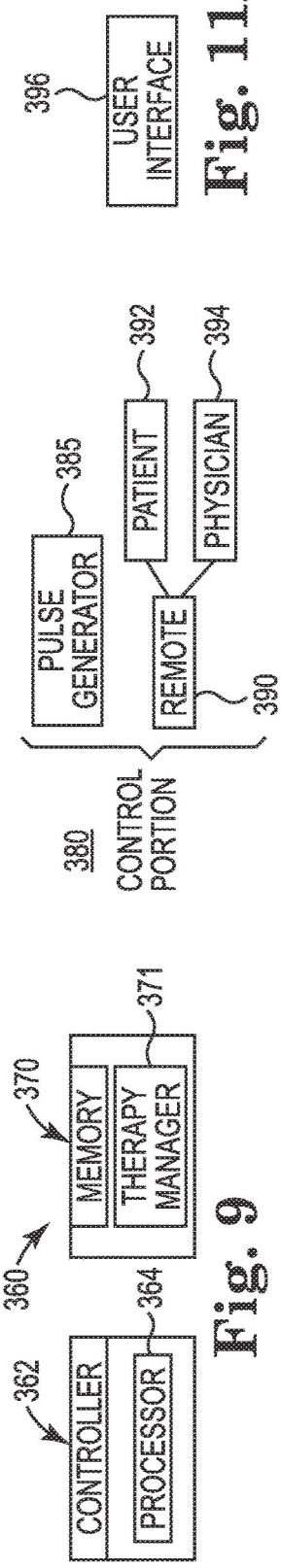


Fig. 9

Fig. 10

Fig. 11A

Fig. 11B

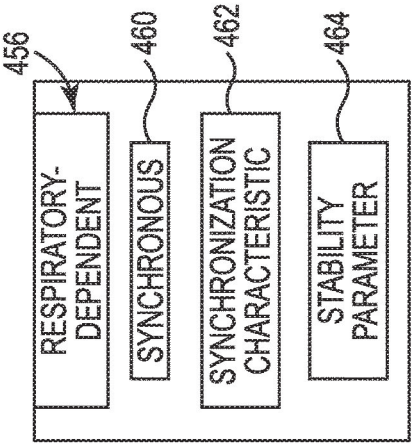


Fig. 13

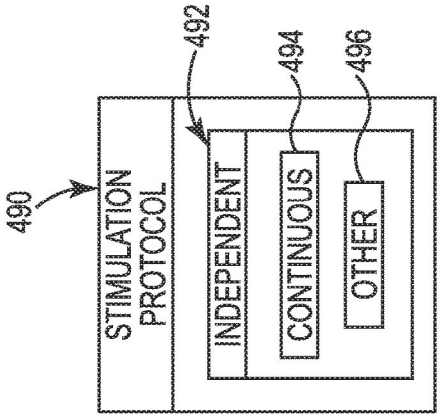


Fig. 15A

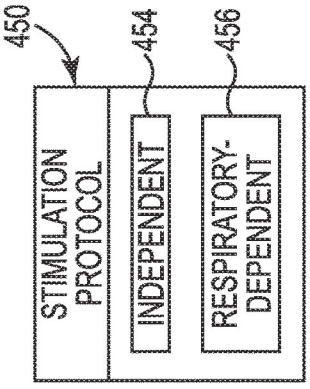


Fig. 12

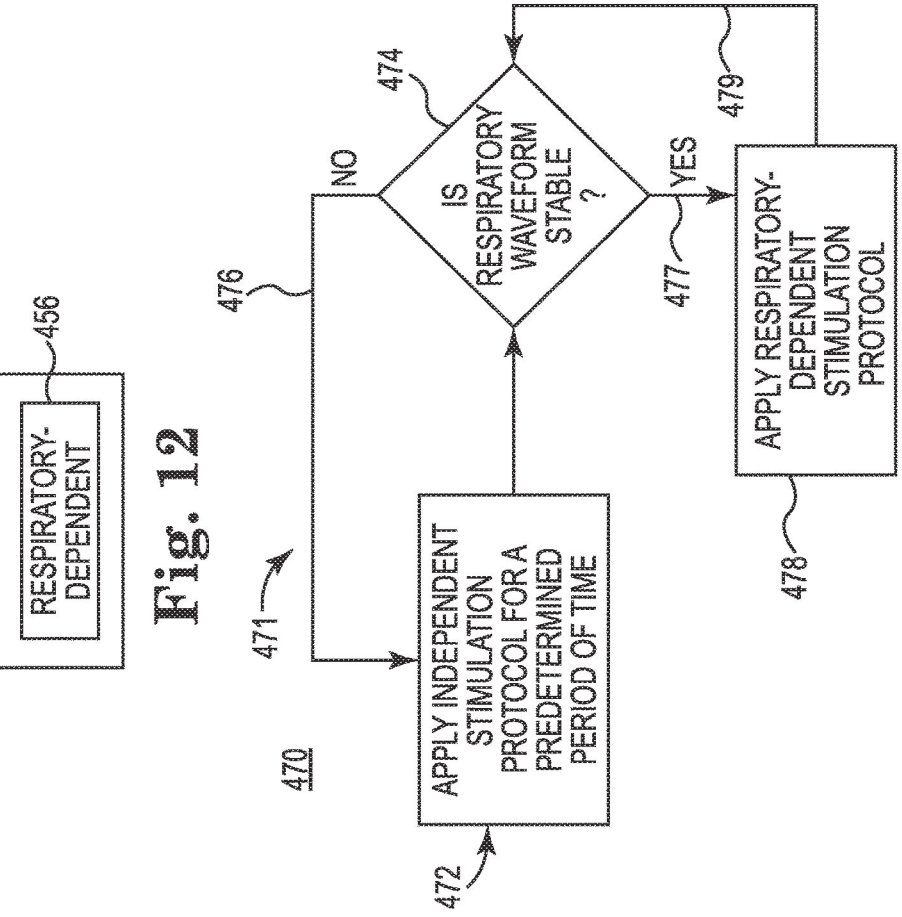


Fig. 14

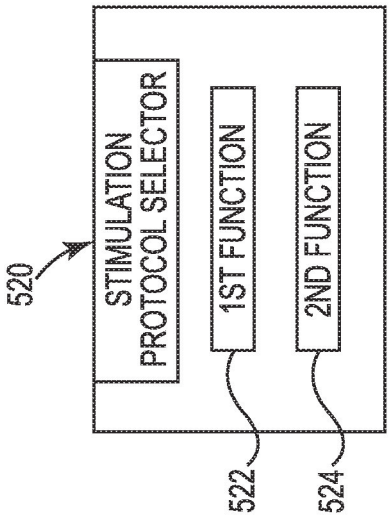


Fig. 15C

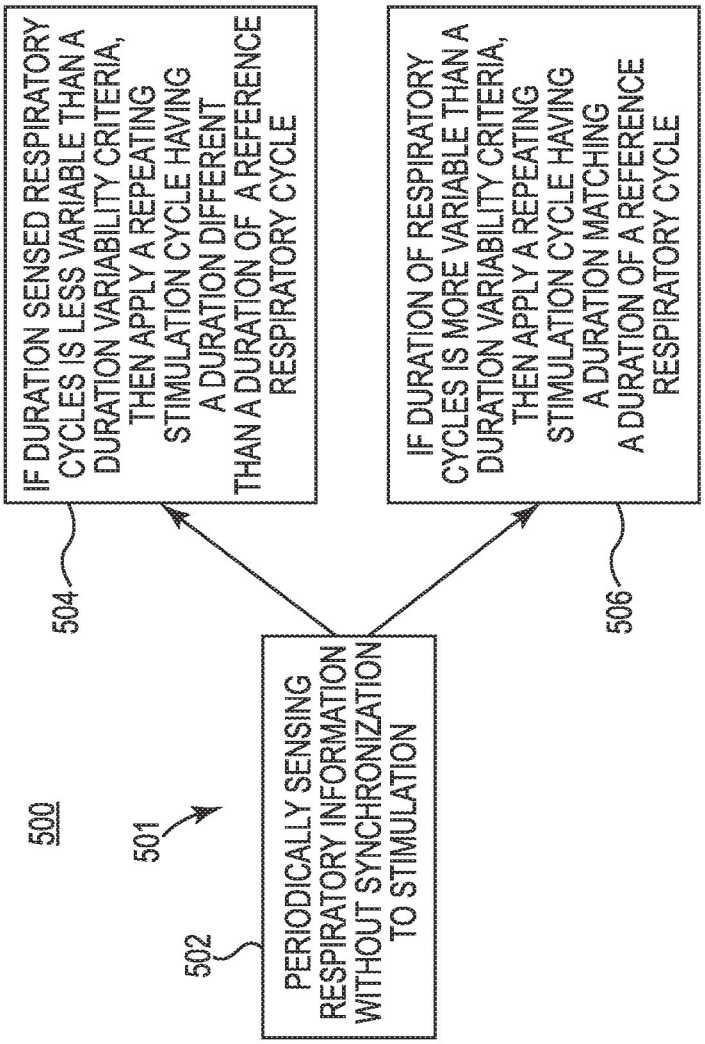


Fig. 15B

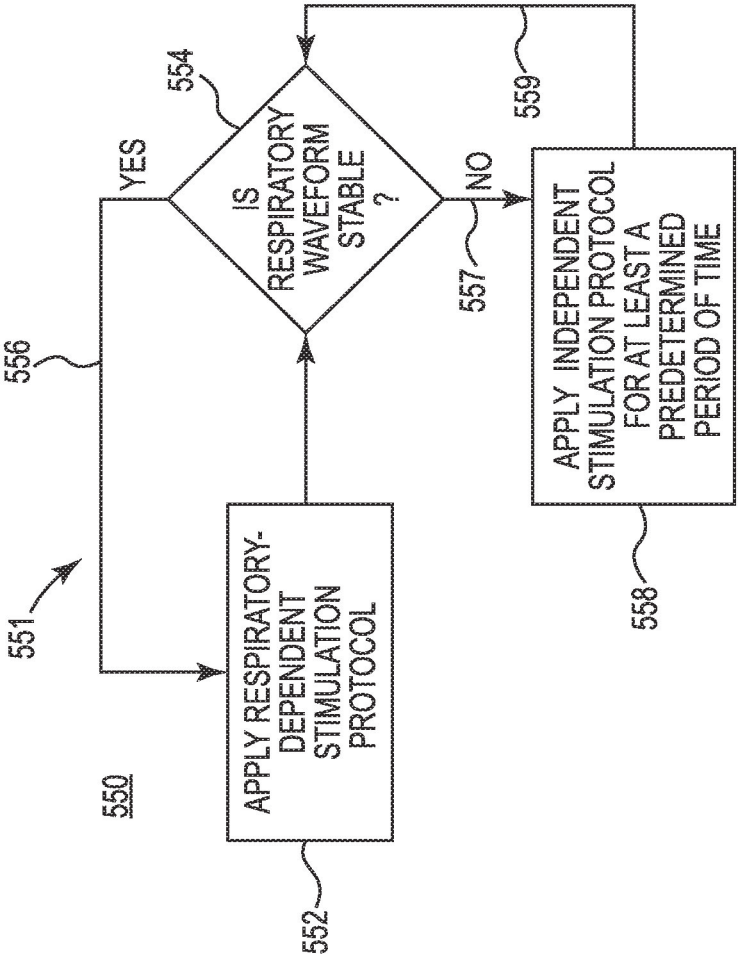

550
551
552
554
556
557
558
559
APPLY RESPIRATORY-DEPENDENT STIMULATION PROTOCOL
IS RESPIRATORY WAVEFORM STABLE ?
YES
NO
APPLY INDEPENDENT STIMULATION PROTOCOL FOR AT LEAST A PREDETERMINED PERIOD OF TIME

Fig. 15D

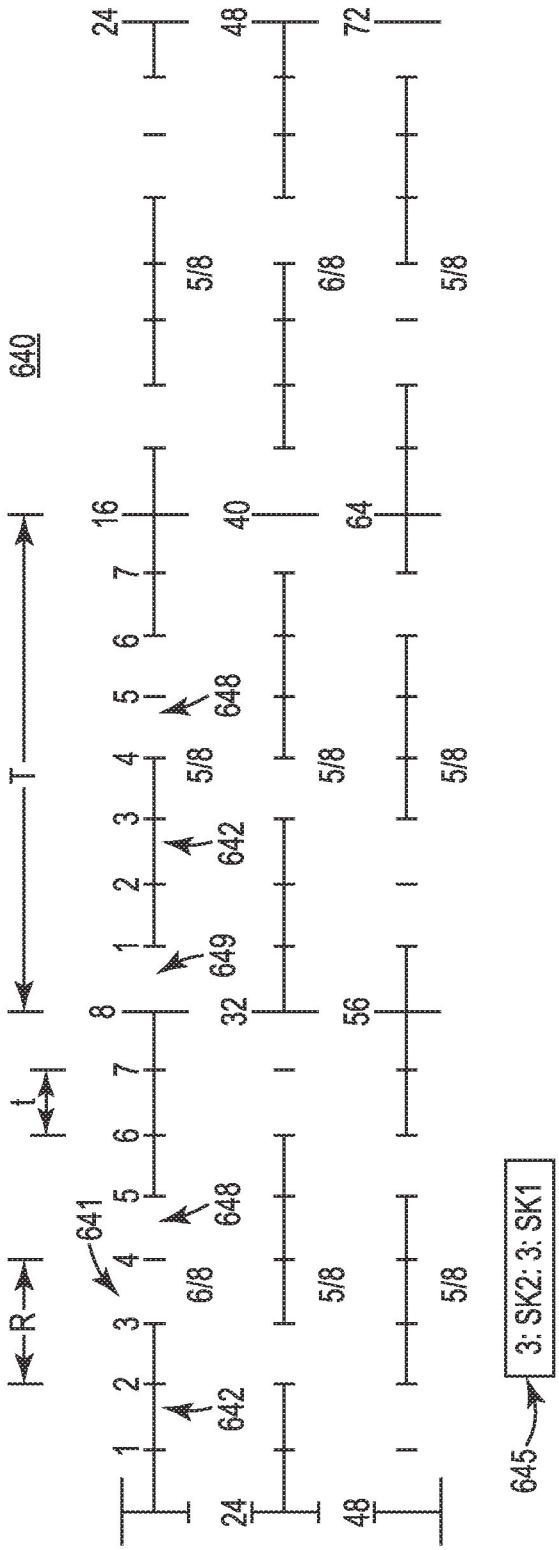

640
R
T
t
641
642
648
649
645
3: SK2: 3: SK1
1
2
3
4
5
6
7
8
16
40
64
24
48
72
5/8
6/8

Fig. 16A

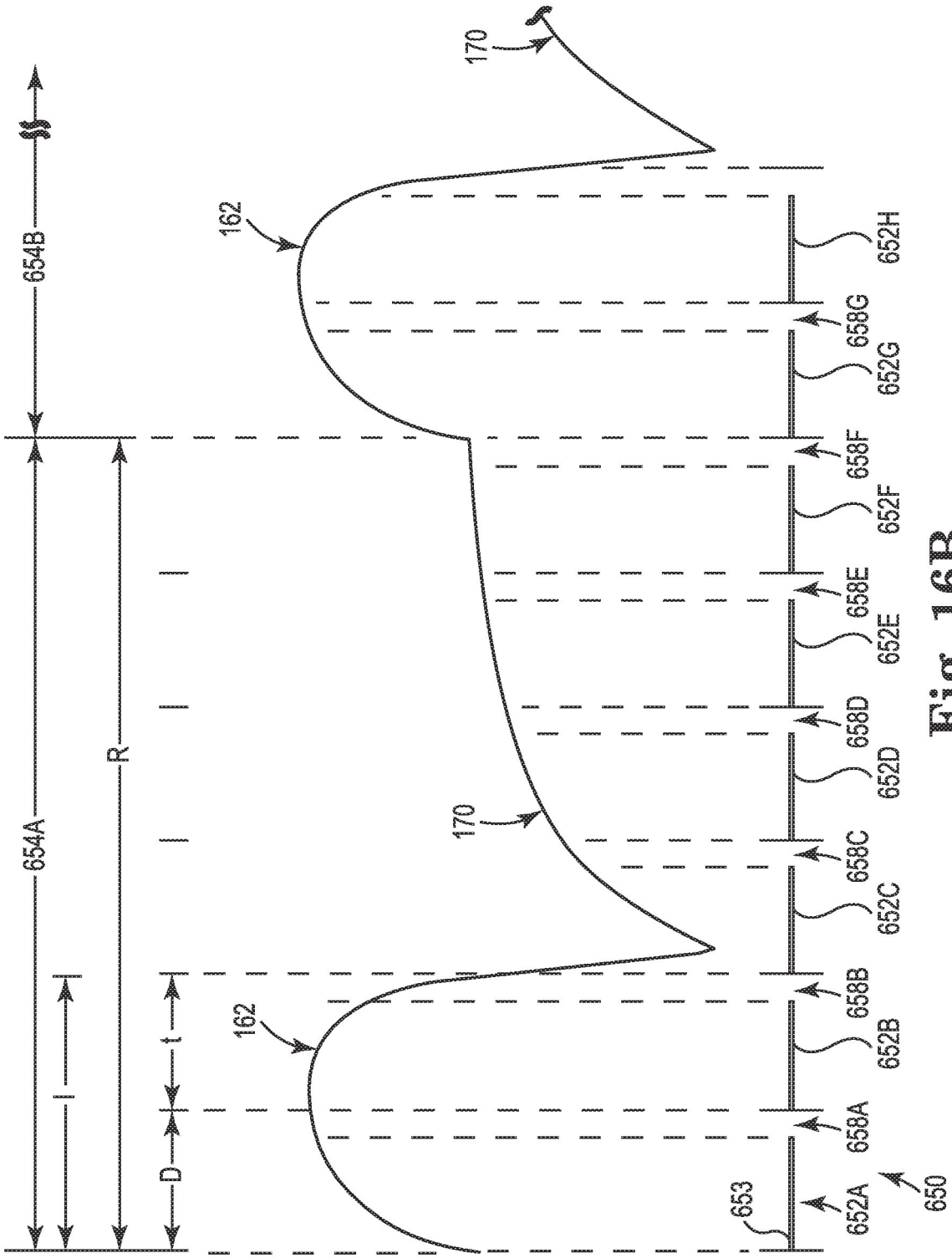

654B
654A
R
l
t
D
162
170
653
650
652A
652B
652C
652D
652E
652F
652G
652H
658A
658B
658C
658D
658E
658F
658G

Fig. 16B

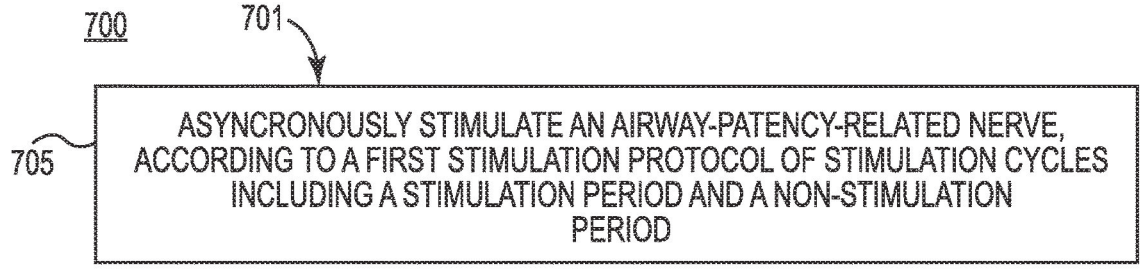


Fig. 17A

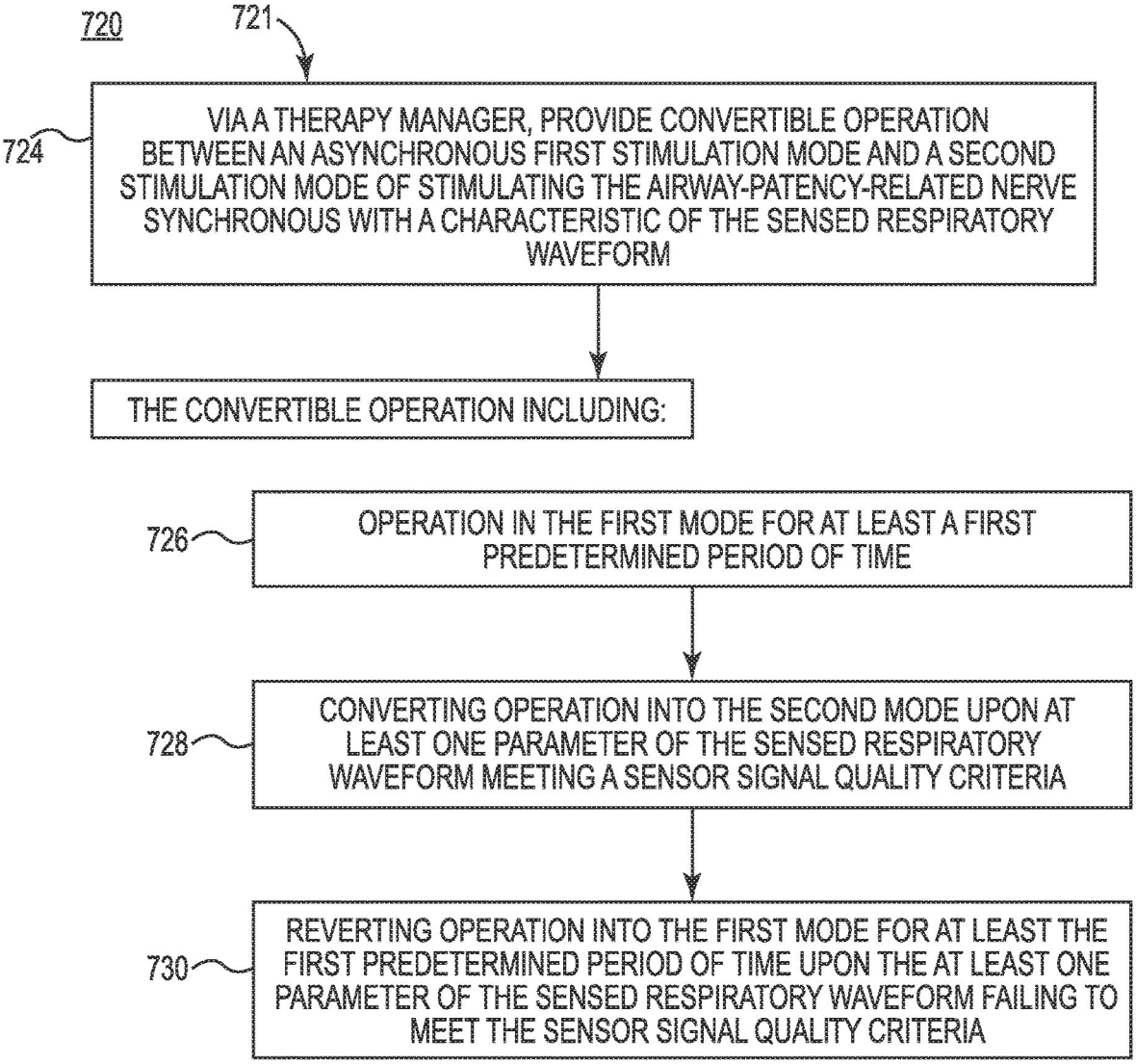


Fig. 17B

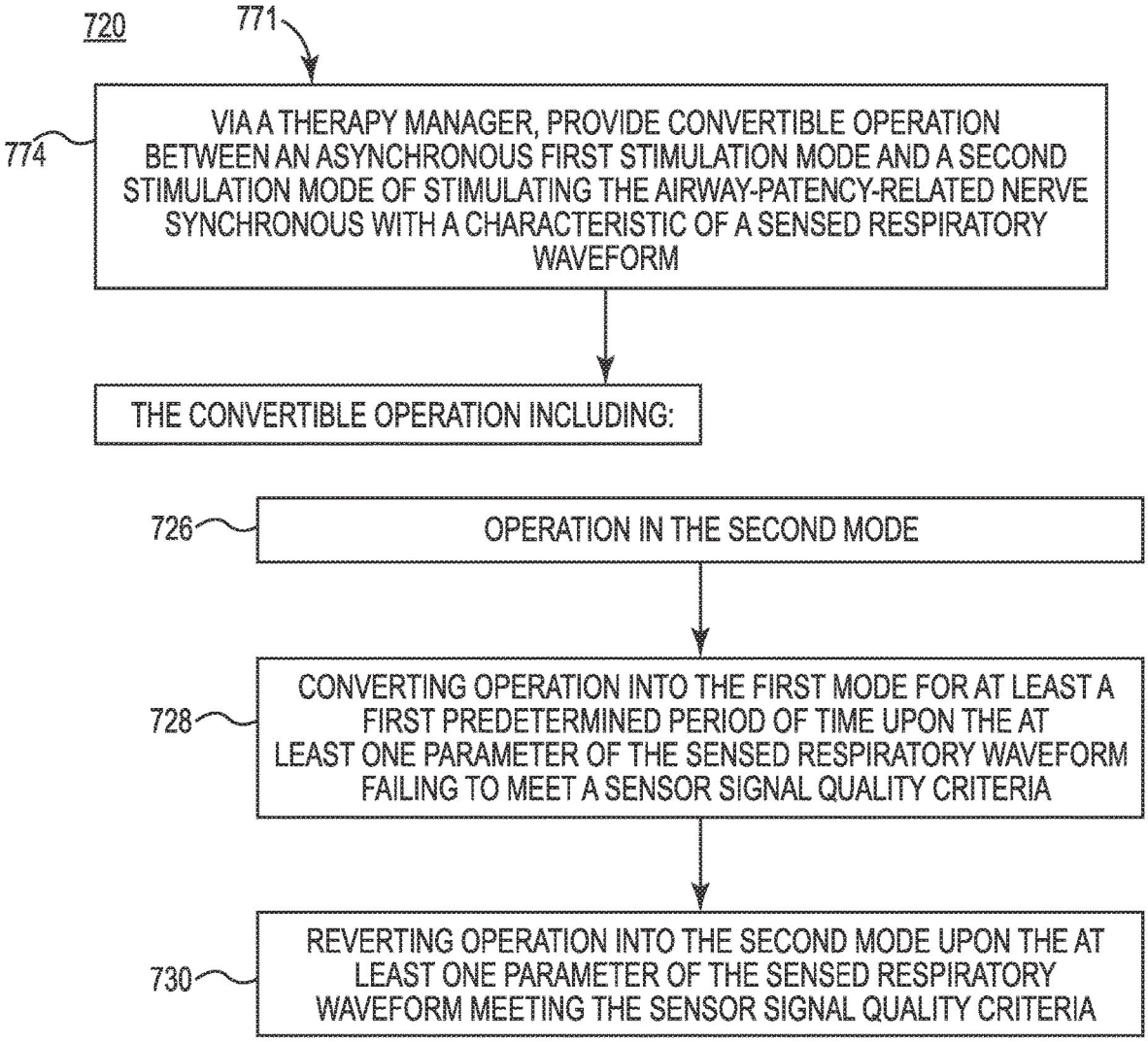


Fig. 17C

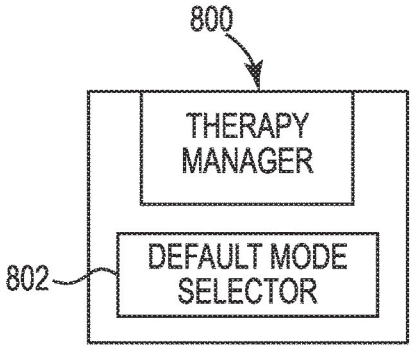


Fig. 18

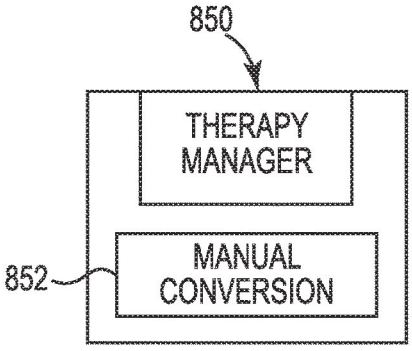


Fig. 19

STIMULATION FOR TREATING SLEEP DISORDERED BREATHING

CROSS-REFERENCE TO RELATED APPLICATIONS

This 371 National Phase Application claims benefit of PCT Patent Application No. PCT/US2016/022611, filed Mar. 16, 2016, entitled STIMULATION FOR TREATING SLEEP DISORDERED BREATHING, which claims benefit from U.S. Provisional Patent Application 62/135,305, filed Mar. 19, 2015, both of which are incorporated by reference herein.

BACKGROUND

Targeted electrical stimulation of a nerve shows great promise in a number of therapies. In one example, such stimulation of a hypoglossal nerve is known to alleviate obstructive sleep apnea by helping to maintain and/or restore upper airway patency.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1**A is a block diagram schematically illustrating a stimulation element, according to one example of the present disclosure.

FIG. **1**B is a block diagram schematically illustrating a therapy manager, according to one example of the present disclosure.

FIG. **2**A is a diagram schematically illustrating an at least partially implantable stimulation system relative to a patient, according to an example of the present disclosure.

FIG. **2**B is a block diagram schematically illustrating an implantable pulse generator, according to one example of the present disclosure.

FIG. **2**C is a block diagram schematically illustrating a control portion for the at least partially implantable stimulation system, according to one example of the present disclosure.

FIG. **2**D is block diagram schematically illustrating a stimulation system, according to one example of the present disclosure.

FIG. **2**E is top view schematically illustrating a stimulation electrode, according to one example of the present disclosure.

FIG. **3**A is a diagram schematically illustrating a respiratory cycle in one example breathing pattern, according to one example of the present disclosure.

FIG. **3**B is a diagram schematically illustrating a series of reference respiratory cycles juxtaposed relative to a stimulation protocol, according to one example of the present disclosure.

FIG. **3**C is a diagram schematically illustrating a series of reference respiratory cycles juxtaposed relative to a stimulation protocol, according to one example of the present disclosure.

FIG. **3**D is a diagram schematically illustrating a series of reference respiratory cycles juxtaposed relative to a stimulation protocol, according to one example of the present disclosure.

FIG. **3**E is a diagram schematically illustrating a series of reference respiratory cycles juxtaposed relative to a stimulation protocol, according to one example of the present disclosure.

FIG. **4** is a block diagram schematically illustrating a plurality of stimulation parameters, according to one example of the present disclosure.

FIG. **5** is a block diagram schematically illustrating a stimulation protocol element, according to one example of the present disclosure.

FIG. **6** is a block diagram schematically illustrating power source components of the at least partially implantable stimulation system, according to one example of the present disclosure.

FIG. **7**A is a block diagram schematically illustrating a sensing element of the at least partially implantable stimulation system, according to one example of the present disclosure.

FIG. **7**B is a diagram schematically illustrating an at least partially implantable stimulation system relative to a patient and including sensing elements, according to an example of the present disclosure.

FIG. **8** is a block diagram schematically illustrating therapeutic respiratory parameters, according to one example of the present disclosure.

FIG. **9** is a block diagram schematically illustrating a control portion of an at least partially implantable stimulation system, according to one example of the present disclosure.

FIG. **10** is a block diagram schematically illustrating aspects of a control portion, according to one example of the present disclosure.

FIG. **11**A is a block diagram schematically illustrating a user interface, according to one example of the present disclosure.

FIG. **11**B is a block diagram schematically illustrating a user interface, according to one example of the present disclosure.

FIG. **12** is a block diagram schematically illustrating a stimulation protocol element, according to one example of the present disclosure.

FIG. **13** is a block diagram schematically illustrating a respiratory-dependent stimulation element, according to one example of the present disclosure.

FIG. **14** is a diagram schematically illustrating at least some aspects of stimulation protocol selection, according to one example of the present disclosure.

FIG. **15**A is a block diagram schematically illustrating a stimulation protocol element, according to one example of the present disclosure.

FIG. **15**B is a diagram schematically illustrating at least some aspects of stimulation protocol selection, according to one example of the present disclosure.

FIG. **15**C is a block diagram schematically illustrating a stimulation protocol selector, according to one example of the present disclosure.

FIG. **15**D is a diagram schematically illustrating at least some aspects of stimulation protocol selection, according to one example of the present disclosure.

FIG. **16**A is a diagram schematically illustrating a stimulation protocol, according to one example of the present disclosure.

FIG. **16**B is a diagram schematically illustrating a stimulation protocol, according to one example of the present disclosure.

FIG. **17**A is a flow diagram schematically illustrating a method of nerve stimulation, according to one example of the present disclosure.

FIG. **17**B is a flow diagram schematically illustrating a method of nerve stimulation, according to one example of the present disclosure.

FIG. **17**C is a flow diagram schematically illustrating a method of nerve stimulation, according to one example of the present disclosure.

FIG. **18** is a block diagram schematically illustrating a therapy manager, according to one example of the present disclosure.

FIG. **19** is a block diagram schematically illustrating a therapy manager, according to one example of the present disclosure.

DETAILED DESCRIPTION

In the following Detailed Description, reference is made to the accompanying drawings, which form a part hereof, and in which is shown by way of illustration specific examples in which the invention may be practiced. In this regard, directional terminology, such as "top," "bottom," "front," "back," "leading," "trailing," etc., is used with reference to the orientation of the Figure(s) being described. Because components of examples can be positioned in a number of different orientations, the directional terminology is used for purposes of illustration and is in no way limiting. It is to be understood that other examples may be made without departing from the scope of the present disclosure. The following detailed description, therefore, is not to be taken in a limiting sense.

At least some examples of the present disclosure are directed to methods of treating obstructive sleep apnea via applying nerve stimulation. By doing so, upper airway patency may be maintained and/or increased while preventing or minimizing collapse of the upper airway. At the same time, by using targeted stimulation, one can limit the overall volume of stimulation applied to a given nerve or set of nerves.

In some examples, nerve stimulation is applied during a treatment period. In some examples, a treatment period corresponds to the patient engaging in sleeping behavior, and during which sleep disordered breathing is to be avoided. The treatment period can be manually initiated by the patient or automatically initiated by a device that applies the nerve stimulation.

In some examples, an at least partially implantable stimulation system for treating sleep disordered breathing includes an independent stimulation element to stimulate an airway-patency-related nerve without synchronization relative to characteristics of respiratory wave form. Accordingly, in some examples, the independent stimulation element forms part of a system that omits any sensing elements. In some examples, the stimulation element comprises a stimulation engine to determine and administer a stimulation protocol. In some examples, the stimulation element further includes and/or acts in cooperation with a pulse generator and stimulation electrode to deliver the stimulation to a target nerve. In such examples, the pulse generator includes the stimulation engine or the stimulation engine is in communication with the pulse generator. In some examples, the pulse generator is implantable and in some examples, the pulse generator is external to the patient's body. In some examples, the stimulation element is in communication with a therapy manager or is incorporated within a therapy manager. In some examples, the therapy manager is in communication with the pulse generator and/or incorporated within the pulse generator. In some examples, at least some components, functions, elements, etc. of the therapy manager are incorporated within a physician programmer external to the patient or a patient remote external to the patient.

In some examples, the at least partially implantable stimulation system includes sensing element(s) to receive and/or obtain respiratory information but that information is not employed to trigger stimulation by synchronizing the stimulation relative to characteristics of the sensed respiratory waveform. Rather, in these examples, the sensed respiratory information is used to detect and evaluate sleep disordered breathing behavior. When the detected behavior meets or exceeds a severity threshold, the therapy manager generally activates stimulation via the independent stimulation element. In some examples, the severity threshold is based on at least a frequency and/or an intensity of apneic events. In some instances, the severity threshold also may be expressed as an obstructive sleep apnea (OSA) burden, i.e. a quantity and/or intensity of apneas which are occurring. In some examples, the severity threshold or OSA burden is expressed as an Apnea-Hypopnea Index (AHI). However, despite the respiratory sensing occurring in these examples, the stimulation is performed via a protocol that remains independent of the particular characteristics of a real-time sensed respiratory waveform. In other words, individual stimulation periods are not triggered and/or synchronized relative to respiratory characteristics, such as the inspiratory phase.

In some examples, the independent stimulation element is configured to asynchronously stimulate an airway-patency-related nerve, according to a first stimulation protocol independent of sensed respiratory information and in which each stimulation cycle includes a stimulation period and a non-stimulation period. In some instances, the first stimulation protocol is referred to as being independent because the first stimulation protocol is not synchronized relative to sensed respiratory information. In some instances, the independence of the first stimulation protocol also may be referred to as being an asynchronous stimulation protocol because the first stimulation protocol is not synchronized relative to the sensed respiratory information.

In some examples, each stimulation period within a stimulation cycle includes continuous stimulation. In some examples, continuous stimulation refers to a train of stimulation pulses which occur in a relatively short time frame. For instance, in some examples, continuous stimulation corresponds to at least a finite number (e.g. 5, 10, etc.) of stimulation pulses per second. In some examples, continuous stimulation corresponds to at least 20 stimulation pulses per second. In some examples, continuous stimulation corresponds to at least 30 stimulation pulses per second. In some examples, the number of stimulation pulses per second is selectable by an operator via a control portion (e.g. **56** in FIG. **2**C).

In some examples, during the above-described continuous stimulation, each stimulation pulse within a train of stimulation pulses includes a primary stimulation pulse followed by a separate recharge pulse, which is in turn followed by a non-stimulation phase before the next primary stimulation pulse.

In some examples, the stimulation period has a minimum duration equal to or greater than an inspiratory reference. In some examples, the inspiratory reference corresponds to a duration of an inspiratory phase of a reference respiratory cycle. In some examples, each stimulation cycle of the first stimulation protocol includes the stimulation period having a duration greater than a duration of the inspiratory reference followed by the non-stimulation period, which has a duration less than the duration of the stimulation period.

In some examples, the reference respiratory cycle is defined by a historical patient-specific average respiratory cycle for stable respiration. In some examples, the reference

respiratory cycle is defined by a multi-patient average respiratory cycle for stable respiration.

Because the overall duration of the stimulation cycle (both stimulation period and non-stimulation period) intentionally does not match the duration (R) of the reference respiratory cycle in at least some examples, the stimulation protocol ensures that each successive stimulation period within the series of stimulation cycles will fall along a different portion of each of the successive reference respiratory cycles. Accordingly, even though the stimulation is not synchronized relative to a characteristic (e.g. inspiration) of reference respiratory waveform (which includes the series of reference respiratory cycles), no matter where the stimulation protocol is started relative to the ongoing pattern of reference respiratory cycles, the stimulation period of each stimulation cycle will overlap with at least a portion of the inspiratory phase of the respective reference respiratory cycles for a significant majority of the treatment period. Accordingly, even if the stimulation protocol happens to be initiated at a time that the non-stimulation period of the initial stimulation cycle at least partially overlaps with the inspiratory phase of a reference respiratory cycle, the stimulation periods of the successive stimulation cycles will at least partially overlap the inspiratory phase of the next reference respiratory cycles. Moreover, at least some of the later successive stimulation periods will significantly overlap (e.g. overlap at least a majority of the inspiratory phase) the inspiratory phase of the at least some of the respective successive reference respiratory cycles. In some instances, such significant overlap may include a complete overlap of the inspiratory phase.

Via this arrangement, it becomes feasible to stimulate an airway-related-nerve to treat sleep disordered breathing either without any sensing elements at all or with minimal use of sensing elements. In this sense, the stimulation is performed asynchronously, i.e. without synchronization relative to sensed respiratory information. Among other benefits, this may reduce the cost of the stimulation system, may simplify its implantation, and may simplify operation of the stimulation system. Moreover, the presence of non-stimulation periods helps to minimize potential muscle fatigue that might otherwise be caused. Finally, providing asynchronous stimulation via the independent stimulation element may help to overcome situations in which sensor-based systems or synchronous systems are unable to achieve synchronization and/or the sensing signal become unstable (or is unavailable).

However, it will be understood that in some examples, an asynchronous independent stimulation protocol is implemented while still performing sensing respiratory information for non-synchronization purposes, such as evaluating stimulation therapy effectiveness and/or provide information to adjust parameters of the independent stimulation protocol.

In another aspect, providing stimulation asynchronously via the independent stimulation element may enable leveraging a greater number of different stimulation protocols because of fewer constraints on how the stimulation cycles of the stimulation protocols relate to characteristics of a respiratory waveform. Moreover, in some examples, the stimulation element applies nerve stimulation while rotating application through the plurality of different stimulation protocols, which in some instances provides a more robust therapy than using a single stimulation protocol. In some examples, this rotation also can be used to sort through the relative effectiveness of the different stimulation protocols and select the most effective stimulation protocol for a particular patient.

In some examples, an independent stimulation protocol is implemented in which the inspiratory phase of a majority of reference respiratory cycles are at least partially overlapped by a stimulation period, with more occurrences of such overlapping being preferred over fewer such occurrences. Similarly, in some examples, it is generally preferred to implement such an independent stimulation protocol via providing the sequence of stimulation periods to result in a greater degree of overlap with the inspiratory phase of the reference respiratory cycles rather than a lesser degree of overlap.

In some examples, the therapy manager includes a stimulation protocol element that provides convertible operation between the above-described independent (i.e. asynchronous) first stimulation mode and a synchronous second stimulation mode of stimulating the airway-patency-related nerve synchronous with a characteristic of the sensed respiratory waveform. In this arrangement, the therapy manager causes: operation in the first stimulation mode for at least a first predetermined period of time; conversion of operation into the second stimulation mode upon at least one parameter of the sensed respiratory waveform meeting a sensor signal quality criteria; and reversion of operation into the first stimulation mode for at least the first predetermined period of time upon the at least one parameter of the sensed respiratory waveform failing to meet the sensor signal quality criteria. Accordingly, in one aspect, the first stimulation mode comprises the default mode of stimulation.

In some examples, the conversion between the first stimulation mode and the second stimulation mode is automatic. In some examples, the therapy manager includes a user selection function to enable user selection of either the first mode or the second mode as a default mode.

In some examples, the therapy manager includes an operator selection function to selectively cause conversion between the two different stimulation modes. In one aspect, such selective conversion can be implemented manually during operator titration of the therapeutic treatment as the operator adjusts parameters of the stimulation protocols for a particular patient.

In some examples the first predetermined period of time corresponds to a period sufficient to establish a steady state in which filtering is established, inspiration and expiration are being detected reliably, signal gain control is realized, etc. In some examples, the first predetermined period of time does not correspond to a test mode for evaluating the operational fitness of the stimulation system. Stated differently, activities occurring during the first predetermined period of time may sometimes be referred to as a non-test mode.

Via this arrangement, the independent stimulation element first establishes a stable respiratory pattern. This arrangement therapeutically achieves airway patency while simultaneously increasing the likelihood of later successful synchronization of a respiratory-dependent stimulation protocol. In particular, because some examples dictate that stimulation is not implemented until or unless sleep disordered breathing behavior (above a severity threshold) is detected, the available respiratory signal will likely be a poor signal which attempt synchronization of a stimulation signal.

Accordingly, rather than attempt a likely problematic synchronization, at least some examples of the present disclosure first establish independent nerve stimulation that does not depend on synchronization. This independent stimulation, in turn, helps to establish a stable respiratory pattern or signal, which then in turn, significantly increases

the success of later synchronizing a respiratory-dependent stimulation protocol relative to the respiratory signal. Once a robust synchronization is established, then the system is well positioned to maintain a stable respiratory period using less overall stimulation by stimulating on a synchronized basis in which stimulation is limited to generally coinciding with an inspiratory phase (or other characteristic of the sensed respiratory waveform).

Of course, in the event the sensed respiratory signal changes in a way that hinders synchronization and/or delivery of effective therapeutic stimulation, then in at least some examples, the therapy manager will cause operation to revert to the independent stimulation mode.

With this arrangement, the independent stimulation mode enables initially applying a higher intensity stimulation to establish and ensure a stable respiratory pattern, which in turn, increases the likelihood of being able to later establish and maintain a lower intensity stimulation via the synchronized, respiratory-dependent stimulation mode. In this way, it is expected that overall muscle fatigue is minimized because of the likelihood of the synchronization mode successfully operating for a longer period of time than if the independent stimulation mode were not applied first.

Accordingly, in some examples, an independent stimulation element is implemented alone to treat sleep disordered breathing. However, in some examples, treatment is accomplished via a complementary combination of an independent (i.e. asynchronous) stimulation mode and a synchronous stimulation mode.

As noted above, in some examples, a stimulation protocol element may provide convertible operation between the above-described independent (i.e. asynchronous) first stimulation mode and a synchronous second stimulation mode of stimulating the airway-patency-related nerve synchronous with a characteristic of the sensed respiratory waveform. However, in one example arrangement, the therapy manager causes: operation in the second stimulation mode and conversion of operation into the first stimulation mode upon at least one parameter of the sensed respiratory waveform failing to meet a sensor signal quality criteria. Later, reversion of operation into the second stimulation mode is made upon the at least one parameter of the sensed respiratory waveform meeting the sensor signal quality criteria. Accordingly, in one aspect, the second stimulation mode comprises the default mode of stimulation.

These examples, and other examples, are further described in association with at least FIGS. **1-19**.

FIG. **1**A is block diagram schematically illustrating a stimulation element **12**, according to one example of the present disclosure. In some examples stimulation element **12** directs and controls nerve stimulation to treat obstructive sleep apnea. In some examples, stimulation element **12** includes an independent stimulation function **14**, which in general terms, applies electrical stimulation via a stimulation protocol to an airway-patency-related nerve to treat upper airway obstructions. In some examples, such airway-patency-related nerves include at least the protrusor branches of the hypoglossal nerve.

In some examples, the independent stimulation function **14** operates to stimulate an airway-patency-related nerve, according to a first stimulation protocol not synchronized relative to sensed respiratory information and in which each stimulation cycle includes a stimulation period and a non-stimulation period. Accordingly, in some examples, via the independent stimulation function **14**, nerve stimulation is applied independent of characteristics of sensed respiratory information. In other words, once the independent stimulation function **14** has been activated, the initiation and termination of individual nerve stimulation periods is not synchronized relative to a characteristic, such as onset of the inspiratory phase of the patient respiratory cycle and/or other characteristics. In at least this context, operation of independent stimulation function **14** (FIG. **1**A) may be referred to as an asynchronous stimulation function or mode.

In some examples, once a treatment period begins, such as when the patient is engaging in sleeping behavior (and during which sleep disordered breathing is to be avoided), the nerve stimulation function **14** is always in an "on" or active mode, and therefore stimulation cycles are applied to the nerve. In such examples, activation or deactivation of the independent stimulation function **14** is independent of whether or not apneas are occurring. For instance, the general activation and/or deactivation of the independent stimulation function **14** can be controlled according to a selectable time schedule, such as a predetermined start time (e.g. 10 p.m.) and predetermined end time (e.g. 6 a.m.).

FIG. **1**B is a block diagram schematically illustrating a therapy manager **16**, according to one example of the present disclosure. In general terms, therapy manager **16** directs a therapeutic regimen for controlling sleep disordered breathing such as, but not limited to, obstructive sleep apnea. The therapy manager **16** operates as part of, or in cooperation with, an at least partially implantable nerve stimulation system. In some examples, therapy manager **16** forms at least part of a control portion such as, but not limited to, control portion **360** as later described in association with at least FIGS. **9-10**, and as such, in some examples, therapy manager **16** includes at least some of substantially the same features and attributes as therapy manager **371** described in association with at least FIG. **9**.

In some examples, therapy manager **16** is in communication with and/or incorporates at least some aspects of stimulation element **12**. In some examples, the therapy manager has access to physiologic sensing information via sensing elements (e.g. at least FIGS. **7**A-**7**B). In such examples, general activation and/or general deactivation of the independent stimulation function **14** is controlled according to a likelihood of sleep behavior, which is determined according to at least body position, body posture, body motion, and/or body activity parameters, which can be sensed via an accelerometer or other sensing elements. In some examples, determining likelihood of sleep behavior is supplemented via additional sensed physiologic information, including but not limited to sensed respiratory information.

In some of the examples in which the therapy manager **16** has access to sensed physiologic information (at least FIGS. **7**A-**8**), once a treatment period begins, the nerve stimulation function **14** is not generally activated and/or deactivated to stimulate a nerve until prompted to do so based on respiratory behavior criteria (e.g. whether apneas are likely or are occurring, etc.). This determination is separate from, and independent of, timing or synchronizing individual stimulation periods relative to particular characteristics (e.g., inspiration, expiration, etc.) of sensed respiratory information. Accordingly, in these examples, whether or not a patient receives any stimulation at all is governed by whether or not the patient experiences a sufficient quantity, frequency, or intensity of apneas.

In other words, in some examples, therapy manager **16** operates to apply stimulation when the patient is experiencing apneas or likely to experience apneas. In this way, nerve stimulation is limited to an as needed basis, thereby conserving energy of the stimulation system **20** and reducing

potential muscle fatigue. As to the particular strength of the stimulation signal and whether it is applied in view of the relative severity of the sleep disordered respiratory behavior, at least some examples of automatic adjustment of a level of stimulation therapy is described in at least Christopherson, METHOD OF TREATING SLEEP DISORDERED BREATHING, published on Oct. 27, 2011 as US 2011-0264164.

In some examples, the detection of flow limitations and/or associated apneas, as well as the detection of the beginning and end of the respective inspiratory and expiratory phases of the respiratory cycle, is performed according to, or in cooperation with, known methods and devices for doing so. Some non-limiting examples of such devices and methods to recognize and detect the various features and patterns associated with respiratory effort and flow limitations include, but are not limited to: PCT Publication WO/2010/059839, titled A METHOD OF TREATING SLEEP APNEA, published on May 27, 2010; Christopherson U.S. Pat. No. 5,944,680, titled RESPIRATORY EFFORT DETECTION METHOD AND APPARATUS; and Testerman U.S. Pat. No. 5,522,862, titled METHOD AND APPARATUS FOR TREATING OBSTRUCTIVE SLEEP APNEA.

In some examples, the stimulation element **12** comprises a stimulation engine to determine and administer a stimulation protocol. In some examples, the stimulation element **12** further includes and/or acts in cooperation with a pulse generator and stimulation electrode to deliver the stimulation to a target nerve, such as later described in association with at least FIGS. **2**A-**2**D and **7**B. In such examples, the pulse generator includes the stimulation engine or the stimulation engine is in communication with the pulse generator.

In some examples, the therapy manager **16** is in communication with the pulse generator and/or incorporated within the pulse generator. In some examples, at least some components, functions, elements, etc. of the therapy manager **16** are incorporated within a physician programmer external to the patient or a patient remote external to the patient.

Details regarding particular stimulation protocols implemented via the independent stimulation function **14** are later described in association with at least FIGS. **3**B-**3**E. In particular, at least some details are provided regarding how asynchronous stimulation may increase therapeutic effectiveness in treating sleep disordered breathing.

FIG. **2**A is a schematic diagram of an at least partially implantable stimulation system **20**, according to an example of the present disclosure. In general terms, the stimulation element **12** of FIG. **1**A (and/or therapy manager **16** of FIG. **1**B) is incorporated within and/or operates in association with stimulation system **20** to deliver stimulation.

As illustrated in FIG. **2**A, in one example system **20** includes an implantable pulse generator (IPG) **35** and a stimulation lead **32** electrically coupled with the IPG **35** via a connector (not shown) positioned within a connection port of the IPG **35**. In some examples, the IPG **35** is surgically positioned within a pectoral region of a patient **22**. The lead **32** includes a stimulation electrode portion **45** and extends from the IPG **35** so that the stimulation electrode portion **45** is positioned in contact with a desired nerve, such as an airway-patency-related nerve **33** of the patient **10**, to enable stimulation of the nerve **33**, as described below in detail. In some examples, the stimulation electrode portion **45** comprises a self-sizing cuff such as described in U.S. Pat. No. 8,340,785 to Bonde et al. In some examples, in association with electrode **45**, lead **32** includes at least some of the features and attributes described in U.S. Patent Publication 20110160827 to Bonde et al. In some examples, lead **32** includes features and attributes at least consistent for use in an implantable stimulation system as described in U.S. Pat. No. 6,572,543 to Christopherson et al.

As later described more fully in association with at least FIGS. **9**-**10**, in some examples the therapy manager **16** controls the IPG **35**, and is implemented externally of the IPG **35**, entirely within the IPG **35**, or partially within the IPG **35**.

In some examples, stimulation electrode portion **45** comprises a cuff electrode including a single operative contact group of at least two electrodes through which the stimulation is deliverable non-selectively to the airway-patency-related nerve. FIG. **2**E is a top view schematically illustrating one example of such an electrode **50** including a single operative contact group of at least two electrodes **52**. In some examples, the stimulation electrode portion **45** comprises a cuff electrode including at least one operative contact group through which the stimulation is deliverable non-selectively to the airway-patency-related nerve. Accordingly, more than one operative contact group of electrodes can be incorporated in a single cuff electrode. In some examples, the stimulation electrode portion **45** can include multiple, separate cuff electrodes with each having at least one operative contact group of electrodes.

In some examples, the stimulation system for treating obstructive sleep apnea is a totally implantable system which provides therapeutic solutions for patients diagnosed with obstructive sleep apnea. However, in some examples, one or more components of the system are not implanted in a body of the patient, thereby providing an at least partially implantable system. A few non-limiting examples of such non-implanted components include an external processing unit and/or an external power source, as later noted in association with at least FIG. **6**.

In some examples, the at least partially implantable stimulation system **20** does not include any sensing elements. Accordingly, to the extent that the system **20** and its therapy manager **16** apply stimulation protocols to treat respiratory behavior, any patient-specific respiratory information would be received and/or obtained prior to, and/or during, implantation of the system **20**. Alternatively, a temporary external sensing system could be employed to periodically calibrate and/or evaluate therapeutic efficacy of the at least partially implantable stimulation system **20** operating according to an independent stimulation function **14** (FIG. **1**A).

At least some examples of the sensor-less stimulation system **20** use significantly less power than some sensor-based systems and are easier to implant. Moreover, in such examples, the system **20** is significantly easier to construct and/or operate because the sensors, certain sensing-related circuitry, and certain operational programming can be omitted.

However, it will be understood that in some examples, the stimulation system **20** includes sensing elements, at least in the manner later described in association with at least FIGS. **7**A-**7**B. In at least some of these examples, the sensing elements are used to evaluate therapy and particular stimulation protocols but are not used to synchronize stimulation relative to characteristics of the sensed respiratory waveforms.

FIG. **2**B is block diagram of an implantable pulse generator (IPG) **50**, according to one example of the present disclosure. In some examples, IPG **50** includes at least some of substantially the same features and attributes as IPG **35** (FIG. **2**A). However, in some examples, IPG **50** includes at least some features and attributes different than those in IPG **35** (FIG. **2**A). As such, in some examples, IPG **50** can take

different forms and be implanted in locations other than those shown in FIG. **2**A (and also FIG. **7**B).

With further reference to FIG. **2**B, in some examples the implantable pulse generator **50** includes a stimulation element **52** and a communication element **54**. The stimulation element **52** generates and applies a neuro-stimulation signal via electrode(s) (such as stimulation electrode(s) **45** in FIG. **2**A) according to a treatment regimen programmed by a physician and/or in cooperation with therapy manager **16**. In some examples, stimulation element **52** comprises at least some of substantially the same features and attributes as stimulation element **12** as previously described in association with FIG. **1**A.

The communication element **54** provides a communication pathway to enable transmission of data, power, and/or controls signals both to and from the implanted portions of the system **20** relative to the external portions of the system **20**. For instance, in some examples, the communication element **54** is configured to report activities of the IPG **50** (including sensed physiologic data, stimulation history, number of apneas detected, etc.) and is configured to receive initial or further programming of the IPG **50** from an external source, such as a patient programmer, clinician programmer, etc. as later noted in association with at least FIG. **10**. In some examples, the communication element **54** utilizes a radiofrequency (RF) telemetry link or other wireless communication protocols.

In some examples, the implantable pulse generator **50** includes a control portion or at least part of a control portion such as control portion **56** shown in FIG. **2**C. In general terms, control portion **56** directs operation of the pulse generator **50** and the at least partially implantable stimulation system. Further details regarding such a control portion **56** are described later in association with at least FIGS. **9**-**10**. Moreover, in some examples, control portion **56** is operable in association with a user interface, such as described later in association with at least FIGS. **11**A-**11**B.

FIG. **2**D is a block diagram **70** schematically illustrating an at least partially implantable stimulation system **80**, according to an example of the present disclosure. In some examples, system **80** includes at least some of substantially the same features and attributes as system **20** (FIG. **2**A), pulse generator **50** (FIG. **2**B), and control portion **56** (FIG. **2**C), except for system **80** having some portions in a non-pectoral location and located in close proximity to a target nerve to be stimulated, as further illustrated in association with at least FIG. **2**D.

In some examples, system **80** is a sensor-less system in a manner substantially similar to the above-described system **20**. In other words, as at least partially implanted in the patient's body, system **80** omits a sensor.

As shown in FIG. **2**D, in some examples system **80** includes a nerve-coupling electrode portion **82** and a pulse generator **84**. In some examples, the nerve-coupling electrode portion **82** comprises an element which is at least electrically coupled relative to a target nerve **72** suitable to maintain or restore airway patency, such as but not limited to, the hypoglossal nerve.

In some examples, the electrode portion **82** comprises a cuff, such as one of the stimulation electrode portions **45** described in association with FIG. **2**A in which the electrode portion is both mechanically and electrically coupled relative to the nerve **72**. However, in some examples, the nerve-coupling electrode portion **82** comprises a cuff-less structure that is both mechanically and electrically coupled relative to the nerve **72**.

In some examples, the nerve-coupling electrode portion **82** is not mechanically coupled to the nerve **72**, but is mechanically coupled or secured in a location in close proximity to the nerve **72** and that enables electrically coupling of the electrode portion **82** relative to the nerve **72**. In one instance, such examples include the electrode portion **82** being delivered to the target nerve **72** via a percutaneous access delivery. In one instance, such examples include the electrode portion **82** being delivered to the target nerve **72** via a transvenous delivery method in which the electrode portion **82** is delivered on a lead maneuvered within and through the vasculature of the patient.

In some examples, in a manner consistent with the previously described pulse generator **50** (FIG. **2**B) pulse generator **84** includes a stimulation element **52** and a communication element **54**. In some examples, pulse generator **84** includes solely internal components **90**, which are internally within the body below the skin/tissue. However, in some examples, pulse generator **84** includes a combination of some internal components **90** and some external components **92**, which are external to the body being above or outside the skin/tissue.

In some examples, via communication element **54** (FIG. **2**B), system **80** includes a wired communication path **94** and/or a wireless communication path **96** between the pulse generator **84** and the nerve-coupling electrode portion **82**, as shown in FIG. **2**D. In some examples, either or both such communication pathways **94**, **96** are also employable for communication between internal and external components **90**, **92** of a pulse generator **84**.

In some examples, in order to utilize and/or evaluate sensed respiratory information, the therapy manager **16** uses a reference point, such as a normal breathing pattern **150**, as shown in FIG. **3**A. Of course, variances may exist from patient-to-patient so it will be understood that the normal breathing pattern **150** is a representative example provided for illustrative purposes and is not intended to strictly define a breathing pattern that is universally normal for all patients. With this in mind, in some examples, the system **20** uses the particular breathing pattern of a specific patient (to which the method is applied) as the reference point to utilize and/or evaluate sensed respiratory information.

In the example of normal breathing pattern **150** shown in FIG. **3**A, a respiratory cycle **160** includes an inspiratory phase **162** and an expiratory phase **170**. The inspiratory phase **162** includes an initial portion **164**, intermediate portion **165**, and end portion **166** while expiratory phase **170** includes an initial portion **174**, intermediate portion **175**, end portion **176**, and an expiratory peak **177**. A first transition **180** occurs at a junction between the end inspiratory portion **166** and the initial expiratory portion **174** while a second transition **182** occurs at a junction between the end expiratory portion **176** and the initial inspiratory portion **164**. In some instances, end expiratory portion **176** includes and/or is referred to as an expiratory pause that occurs just prior to onset of the initial inspiratory portion **164**.

FIG. **3**B is a diagram **200** schematically illustrating a stimulation protocol **210** implemented via independent stimulation function **14** (FIG. **1**A), according to one example of the present disclosure. In some examples, after initializing the system according to the known/applicable respiratory cycle for that patient and after general activation of the independent stimulation function **14**, the initiation, operation, and termination of the stimulation protocol **210** operates without regard to sensed respiratory information. In one aspect, FIG. **3**B illustrates a respiratory pattern **202** including a series of reference respiratory cycles **204**A-**204**H, with

each cycle having substantially the same features and attributes as the respiratory cycle **160**. Accordingly, each reference respiratory cycle **204**A-**204**H has a duration R.

In one aspect, the pattern **202** represents a stable respiratory pattern that occurs during normal daytime breathing and/or that results from application of stimulation protocol **210**.

In some examples, because stimulation via the stimulation protocol **210** is not synchronized relative to characteristics of actively-sensed respiratory cycles (such as via real-time measure of respiratory effort), the stimulation protocol **210** operates based on a reference respiratory cycle. In some examples, the reference respiratory cycle includes at least one of a historical patient-specific average respiratory cycle for stable respiration and a multi-patient average respiratory cycle for stable respiration. This historical and/or predictive information is employed in at least some examples in which the therapy manager **16** (FIG. **1**B) is not actively sensing respiratory waveforms during operation of the at least partially implantable stimulation system **20**.

As shown in FIG. **3**B, stimulation protocol **210** includes a series of separate stimulation periods (e.g. pulses) **212**A-**212**J spaced apart by a non-stimulation periods **218**A-**281**I, each of which are interposed between an adjacent pair of stimulation periods. For instance, non-stimulation period **218**B is interposed between stimulation periods **212**B, **212**C. In one aspect, each stimulation period (**212**A-**212**I) has a first end **214** and an opposite second end **216**.

In some examples, in order to demonstrate the manner in which the stimulation protocol **210** is juxtaposed relative to the respiratory pattern **202**, FIG. **3**B further illustrates each respiratory cycle being apportioned into a discrete number (e.g. 3, 4, 5, 6, 7, 8, etc.) time units, with each time unit having a duration t. In the example shown in FIG. **3**B, each respiratory cycle has a duration R and is divided into six time units t.

In some examples, the duration R is patient specific and is based on a long term average duration of a respiratory cycle. In some examples, the duration R is not patient specific and is based on an average duration of a respiratory cycle for many different patients. In some examples, duration R is about 3 to about 6 seconds. In some examples, via therapy manager **16**, the duration R can be adjusted to a preferred duration. In some examples, the therapy manager **16** uses the patient-specific information regarding durations.

However, in some examples, where such information is not available or is problematic, the therapy manager **16** uses multi-patient information. For instance, for at least some patient populations a duration of an entire respiratory period is about 3 to 6 seconds, which corresponds to a general respiratory rate of about 10-18 breaths/minute. Moreover, generally speaking inspiration (e.g. an inspiratory phase) is a minority of the entire respiratory period which includes inspiration, expiration, and expiratory pause.

In at least some patient populations, an apnea and/or hypopnea has a minimum duration of about 10 seconds, which corresponds to a minimum duration about 2-3 breaths.

In some examples, an apnea may be avoided via implementation of a stimulation protocol which avoids missing (either completely missing or significantly missing) stimulation for more than one breath (e.g. one inspiratory phase).

With further reference to FIG. **3**B, as represented by the legend **209**, the stimulation protocol **210** operates according to a stimulation cycle in which the duration of the stimulation cycle is less than the duration (R) of the reference respiratory cycle. In some examples, the duration of the stimulation period exceeds the duration of the non-stimulation period by a factor of 3. In some examples, as shown by legend **209**, the stimulation period and the non-stimulation period are in a proportion of 4 to 1. In such examples, each stimulation cycle includes a continuous stimulation period of 4 time units followed by a non-stimulation period of 1 time units, with this stimulation cycle being repeated continuously when nerve stimulation is generally activated. The total duration of the stimulation cycle (e.g. 4 time units of stimulation and 1 time unit of non-stimulation) is 5 time units, which is less than the duration R of the respiratory period, which is 6 time units in this example. In one aspect, this example arrangement in which the stimulation period is in much greater proportion to the non-stimulation period may benefit some patients by minimizing tongue rubbing by minimizing the frequency or total volume of tongue motion incident to tongue protrusion intentionally caused by the stimulation therapy to restore airway patency.

In FIG. **3**B, the first end **214** of stimulation period **212**A is shown as coinciding with the beginning of an inspiratory phase **162** of the respiratory cycle **204**A. However, it will be understood that the beginning **214** of the stimulation period **212**A is not synchronized relative to the inspiratory phase **162**. Rather, the beginning **214** of stimulation period **212**A is shown as coinciding with the beginning of inspiratory phase **162** for illustrative simplicity in juxtaposing the stimulation protocol **210** relative to the respiratory cycles **204**A-**204**H. Accordingly, it will be understood that when stimulation (according to stimulation protocol **210**) is initiated during a treatment period, the beginning of the stimulation period **212**A may coincide with a different portion of the respiratory cycle (e.g. **204**A) than shown in FIG. **3**B.

With further reference to the stimulation protocol **210** in FIG. **3**B, in one aspect, each respective non-stimulation period **218**A-**218**I has a duration less than a duration of each respective stimulation periods **212**A-**212**J. In one aspect, the duration of the stimulation period **212**A is less than a duration (R) of the reference respiratory cycle **204**A. In one aspect, the relative duration of the respective stimulation periods (e.g. **212**A) and non-stimulation periods (e.g. **218**A) causes each successive stimulation period (e.g. **212**B) to begin at a different place along a successive respiratory cycle, such that the stimulation pattern is independent of (i.e. not synchronized relative to) the characteristics of the respiratory cycle. For instance, it can be seen from FIG. **3**B that the first end **214** of stimulation period **212**D coincides with a portion of the expiratory phase **170** of respiratory cycle **204**C while the first end **214** of stimulation period **212**E coincides with a portion of inspiratory phase **162** of the successive respiratory cycle **204**D.

As shown in FIG. **3**B, each of the respective stimulation periods **212**A, **212**B, **212**C overlaps the entire inspiratory phase **162** of the respective respiratory cycles **204**A-**204**C while stimulation period **212**D at least partially overlaps the inspiratory phase **162** of respiratory cycle **204**D.

Because the overall duration of the stimulation cycle (both stimulation period and non-stimulation period) does not match the duration (R) of the reference respiratory cycle, the stimulation protocol **210** ensures that each successive stimulation period within the series of stimulation cycles will fall along a different portion of the successive respiratory cycles. Accordingly, even though the stimulation is not synchronized relative to a characteristic (e.g. inspiration) of the respiratory waveform, no matter where the stimulation protocol **210** is started relative to a series of respiratory cycles, the stimulation periods will overlap with at least a portion of the inspiratory phase of the respective reference

respiratory cycles for a significant majority of the treatment period. Accordingly, even if the stimulation protocol **210** happens to be initiated at a time that the non-stimulation period (e.g. **218**D, **218**E) at least partially overlaps with the inspiratory phase **162** of a respiratory cycle (e.g. **204**D, **204**E), the succeeding stimulation periods **212**F, **212**G, etc. at least partially overlaps the inspiratory phase **162** of the next respiratory cycle **204**F, **204**G, etc., with these later successive stimulation periods significantly overlapping (e.g. stimulation period **212**F, which overlaps by at least a majority) or even completely overlapping (e.g. stimulation period **212**G) the inspiratory phase **162** of the respective successive respiratory cycles (e.g. **204**F, **204**G).

In one aspect, in stimulation protocol **210** the duration of each stimulation period (e.g. **212**A-**212**J) is less than a duration (R) of the reference respiratory cycles (**204**A-**204**H) but greater than a duration of the inspiratory phase **162** of an individual respiratory cycle (e.g. **204**A).

In one aspect, a duty cycle for the stimulation cycle varies on a respiratory cycle-by-respiratory cycle basis. For instance, during respiratory cycles **204**A, **204**B, **204**C, **204**D, **204**F, **204**G, **204**H the duty cycle is 5 time units of continuous stimulation and 1 time unit of non-stimulation, which equals about 83%. However, during respiratory cycle **204**E, the duty cycle is 4 time units of continuous stimulation and 2 time units of non-stimulation, which equals about 67%. Every 5 respiratory cycles, the series of stimulation cycles repeats itself, as illustrated at respiratory cycle **204**F, at which the first end **214** of the stimulation period **212**G once again coincides with the beginning of the inspiratory phase **162** of the respiratory cycle **204**F in a manner similar to respiratory cycle **204**A. Accordingly, in one aspect, the long term duty cycle over an indefinite number of respiratory cycles (or average duty cycle over a sufficient number of time frames) is about 80%.

In some examples, via stimulation protocol **210**, no sequence of four respiratory cycles occurs without a stimulation period significantly overlapping the inspiratory phase **162** (e.g. overlapping at least majority of the inspiratory phase **162**) of respiratory cycles in FIG. **3**B. This criteria is based on the longest period of time, in at least some examples, that a patient can go without a breath while avoiding a respiratory-event related arousal and/or to maintain near normal blood oxygenation.

In some examples, via stimulation element **12** (FIG. **1**A) and/or therapy manager **16** (FIG. **1**B) a clinician can implement a stimulation protocol in which a quantity (e.g. 2, 3, 4) is selected by the operator regarding how many respiratory cycles can pass without a significantly overlapping stimulation period, according to a predetermined amount of time and/or a predetermined number of respiratory cycles for a particular patient.

It will be understood that each inspiratory phase **162** of each respiratory cycle (**204**A-**204**H) is shown in its ideal form in FIG. **3**B, and that in some instances where the inspiratory phase **162** at least partially coincides with one of the respective non-stimulation periods (e.g. **218**D), the inspiratory phase may sometimes have an irregular shape compared to the idealized shape shown in FIG. **3**B.

Accordingly, via stimulation protocol **210**, the independent stimulation function **14** of stimulation element **12** (FIG. **1**A) employs asynchronous nerve stimulation to achieve stable respiration despite potential sleep disordered breathing.

With the example of pattern **202** and stimulation protocol **210** as a foundation, it will be understood that in some examples, a stimulation protocol is adopted in which the duration of the stimulation period of each stimulation cycle is at least 50 percent of the duration of the reference respiratory cycle. In at least some contexts, this arrangement may ensure that the probability of entirely missing inspiration in an asynchronous stimulation protocol is less than 50%, such that a majority of the treatment period, stimulation will be delivered during at least a portion of inspiration, which may be sufficient to minimize or prevent sleep disordered breathing (e.g. apneas).

In some examples, a stimulation protocol is adopted in which the duration of the stimulation period of each stimulation cycle is 80 percent of the duration of the reference respiratory cycle. For instance, such an arrangement might be employed in some example patients having severe obstructive sleep apnea in which an inspiration can be missed for no more than 1 of 5 breaths. When applied asynchronously, such a duty cycle may likely ensure effective treatment (assuming other stimulation parameters are effective) while still allowing the protrusor muscles to rest sufficiently.

While not depicted in FIG. **3**B, in some examples, a stimulation protocol is adopted in which the duration of the stimulation period of each stimulation cycle is at least 25 percent of the duration of the reference respiratory cycle. When employed in an asynchronous arrangement, such an arrangement will likely ensure that at least one stimulation period significantly overlaps with the inspiratory phase at least one breath (e.g. one respiratory cycle) out of every three breaths (i.e. three respiratory cycles). For some patients which exhibit less severe apneas, this arrangement can be sufficient to prevent obstructive events.

FIG. **3**C is a diagram **221** schematically illustrating a stimulation protocol **220** implemented via independent stimulation function **14** (FIG. **1**A), according to one example of the present disclosure. In one example, diagram **221** includes at least some of substantially the same features and attributes as diagram **201**, except for having a different stimulation protocol **220**.

Moreover, as represented by the legend **229**, the stimulation protocol **220** operates according to a stimulation cycle in which the duration of the stimulation cycle is greater than the duration (R) of the reference respiratory cycle. In some examples, the duration of the stimulation period exceeds the duration of the non-stimulation period by a factor of at least 1.5. As represented via legend **229**, in some examples stimulation protocol **220** includes a stimulation cycle including a stimulation period of 4½ time units and a non-stimulation period of 2½ time units, with the overall stimulation cycle of 7 time units having a duration greater than the duration R of the respiratory cycle (e.g. **204**A) of 6 time units.

In a manner substantially the same as previously noted for stimulation protocol **210**, even though stimulation protocol **220** is not synchronized relative to a characteristic (e.g. inspiration) of the respiratory waveform, no matter where the stimulation protocol **220** is started relative to a series of respiratory cycles, the stimulation periods will overlap with at least a portion of the inspiratory phase of the respective reference respiratory cycles for a significant majority of the treatment period. For instance, even if the stimulation protocol happens to be initiated at a time that the non-stimulation period **228**B generally coincides with the inspiratory phase **162** of a respiratory cycle **204**C, the succeeding stimulation period **222**C at least partially overlaps the inspiratory phase **162** of the next respiratory cycle **204**D, and with later successive stimulation periods significantly overlapping (e.g. stimulation period **222**D, exhibiting at

least a majority overlap) or completely overlapping (e.g. stimulation period **222**E) the inspiratory phase **162** of the respective successive respiratory cycles (e.g. **204**E, **204**F).

In some examples, a stimulation protocol is applied in which a total duration of stimulation via the first stimulation protocol during a treatment period is greater than 30 percent of the total duration of the treatment period.

In one aspect, in stimulation protocol **220** the duration of each stimulation period (e.g. **222**A-**222**G) is less than a duration (R) of the respiratory cycles **204**A-**204**H) but greater than a duration of the inspiratory phase **162** of an individual respiratory cycle (e.g. **204**A).

In one aspect, a duty cycle exhibited by the repeating stimulation cycle varies on a respiratory cycle-by-respiratory cycle basis. For instance, during respiratory cycles **204**D, **204**E, **204**F, **204**G the stimulation duty cycle is 3½ time units of continuous stimulation and 2½ time units of non-stimulation, which equals about 58%. However, during respiratory cycles **204**A and **204**B the stimulation duty cycle is 4½ time units of continuous stimulation and 1½ time units of non-stimulation, which equals about 75%. Meanwhile, during respiratory cycles **204**C, the duty cycle is 4 time units of continuous stimulation and 2 time units of non-stimulation, which equals about 67%. Every 8 respiratory cycles, the series of stimulation cycles repeats itself, as illustrated at respiratory cycle **204**H, at which the first end **224** of the stimulation period **222**G once again coincides with the beginning of the inspiratory phase **162** of the respiratory cycle **204**H in a manner similar to respiratory cycle **204**A. Accordingly, in one aspect, the long term or average duty cycle over a long period of time is about 64%.

In some examples, via stimulation protocol **220** no more than four respiratory cycles occur without a stimulation period significantly overlapping (e.g. at least a majority of the) inspiratory phase **162** of respiratory cycles in FIG. **3**C.

FIG. **3**D is a diagram **231** schematically illustrating a stimulation protocol **230** implemented via independent stimulation function **14** (FIG. **1**A), according to one example of the present disclosure. In one example, diagram **231** includes at least some of substantially the same features and attributes as diagram **201** (FIG. **3**B) or diagram **221** (FIG. **3**C), except for having a different stimulation protocol **230**.

Moreover, as represented by the legend **239**, the stimulation protocol **220** operates according to a stimulation cycle in which the duration of the stimulation cycle is greater than the duration (R) of the reference respiratory cycle. In some examples, the duration of the stimulation period exceeds the duration of the non-stimulation period by a factor of at least 3. As represented via legend **239** in FIG. **3**D, in some examples stimulation protocol **230** includes a stimulation cycle including a continuous stimulation period of 7½ time units and a non-stimulation period of 2½ time units, with the overall stimulation cycle of 10 time units having a duration greater than the duration R of the respiratory cycle (e.g. **204**A) of 6 time units.

In a manner substantially the same as previously noted for stimulation protocols **210**, **220**, even though stimulation protocol **230** is not synchronized relative to a characteristic (e.g. inspiration) of the respiratory waveform, no matter where the stimulation protocol **230** is started relative to a series of respiratory cycles, the stimulation periods will overlap with at least a portion of the inspiratory phase of the respective respiratory cycles for a significant majority of the treatment period. Accordingly, even if the stimulation protocol happens to be initiated at a time that the non-stimulation period **238**B generally coincides with the inspiratory phase **162** of a respiratory cycle **204**D, the succeeding stimulation period **232**C at least partially overlaps the inspiratory phase **162** of the next respiratory cycle **204**E.

In one aspect, in stimulation protocol **230** the duration of each stimulation period (e.g. **232**A-**232**D) is greater than a duration (R) of the respiratory cycles **204**A-**204**G) and greater than a duration of the inspiratory phase **162** of an individual respiratory cycle (e.g. **204**A).

In one aspect, a duty cycle exhibited by the repeating stimulation cycle varies on a respiratory cycle-by-respiratory cycle basis. For instance, during respiratory cycle **204**A, the duty cycle is 6 time units of continuous stimulation, which equals 100%. However, during respiratory cycles **204**B and **204**E the stimulation duty cycle is 3½ time units of continuous stimulation and 2½ time units of non-stimulation, which equals about 58%. Meanwhile, during respiratory cycle **204**C, the duty cycle is 5½ time units of continuous stimulation and ½ time units of non-stimulation, which equals about 92 percent. Meanwhile, during respiratory cycle **204**D, the duty cycle is 4 time units of continuous stimulation and 2 time units of non-stimulation, which equals about 66 percent.

Every 5 respiratory cycles, the series of stimulation cycles repeats itself, as illustrated at respiratory cycle **204**F, at which the first end **234** of the stimulation period **232**D once again coincides with the beginning of the inspiratory phase **162** of the respiratory cycle **204**F in a manner similar to respiratory cycle **204**A.

In one aspect, the long term (i.e. average) duty cycle over a sufficient number of respiratory cycles is about 75 percent.

In one aspect, this stimulation protocol provides an occasional 100% duty cycle (e.g. stimulation period **232**D) to ensure that an inspiratory phase will be not missed during a stimulation period, while the overall average duty cycle is 75 percent. In some examples, such stimulation protocols are suitable for a patient in which the pattern of the respiratory waveform varies considerably but where effective therapy can be achieved without using continuous stimulation.

In some examples via stimulation protocol **230** no sequence of four respiratory cycles occurs without a stimulation period at least significantly overlapping the inspiratory phase **162** of respiratory cycles in FIG. **3**D.

FIG. **3**E is a diagram **241** schematically illustrating a stimulation protocol **240** implemented via independent stimulation function **14** (FIG. **1**A), according to one example of the present disclosure. In one example, diagram **241** includes at least some of substantially the same features and attributes as diagram **201**, except for having a different stimulation protocol **240**.

As represented via legend **249** in FIG. **3**E, stimulation protocol **240** includes a stimulation cycle including a continuous stimulation period of 4 time units and a non-stimulation period of 2 time units, with the overall stimulation cycle of 6 time units having a duration generally matching the duration R of the reference respiratory cycle (e.g. **204**A) of 6 time units. As in the prior examples associated with FIGS. **3**A-**3**E, the stimulation protocol **240** is independent, i.e. not synchronized relative to sensing of respiratory information.

In some patients the duration (R) of their respiratory cycle may vary slightly over time as the respiratory cycle might shorten or lengthen. Diagram **241** schematically illustrates just one example in which the reference respiratory cycle represents a situation in which the duration of the respiratory cycle lengthens to R**1** due to lengthening of the expiratory phase **171** of the respiratory cycles of the patient. It will be understood that other characteristics, parameters, features of

the respiratory cycle often change as well, but these changes are not depicted in FIG. **3**E for illustrative simplicity and clarity.

It will be further understood that such changes may develop gradually over time and that FIG. **3**E provides a snapshot of one such change after it has already at least partially developed. Moreover, because this arrangement of independent stimulation operates without synchronization relative to sensed respiratory information, FIG. **3**E schematically represents at least some aspects regarding how stimulation protocol **240** may provide therapeutic effectiveness in this situation of lengthening respiratory cycles (or shortened respiratory cycles) as represented by the reference respiratory cycles **204**A-**245**M in FIG. **3**E.

Accordingly, in this example, the stimulation cycle repeats itself in what otherwise would be exactly matching each reference respiratory cycle, but the elongated duration of the reference respiratory cycle causes the stimulation cycle to no longer coincide with various portions of the respiratory cycle.

It will be understood, of course, as previously noted elsewhere that at the time the stimulation protocol is initiated and while not shown in FIG. **3**E, the first end **244** of the initial stimulation period **242**A may not necessarily coincide with the beginning of an inspiratory phase **162** of a respiratory cycle **245**A.

In some examples, even though stimulation protocol **240** is not synchronized relative to a characteristic (e.g. inspiration) of the respiratory waveform, no matter where the stimulation protocol **240** is started relative to a series of respiratory cycles, the stimulation periods will overlap with at least a portion of the inspiratory phase of the respective respiratory cycles for a significant majority of the treatment period. Accordingly, even if the stimulation protocol happens to be initiated at a time that the non-stimulation period **248**H **248**I, **248**J generally coincides with the inspiratory phase **162** of a respiratory cycle **245**H, **245**I, **245**J, at least some subsequent stimulation periods **242**L, **242**M, **242**N significantly overlap (at least a majority overlap) the inspiratory phase **162** of the next respiratory cycles **245**K, **245**L, **245**M. As further seen in FIG. **3**E, other example stimulation periods also significantly overlap (e.g. stimulation period **242**F) the inspiratory phase **162** of the corresponding respective respiratory cycle **245**F.

In some examples, the stimulation periods **242**A-**242**E, **242**N completely overlap the inspiratory phase **162** of the respective respiratory cycles (e.g. **245**A-**245**E, **245**M). However, it will be understood that in some examples, such complete overlap with the inspiratory phase of some respiratory cycles may not be exhibited, and a significant overlap would suffice to achieve adequate airway patency.

In one aspect, in stimulation protocol **240**, the duration of each stimulation period (e.g. **242**A-**242**M) is less than a duration (R) of the respiratory cycles (**245**A-**245**M) but greater than a duration of the inspiratory phase **162** of an individual respiratory cycle (e.g. **245**A).

In one aspect, the duty cycle associated with the stimulation cycle varies on a respiratory cycle-by-respiratory cycle basis. For instance, during respiratory cycles **245**A, **245**B, **245**C, **245**D, **245**E, **245**F, **245**G, **245**H, **245**M the duty cycle is 4½ time units of continuous stimulation and 2 time units of non-stimulation, which equals about 75 percent. However, during respiratory cycles **245**I, **245**J, **245**K, **245**L the duty cycle is 4 time units of continuous stimulation and 2½ time units of non-stimulation, which equals about 62 percent.

For at least the time that a particular duration (R**1**) of the elongated respiratory cycle persists (as represented by reference respiratory cycles), every 12 respiratory cycles, the series of stimulation cycles repeats itself, as illustrated at respiratory cycle **245**M, at which the first end **244** of the stimulation period **242**N once again coincides with the beginning of the inspiratory phase **162** of the respiratory cycle **245**M in a manner similar to respiratory cycle **245**A.

In one aspect, the long term, average stimulation duty cycle over a sufficient period of time is about 67 percent.

Accordingly, in some examples, via stimulation protocol **240** no sequence of four respiratory cycles occurs without a stimulation period at least partially overlapping or even significantly overlapping the inspiratory phase **162** of respiratory cycles in FIG. **3**E.

It will be further understood that the various stimulation protocols described and illustrated in association with at least FIGS. **3**B-**3**E are implemented via the at least partially implantable stimulation system **20** as described in association with at least FIGS. **1**-**14**. However, in some examples, the various stimulation protocols described and illustrated in association with at least FIGS. **3**B-**3**E are implemented via at least some components, elements, systems etc. other than those described in association with FIGS. **1**-**14**.

While the independent stimulation function **14** (FIG. **1**A) does not use sensed respiratory information to trigger each stimulation period or synchronize each stimulation period, in some examples the independent stimulation mode **14** uses sensed respiratory information to track how a stimulation protocol is matching up relative to the characteristics of the sensed respiratory waveform. Accordingly, upon elongation or shortening of the sensed respiratory cycles, the therapy manager **16** (including independent stimulation function **14**) can choose to maintain or modify which stimulation protocol is being applied in order to ensure that the desired amount and timing of stimulation is being applied. In addition, or as an alternative, the therapy manager **16** uses the sensed respiratory information to adjust or calibrate features of the reference respiratory cycle associated with a particular stimulation protocol.

In some examples, operation of the therapy manager **16** (as part of an at least partially implantable stimulation system **20**) is not limited to the specific stimulation protocols described in association with at least FIGS. **3**B-**3**E, as other stimulation protocols can be implemented with longer or shorter stimulation periods and with longer or shorter non-stimulation periods.

In some examples the independent stimulation function **14** (FIG. **1**A) includes a complex stimulation cycle in which at least two different length stimulation periods is employed and/or at least two different length non-stimulation periods is employed. As one non-limiting example to illustrate the principle, one stimulation protocol could include a first continuous stimulation period of three time units, a first non-stimulation period of two time units, a second continuous stimulation period of three time units, followed by a second non-stimulation period of one time unit. The example later described in association with FIG. **16**A illustrate some aspects of these features.

In some examples, and as illustrated in the diagrams of FIGS. **3**B-**3**E, the stimulation cycles are not centered relative to a characteristic or feature of a respiratory waveform. In other words, the respective continuous stimulation periods or non-stimulation periods (in the example stimulation protocols) are not fixed or tied to a particular landmark or fiducial of the respiratory waveform. Accordingly, the respective continuous stimulation periods and non-stimula-

tion periods within stimulation cycles (of a particular stimulation protocol) vary regarding which portion of a respiratory cycle (of a series of respiratory cycles) with which they coincide.

In some examples, the independent stimulation function **14** provides a stimulation protocol having a duty cycle of 80 percent, where a 100 percent duty cycle would correspond to continuous stimulation over a full respiratory cycle. In one example, a first portion of the duty cycle comprises a continuous stimulation period and a second portion of the duty cycle comprises a continuous non-stimulation period immediately following the first portion. In a non-limiting example in which a respiratory cycle has a duration of 5 seconds, the duty cycle includes applying continuous stimulation for 4 seconds immediately followed by continuous non-stimulation for 1 second, with the duty cycle being repeated.

FIG. **4** is a block diagram **251** schematically illustrating a plurality of stimulation parameters **250**, according to one example of the present disclosure. In general terms, these stimulation parameters may be employed as part of implementing one of the stimulation protocols described in association with FIGS. **3**B-**3**E and/or as part of general operation of stimulation element **12** (FIG. **1**A) and/or therapy manager **16** (FIG. **1**B). In one example, a single parameter is implemented, while in some examples, several of these parameters may be implemented. When several parameters are implemented, they are implemented separately but contemporaneously in some examples and in other examples, they are implemented in combination.

As shown in FIG. **4**, these stimulation parameters **250** include amplitude parameter **252**, a duty cycle parameter **254**, a respiratory cycle duration parameter **260**, a time unit parameter **262**, and a time frame parameter **270**. The amplitude parameter **252** controls an amplitude of the stimulation signal, which can be selected for a particular stimulation protocol.

In some examples, the duty cycle parameter **254** tracks and/or controls a duty cycle of stimulation. In some examples, the stimulation duty cycle is expressed relative to a duration (R) of one respiratory cycle (per parameter **260**) in the manner previously described regarding the stimulations protocols previously described in association with at least FIGS. **3**B-**3**E. The duty cycle parameter **254** comprises a constant function **256** and a variable function **258**. The constant function **256** implements a duty cycle in which the stimulation duty cycle is identical relative to each respiratory cycle, while the variable function **258** implements a duty cycle in which the stimulation duty cycle varies relative to at least some respiratory cycles within a series of respiratory cycles.

As previously described in association with at least FIGS. **3**B-**3**E, in some examples, the stimulation duty cycle is implemented according to a series of stimulation cycles in which each stimulation cycle includes at least one continuous stimulation period and at least one non-stimulation period. At least some stimulation protocols includes stimulation cycles in which the duration of the stimulation period (s) differs relative to the duration of the non-stimulation period(s) through a series of stimulation cycles such that an average duty cycle can be calculated.

Accordingly, the various stimulation protocols provide some duty cycles that vary from one respiratory cycle to the next, while simultaneously providing an overall or average duty cycle. By selecting a particular stimulation cycle, specific duty cycles are implemented on a respiratory-cycle by respiratory-cycle basis and an overall or average duty cycle is achieved.

In some examples, a respiratory cycle duration parameter **260** identifies a duration of a patient-specific average respiratory cycle during reasonably stable respiration (e.g. normal breathing) or a duration of a multi-patient average respiratory cycle during reasonably stable respiration. In some examples, the patient-specific average respiratory cycle is determined according to recent sensed respiration information while in some examples, the patient-specific average respiratory cycle is determined according to long term data gathered for that patient during reasonably stable respiration (e.g. normal breathing).

In some examples, the respiratory cycle duration parameter **260** tracks a duration of the sensed respiratory cycles of a patient and determines an average.

In some examples, the time unit parameter **262** tracks and controls a number of time units by which a stimulation cycle operates. In some examples, the time unit parameter **262** implements time units as a multiple of some natural time unit associated with a respiratory waveform. For instance, in some examples such as the stimulation protocols described and illustrated in association with FIGS. **3**B-**3**E, the time unit parameter **262** equates six time units with a duration of a respiratory cycle, and in which an inspiratory phase comprises one-third of the entire respiratory cycle. However, it will be understood that in some examples, the time units (per parameter **262**) are unit-less. For instance, suppose the respiratory period has a duration R of five seconds, and a convention has been adopted that the respiratory cycle is divisible into six time units. Then, the six time units would be distributed across the five second duration of the respiratory cycle.

In some examples, the time unit parameter **262** implements time units which are entirely arbitrary relative to one or more natural time units associated with a respiratory waveform. For instance, in some examples such as the stimulation protocol described and illustrated in association with FIG. **16**A, the time unit parameter **262** equates eight time units with a duration of a respiratory cycle, and in which an inspiratory phase comprises one-third of the entire respiratory cycle.

In some examples, the time frame parameter **270** in FIG. **4** identifies a respiratory cycle series parameter **272** and a stimulation cycle parameter **274**. The respiratory cycle series parameter **272** identifies and tracks the number of respiratory cycles that occur before a particular portion of a particular stimulation cycle (**274**) would coincide again with a particular portion of a respiratory cycle. For example, it was previously noted in association with at least FIG. **3**C that the stimulation protocol **220** operated based on a time frame of seven respiratory cycles such that a sequence of seven respiratory cycles would occur before a beginning of a stimulation period of a stimulation cycle would coincide with a beginning of an inspiratory phase of the repeating respiratory cycle. While the stimulation protocols associated with independent stimulation function **14** (FIG. **1**A) are not synchronized relative to characteristics (e.g. inspiratory phase) of a sensed respiratory waveform, the time frame parameter **270** enables tracking and adjusting how a given stimulation protocol is juxtaposed relative to sensed patient respiratory behavior.

FIG. **5** is a block diagram of a stimulation protocol element **280**, according to one example of the present disclosure. As shown in FIG. **5**, the stimulation protocol element **280** comprises an array parameter **282**, a rotation

parameter **284**, an automatic parameter **286**, a manual parameter **288**, a static parameter **290**, and a custom parameter **291**.

In some examples, stimulation protocol element **280** includes at least some of substantially the same features and attributes as stimulation protocol element **12**, as previously described in association with at least FIGS. **1**-**4**. In particular, as previously noted, in some examples the independent stimulation function **14** (FIG. **1**A) provides at least one stimulation protocol suitable for delivering electrical stimulation to a nerve of a patient, such as one of the stimulation protocols as previously described and illustrated in association with FIGS. **3**B-**3**E.

With this in mind, array parameter **282** of stimulation protocol element **280** provides an array of stimulation protocols that can be applied, such as but not limited to those illustrated in association with FIGS. **3**B-**3**E.

In some examples, via a rotation parameter **284**, the stimulation protocol **280** enables delivering therapeutic nerve stimulation to a patient while rotating through different stimulation protocols available via array parameter **282**. In some examples, such rotation enables identifying a stimulation protocol that works best for a particular patient on a particular day or on a long term basis. However, in some examples, rotation through different stimulation protocols is maintained for a particular day or on a long term basis to provide a large degree of variability in the overall stimulation pattern to thereby provide a robust therapy regimen when a patient's respiratory behavior is consistently erratic and/or when sensing of a patient's respiratory behavior is consistently problematic.

In some examples, in cooperation with an automatic parameter **286**, the rotation parameter **284** automatically rotates through the different stimulation protocols to achieve goals set by therapy manager **16** (FIG. **1**B). In some examples, via automatic parameter **286**, the therapy manager **16** (FIG. **1**B) automatically selects at least one stimulation protocol suitable for a particular patient. In some examples, the automatic selection of which stimulation protocol(s) is best suited for a particular patient is based on a sensed respiratory waveform of the patient.

In some examples, via a static parameter **290** shown in FIG. **5**, therapy manager **16** (FIG. **1**B) enables selecting and then maintaining a single stimulation protocol indefinitely until and unless a user or operator selects a different stimulation protocol or parameters affecting the selected stimulation protocol. In some examples, if a particularly effective stimulation protocol is identified during operation of the rotation parameter **284**, the therapy manager **16** (FIG. **1**B) deactivates automatic rotation of the stimulation protocols and operates that single, "particularly effective" stimulation protocol, per the static parameter **290**.

In some examples, stimulation protocol element **280** includes custom parameter **291**, which enables adjusting a selected stimulation protocol or making a custom stimulation protocol by selecting a duration of respiratory cycle, duration of stimulation period(s), duration of non-stimulation periods, duration of stimulation cycle, and/or other parameters identified in the plurality of stimulation parameters **250** (FIG. **4**).

In some examples, the range of stimulation protocols available to a patient via stimulation protocol element **280** are selected and/or bounded according to the discretion of a physician or physician programmer.

FIG. **6** is a block diagram of a power element **320**, according to one example of the present disclosure. In one example, power element **320** represents IPG **35**, **50** (FIGS. **2**A-**2**B) as having an external power source **322** and/or an on-board power source **324**.

In some examples, an at least partially implantable stimulation system (according to examples of the present disclosure) operates in cooperation with and/or incorporates sensing functionality. With this in mind, in some examples, such systems include a sensing element **330**, according to one example of the present disclosure, as shown in FIG. **7**A. The sensing element receives and/or obtains respiratory information.

In some examples, the sensing element **330** includes an on-board sensing element **332**, which is physically incorporated into IPG **35** (FIG. **2**A) or IPG **50** (FIG. **2**B) in some manner such that communication between the on-board sensing element **332** and other elements of the IPG **35**, **50** will occur within the case or housing of the IPG. In some examples, the on-board sensing element **332** includes internal components, such as an accelerometer and in some examples, the on-board sensing element **332** includes surface components, such as the external surface of the case or housing of the IPG **35**, **50** acting as a sensing element alone or in combination with other sensing elements.

In some examples, the sensing element **330** includes an implanted sensing input **334** to receive signals from a sensor implanted within the body physically separate from the IPG **35**, **50**, with the sensing input **334** in communication with and/or connected to the IPG **35**, **50** via wired or wireless communication pathways.

In some examples, the sensing element **330** includes an external sensing input **336** to receive signals from a sensor external to the patient's body, with the sensing input **336** in communication with the IPG **35**, **50** via wireless communication pathways.

In some examples, sensing element **330** does not comprise a physically-embodied sensor but rather a sensing input to receive information sensed via sensors separate from, and independent of, sensing element **330** with such sensors in communication with sensing element **330**.

In some examples, sensing element **330** can comprise both a sensing input and a physically-embodied sensor.

Via these various sensing elements and inputs, the sensing element **330** receives and tracks signals from at least one physiologic sensor in order to gather information pertinent to treating sleep disordered breathing. In some examples, this information includes respiratory information such as, but not limited to, determining a respiratory state of a patient, whether or not the patient is asleep or awake, and other respiratory-associated indicators, etc. In some examples, the type of sensed physiologic information received by, and/or the type of physiologic sensors embodied within, one of the sensing elements/inputs **332**, **334**, **336** (FIG. **7**A) include, but are not limited to, a pressure sensing, blood oxygenation sensing, acoustic sensing, posture sensing, motion/activity sensing, differential pressure sensing, electrocardiogram (ECG) sensing, or impedance sensing. Via such sensing modalities, the system can measure thoracic impedance, respiratory pressure, diaphragm-based parameters, electrocardiac monitoring, airflow monitoring, snoring, etc. Gathering of this respiratory information, including information regarding respiratory-related behaviors, may be implemented via either a single sensor or any combination of various physiologic sensors that can provide a reliable and accurate signal. In some examples, these various measures of respiratory-related behavior can be considered alone or together in combination to indicate

respiratory effort, which is at least one type of respiratory information receivable and/or obtainable by the sensing element.

In some examples, the therapy manager **16** (FIG. **1**B) maintains the sensing components of the sensing element **330** in a default, dormant mode (i.e. off or low power) and periodically activates one or more of the available sensing element(s) to gather patient data. After gathering the data, the sensing elements are deactivated, thereby resuming their dormant mode. In some examples, the gathered patient data is used to evaluate the effectiveness of the therapy, such as the number, intensity, and/or frequency of apneas occurring. After such data gathering, the therapy manager **16** (FIG. **1**B) deactivates the sensing element(s), thereby returning them to a dormant mode.

In some examples, the gathered patient data is used to measure the respiratory period to verify its duration and to determine or verify the relative durations (or absolute duration) of the inspiratory and expiratory phases. This information is used to assess a current stimulation protocol and potentially determine whether adjustments to the stimulation protocol are warranted or whether a different stimulation protocol should be employed. For instance, in some examples, the gathered patient data from the temporarily activated sensing elements is used to calibrate the reference respiratory cycle associated with implementation of a particular stimulation protocol.

FIG. **7**B is a schematic diagram of an at least partially implantable stimulation system **340**, according to an example of the present disclosure. In one example, the system **340** includes at least some of substantially the same features and attributes as system **20** (previously described in association with at least FIG. **2**A), except further including sensing functionality via at least one sensing element to sense respiratory information. In some examples, this sensing functionality is implemented via sensing element **330** (FIG. **7**A).

In some examples, the system **340** comprises an additional lead **137** including at least one sensor portion **341** (electrically coupled to the IPG **35** and extending from the IPG **35**) positioned in the patient **22** for sensing respiratory information, such as respiratory effort, respiratory pressure, etc. In some examples, this information includes identifying and tracking characteristics and parameters of sensed respiratory waveforms.

In some examples, the sensor portion **341** is a pressure sensor. In one example, the pressure sensor detects pressure in the thorax of the patient. In some examples, the sensed pressure could be a combination of thoracic pressure and cardiac pressure (e.g., blood flow). Via sensor portion **341**, therapy manager **16** (FIG. **1**B) is configured to analyze this pressure sensing information to identify, track, and evaluate the respiratory patterns of the patient.

In some examples, the respiratory sensor portion **341** comprises a bio-impedance sensor or forms one of a pair of bio-impedance sensors. In some examples, the respiratory sensor portion **341** is located in regions other than the pectoral region. In some examples, the sensor portion **341** is used to sense impedance in cooperation with other electrodes (e.g. a stimulation electrode) or with an electrically conductive exterior housing of the IPG **35**, **50** (FIGS. **2**A-**2**B, **7**B). In some examples, as shown in FIG. **7**B, additional sensors **347**, **348**, **349** are distributed about the chest area for measuring a trans-thoracic bio-impedance signal, an electrocardiogram (ECG) signal, or other respiratory-associated signals. In some examples, sensor portion **341** is omitted and sensors **347**, **348**, **349** are implemented.

In some examples, the system **340** for treating obstructive sleep apnea is a totally implantable system which provides therapeutic solutions for patients diagnosed with obstructive sleep apnea. However, as identified in various examples, in some examples, the system is partially implantable with some components (e.g. power source, sensing elements, or control circuitry) being at least partially or completely external to the patient's body.

In some examples, the previously-described at least partially implantable system **80** (FIG. **2**D) includes at least some of substantially the same features described and illustrated in association with FIGS. **4**-**7**B, except for system **80** having a non-pectoral location and those attributes specific to system **80** as described in association with FIG. **2**D.

In some examples, the respiratory information and/or other physiologic information gathered via the sensing element **330** (FIG. **7**A) and associated sensor schemes (FIG. **7**B) is used to identify, track, evaluate, etc. various therapeutic parameters. Accordingly, in some examples the at least partially implantable stimulation system includes a therapeutic monitoring element **350**, which as shown in FIG. **8**, includes a plurality of therapeutic parameters. In some examples, these parameters include identifying, tracking, and evaluating apnea events per parameter **352** and/or computing and tracking an apnea severity index **354**, such as AHI or other index. The index parameter **354** determines a frequency, intensity, duration, etc. of detected apneas to indicate the relative severity of sleep disordered breathing for the patient.

In some examples, one therapeutic parameter of monitoring element **350** includes a minute ventilation parameter **356** to track minute ventilation of the patient before, during, or after a therapy regimen. In some examples, one therapeutic parameter of monitoring element **350** includes a tidal volume parameter **357** to track the tidal volume of a patient before, during, or after a therapy regimen.

In some examples, one therapeutic parameter of monitoring element **350** includes a body position parameter **358**. In some examples, one therapeutic parameter of monitoring element **350** includes a posture parameter **359**. Together or separately, the body position parameter **358** and posture parameter **359** determine and track a body position of the patient and posture of the patient. Among other uses, such information can be used to activate or deactivate a therapy, to select a therapeutic regimen (e.g. stimulation protocol), and/or to adjust a therapeutic regimen. It will be understood that these example parameters are not exhaustive and can be employed separately from each other or in various combinations.

In some examples, this information obtained via any one or several parameters **352**, **354**, **356**, **357**, **358**, **359** of the therapeutic monitoring element **350** is used to initiate, terminate, select, and/or adjust stimulation applied via the IPG **35**, **50** and stimulation electrode **45**. For instance, upon determining that the number and/or intensity of apneic events has met or exceeded a severity threshold, the therapy manager **16** (FIG. **1**B) can utilize control portion **56** (FIG. **2**C) to initiate application of stimulation to the airway-patency related nerves to open the airway and thereby reduce the associated sleep disordered breathing behavior. However, it will be understood that in at least some examples, this arrangement does not include causing (or depend on) the stimulation signal to become synchronized relative to a characteristic (e.g. inspiratory phase, expiratory phase, etc.) of the respiratory waveform. Rather, as noted in association with at least FIG. **1**A, in the examples described

thus far in association with FIGS. **1-8**, such stimulation is applied independent of such synchronization.

In some examples, the therapeutic parameters element **350** may be employed to select one of a plurality of stimulation protocols and/or to evaluate the therapeutic effectiveness of a particular stimulation protocol(s) for a particular patient for a given period of time or on a long term basis.

In at least this context and/or other contexts in at least some examples of the present disclosure, therapeutic effectiveness may correspond to alleviating sleep disordered breathing, which in some instances is measurable via a severity threshold, such as an apnea-hypopnea index (AHI) and/or other scoring mechanisms. In some examples, the therapeutic effectiveness may also be measured or evaluated relative to sensor signal quality, such as via sensor signal quality criteria as described in at least some of the examples of the present disclosure.

FIG. **9** is a block diagram schematically illustrating a control portion **360**, according to one example of the present disclosure. In some examples, control portion **360** includes a controller **362** and memory **370**. In some examples, therapy manager **371** is stored in memory **370**, and in some examples, therapy manager **371** includes at least some of substantially the same features and attributes as therapy manager **16** (FIG. **1**B), as previously described in association with at least FIGS. **1-8**.

In general terms, controller **362** of control portion **360** comprises at least one processor **364** and associated memories that are in communication with memory **370** to generate control signals to direct operation of at least some components of the systems and components described throughout the present disclosure. In some examples, these generated control signals include, but are not limited to, employing therapy manager **371** to manage operation of the stimulation system to control sleep disordered breathing. In some examples, a control portion **360** is present in the IPG **35**, **50**, **84** (FIGS. **2**A, **2**B, **2**D) as control portion **56** (FIG. **2**C) and/or is accessible to the IPG **35**, **50**, **84**. In some examples, at least some aspects of stimulation element **12** (FIG. **1**A) are at least partially implemented via control portion **360** and/or in communication with control portion **360**, with at least some aspects of stimulation element **12** being storable in memory **370** with or as part of therapy manager **371**.

In particular, in response to or based upon commands received via a user interface **396**, **400** (FIGS. **11**A, **11**B) and/or machine readable instructions (including software), controller **362** generates control signals to implement a nerve stimulation protocol to control sleep disordered breathing, in accordance with at least some of the previously described examples and/or later described examples of the present disclosure. In some examples, controller **362** is embodied in a general purpose computer while in other examples, controller **362** is embodied in at least some of the components described throughout the present disclosure, such as IPG **35**, **50**, **84** or external components operatively coupled to implantable pulse generator **35**, **50**, **84**. For purposes of this application, in reference to the controller **362**, the term "processor" shall mean a presently developed or future developed processor (or processing resources) that executes sequences of machine readable instructions contained in a memory. In some examples, execution of the sequences of machine readable instructions, such as those provided via therapy manager **371** stored in memory **370** of control portion **360**, cause the processor to perform actions, such as operating controller **362** to implement stimulation protocols as generally described in (or consistent with) at least some examples of the present disclosure. The machine readable instructions may be loaded in a random access memory (RAM) for execution by the processor from their stored location in a read only memory (ROM), a mass storage device, or some other persistent storage (e.g., non-transitory tangible medium or non-volatile tangible medium), as represented by memory **370**. In some examples, memory **370** comprises a computer readable tangible medium providing non-volatile storage of the machine readable instructions executable by a process of controller **362**. In other examples, hard wired circuitry may be used in place of or in combination with machine readable instructions to implement the functions described. For example, controller **362** may be embodied as part of at least one application-specific integrated circuit (ASIC). In at least some examples, the controller **362** is not limited to any specific combination of hardware circuitry and machine readable instructions, nor limited to any particular source for the machine readable instructions executed by the controller **362**.

In some examples, user interface **396** shown in FIG. **11**A comprises a user interface or other display that provides for the simultaneous display, activation, and/or operation of at least some of the various components, functions, features, and of stimulation element **12** (FIG. **1**A), therapy manager **16** (FIG. **1**B), control portion **360** (FIG. **9**), IPG **35**, **50**, **84** (FIGS. **2**A, **2**B, **2**D), and related elements, as described throughout the present disclosure. In some examples, at least some portions or aspects of the user interface **396** are provided via a graphical user interface (GUI) and may include an input and a display.

In some examples, user interface **396** includes at least some of the components illustrated in user interface **400** schematically depicted in FIG. **11**B.

As shown in FIG. **11**B, user interface **400** includes at least some of the various components, functions, elements, and features as described and illustrated in association with at least stimulation protocol elements **280** (FIG. **5**), **490** (FIG. **15**A), therapeutic monitoring element **350** (FIG. **8**), stimulation parameters **250** (FIG. **4**), stimulation protocol element **450** (including independent function **454**, respiratory-dependent function **456** in FIG. **12**), automatic protocol selector **470** (FIG. **14**), and stimulation protocol selection **500** (FIG. **15**B).

FIG. **10** is a diagram **380** schematically illustrating a manner in which the control portion **360** is implemented, according to one example of the present disclosure. In some examples, control portion **360** is entirely implemented within or by an implantable pulse generator **385**, which has at least some of substantially the same features and attributes as pulse generator (IPG) **35**, **50**, **84** as previously described in association with at least FIGS. **1-9**. In some examples, control portion **360** is entirely implemented within or by a remote control **390** (e.g. a programmer) external to the patient's body, such as a patient control **392** and/or a physician control **394**. In some examples, the control portion **360** is partially implemented in the pulse generator **385** and partially implemented in the remote control **390** (at least one of patient control **392** and physician control **394**).

In some examples, in association with control portion **360**, user interface (**396** in FIG. **11**A; **400** in FIG. **11**B) is implemented in remote control **390**.

FIG. **12** is a block diagram of a stimulation protocol element **450**, according to one example of the present disclosure. As shown in FIG. **12**, stimulation protocol element **450** includes an independent stimulation function **454** and a respiratory-dependent function **456**. In some examples, the independent stimulation function **454** includes

at least some of substantially the same features as independent stimulation function **14** associated with stimulation element **12** (FIG. **1**A) and/or therapy manager **16** (FIG. **1**B) as part of an at least partially implantable stimulation system, as previously described in association with FIGS. **1**-**11**B. Meanwhile, FIG. **13** is a block diagram of a respiration-dependent function **456**, according to one example of the present disclosure.

After describing the features and attributes associated with the respiration-dependent stimulation function **456**, at least some examples regarding the relationship and relative operation of the independent stimulation function **454** and respiratory-dependent stimulation function **456** will be addressed.

As shown in FIG. **13**, in some examples, the respiratory-dependent function **456** includes a synchronous parameter **460**, a synchronization characteristic parameter **462**, and a stability parameter **464**.

In some examples, via the synchronous parameter **460**, respiratory-dependent function **456** implements a stimulation protocol in which each individual nerve stimulation period (within a treatment period) is triggered by and/or synchronized relative to a synchronization characteristic of the patient's respiratory waveform. For instance, in some examples, respiratory-dependent function **456** causes individual stimulation periods to occur substantially simultaneous with the inspiratory phase (e.g. **162** in FIG. **3**B) of the patient's respiratory cycle (e.g. **204**A in FIG. **3**B) such that stimulation is considered to be synchronous with inspiration.

In some examples, per synchronization characteristic parameter **462**, one can select (or a therapy manager can automatically select) the characteristic to which stimulation will be synchronized. In some examples, via parameter **462** respiratory-dependent stimulation function **456** causes nerve stimulation periods to be synchronized relative to a junction or transition between expiratory pause and the onset of inspiration. In some examples, via parameter **462**, nerve stimulation periods are synchronized relative to a junction or transition between inspiration and the onset (i.e. beginning) of expiration. In some examples, the characteristic to which stimulation will be synchronized can be peak inspiration, peak expiration, or expiratory pause.

In some examples, stability parameter **464** of respiratory-dependent stimulation function **456** (FIG. **13**) tracks and determines at least one parameter of a sensed respiratory waveform to determine the relative stability of the respiratory waveform (e.g. sensor signal quality) to provide a reliable, accurate indication of respiratory behavior to the therapy manager (**371** in FIG. **9**). Without a reasonably stable respiratory waveform, the respiratory-dependent function **456** cannot be implemented. In such a situation, the independent stimulation function **454** is implemented until the control portion **360** determines via stability parameter **464** that a reasonably stable respiratory waveform is available (e.g. the sensor signal has sufficient quality) and by which stimulation can be triggered and/or synchronized relative to a characteristic of the respiratory waveform.

Via the stability parameter **464**, the control portion **56** of FIG. **2**C (control portion **360** in FIG. **9**) determines whether the respiratory waveform is stable enough (e.g. sensor signal quality is sufficient) to support synchronizing stimulation relative to characteristics (e.g. inspiratory phase) of the respiratory waveform. In some examples, the stability parameter **464** identifies and tracks parameters such as a peak-to-peak amplitude, a respiratory rate, sensor signal frequency content, signal morphology, and a duty cycle associated with at least one of inspiration, expiration, and expiratory pause, or various combinations of these parameters. In some examples, the at least one parameter comprises a statistical stability of these identified parameters. In some examples, a determination of such statistical stability may be performed relative to a known good state for the patient or a moving baseline of known good state for the patient. In some examples, a known good state corresponds to a period of respiration free from obstructive sleep apnea. In some examples, the determination of statistical stability may be performed relative to an independent threshold of statistical goodness.

In some examples, the inspiratory duty cycle is defined as the ratio of inspiration duration to the duration of respiratory period.

In some examples, the above-noted waveform signal stability or quality parameter may be evaluated after sufficient gain is applied to the signal to enable analysis. For instance, if the peak to peak amplitude is low and sensor signal quality is low, then signal gain can be increased to determine if signal quality analysis can be performed. In some examples, a sensed signal can be subject to a process in which a sensor obtains a physiologic signal, to which gain is applied prior to quality analysis, and then potentially used for synchronization of a stimulation protocol relative to the sensed respiratory waveform. In some examples, an automatic gain control mechanism is employed and queried to determine if the gain is stable so the signal may be reliably analyzed.

In some examples, via therapy manager **16**, **371** (FIGS. **1**B, **9**), the respiratory-dependent stimulation function **456** can be disabled so that therapy is selectively applied entirely via the independent stimulation function **14** (FIG. **2**A), **454** (FIG. **12**). Of course, in some examples as previously described, the respiratory-dependent stimulation function **456** is not even present with the independent stimulation function **14**, **454** being the sole mechanism to apply nerve stimulation.

FIG. **14** is a diagram **470** schematically illustrating a relationship between, and automatically selection between, the independent stimulation protocol **454** (FIG. **12**) and the respiration-dependent stimulation protocol **456** (FIG. **12**), according to one example of the present disclosure. In some examples, at least some aspects of stimulation protocol selection in diagram **470** can be embodied as a method while in some examples, at least some aspects of stimulation protocol selection in diagram **470** can be embodied as operational aspects of a stimulation protocol manager of a therapy manager, as described in association with at least FIGS. **11**B-**13**.

In some examples, operation of the at least partially implantable stimulation system is implemented via providing cooperation or complementary deployment of the respective stimulation protocols **454**, **456**. In some examples, an independent stimulation protocol **454** is applied for a predetermined period of time, as shown at **472** in FIG. **14**. The predetermined period of time corresponds at least to an amount of time for a stable respiration period to be established, which may be ensured based on the independent stimulation of the airway-patency-related nerve. In some examples the first predetermined period of time corresponds to a period sufficient to establish a steady state in which filtering is established, inspiration and expiration are being detected reliably, signal gain control is realized, etc.

In some examples, operation of the first independent stimulation protocol during at least the first predetermined period of time is not a test mode, such as a mode that may otherwise be dedicated to diagnosing or evaluating the

operational fitness of the stimulation system. Rather, the first independent stimulation protocol operates for at least the predetermined period of time to apply therapeutic stimulation to achieve a stable respiratory behavior and a stable respiratory waveform.

In some examples, by applying stimulation protocol(s) via the independent stimulation, a stable respiratory waveform is achieved, thereby increasing the likelihood of being able to transition to operation in the respiratory-dependent stimulation at **478** than if independent stimulation at **472** were not deployed prior to the activation of the respiratory-dependent function at **478**.

With further reference to FIG. **14**, based on monitoring of the sensed respiratory waveform, at repeating intervals, at **474** it is queried whether the respiratory waveform is sufficiently stable to support activation of the respiratory-dependent stimulation. If the answer to the query at **474** is NO, then pathway **476** directs continued operation of independent stimulation at **472**. However, if the answer to the query at **474** is YES, then pathway **477** directs initiation of operation of respiratory-dependent stimulation at **478** of FIG. **14**. During operation of respiratory-dependent stimulation at **478**, the query at **474** is periodically implemented via pathway **479**. If the answer to the query (at **474**) is NO, then operation in respiratory-dependent stimulation n (**456** in FIG. **12**) at **478** in FIG. **14** is terminated as operation is returned (i.e. reverts) via pathway **476** to independent stimulation at **472** in FIG. **14** for at least the predetermined period of time.

For at least the current example, it will be understood that, in the event that no stable respiratory waveform is established, the operation would remain in independent stimulation at **472** without converting to operation in respiratory-dependent stimulation **478**.

In some examples, the query at **474** is performed generally continuously by monitoring parameters indicative of respiratory signal sensing quality (i.e. sensor signal quality criteria), such as but not limited to, peak to peak amplitude, inspiratory duty cycle, respiratory rate, etc. Upon one or more of these parameters failing to meet the sensor signal quality criteria, then the answer to the query (at **474**) would be registered as NO. Upon meeting the sensor signal quality criteria, the answer to the query at **474** is YES.

In some examples, meeting the signal quality criteria (e.g. answer to query is YES) can be defined via a first parameter as an average peak-to-peak respiratory amplitude above a threshold, where the average is computed from the previous two respiratory cycles. In some examples, meeting the signal quality criteria (e.g. answer to query is YES) can be defined via a second parameter as a peak-to-peak respiratory amplitude variability below a threshold, where the threshold is referenced to an average computed over the previous 60 seconds. In some examples, meeting the signal quality criteria (e.g. answer to query is YES) can be defined via a third parameter as a respiratory duration variability below a threshold, where threshold is reference to an average computed of the previous 60 seconds. In some examples, meeting the signal quality criteria (e.g. answer to query is YES) can be defined via a fourth parameter as an average inspiratory phase duration above a threshold, where the average is computed of the previous two respiratory cycles. In some examples, meeting the signal quality criteria (e.g. answer to query is YES) can be defined via various combinations of the respective first, second, third, and fourth parameters, including but not limited to, a combination of all four parameters. It will be understood that the sensor signal quality criteria and/or meeting the sensor signal quality criteria is not exclusively defined by the respective four parameters.

FIG. **15**A is block diagram of a stimulation protocol element **490**, according to one example of the present disclosure. In some examples, stimulation protocol element **490** includes at least some of substantially the same features and attributes as stimulation protocol element **450** as previously described in association with at least FIGS. **12-14**, while further including at least the features shown in FIG. **15**A.

As shown in FIG. **15**A, stimulation protocol element **490** includes an override function **492** to take abrupt and sustained action to achieve a stable respiratory pattern. For instance, in some examples, persistent sleep disordered breathing is observed, which includes a series of unresolvable/intractable respiratory events (e.g. persistent apnea) that occur despite stimulation via either the independent stimulation function **454** or the respiratory-dependent function **456**. In some examples, the override function **492** is activated when a stable respiratory pattern has not been detected for a predetermined period of time, such as 5 or 10 minutes. In some examples, the predetermined period of time is less than 5 minutes, such as when some number (e.g. 3 apneas) of apneas are detected prior to reaching 5 minutes.

Upon activation of the override function **492**, therapy that was being implemented via the independent stimulation function **454** or via the respiratory-dependent function **456** is terminated or converted over to operation via a continuous stimulation function **494** (FIG. **15**A) in which nerve stimulation is applied continuously (a 100% duty cycle) for a predetermined period of time. As previously described, in some examples, continuous stimulation refers to a train of stimulation pulses which occur in a relatively short time frame. For instance, in some examples, continuous stimulation corresponds to at least a finite number (e.g. 5, 10, etc.) of stimulation pulses per second. In some examples, continuous stimulation corresponds to at least 20 stimulation pulses per second. In some examples, continuous stimulation corresponds to at least 30 stimulation pulses per second. In some examples, the number of stimulation pulses per second is selectable by an operator via a control portion (e.g. **56** in FIG. **2**C). In some examples, during such continuous stimulation, each stimulation pulse within a train of stimulation pulses includes a primary stimulation pulse followed by a separate recharge pulse, which is in turn followed by a non-stimulation phase before the next primary stimulation pulse.

In some examples, the override function **492** is implemented via an "other" function, in which nerve stimulation is applied that is not continuous but which has an intensity and duration substantially greater than implemented via the stimulation protocols of one of the independent stimulation function **454** (FIG. **12**) or the respiratory-dependent function **456** (FIG. **12**).

In some examples, operation via the override function **492** is maintained until at least one of a time limit, and/or the therapy manager detecting (via the sensed respiratory waveform) at least one respiratory cycle exhibiting an absence of sleep disordered breathing behavior as measured by a number of respiratory cycles and/or a severity threshold (in one example). In some examples, the time limit is 100 seconds, such as about 20 breaths. However, in some examples, the time limit can be much lower, such as 30 to 40 seconds. In some examples, the continuous stimulation is applied until detected sleep disordered breathing is absent for at least three consecutive respiratory cycles, i.e. a successful inspi-

ration occurs for at least three consecutive respiratory cycles or some operator-selectable quantity (e.g. 2, 4) of consecutive respiratory cycles for a particular patient.

In some examples, the continuous stimulation is applied up to a predetermined maximum period. In some examples, the predetermined maximum period is at least 120 seconds. In some examples, the predetermined maximum period is selectable by an operator and can have values greater or less than 120 seconds, such as 130 seconds, 110 seconds, 90 seconds, etc. In general terms, the predetermined maximum period corresponds to an expired time by which fatigue of the stimulated muscle is complete or nearly complete.

In some examples, upon a determination that detected sleep disordered breathing behavior meets or exceeds the severity threshold, the therapy manager terminates operation in the respective independent and respiratory-dependent stimulation modes and initiates operation in a third mode including a stimulation protocol of a stimulation period and a non-stimulation period in a proportion of at least 3 to 1 wherein the stimulation period has a duration equal to or greater than a duration of at least four respiratory cycles.

In some examples, the duration of the stimulation period is about 30 seconds and the duration of the non-stimulation period is about 10 seconds. In some examples, the duration of the stimulation period is about 30 seconds and the duration of the non-stimulation period is about 5 seconds.

Upon determination that a stable respiratory period has been established, operation in the override function **492** terminates and operation is resumed via the independent stimulation function **454** (FIG. **12**) consistent with the functionality previously described in association with at least FIGS. **12-14**.

FIG. **15**B is a diagram **500** schematically illustrating aspects of selecting a stimulation protocol **501**, according to one example of the present disclosure. In some examples, at least some aspects of selecting a stimulation protocol as expressed in diagram **500** can be embodied as a method while in some examples, at least some aspects of selecting a stimulation protocol as expressed in diagram **500** can be embodied as operational aspects of a stimulation protocol management associated with a therapy manager **16** as described in association with at least FIGS. **1-15**A.

As shown at **502**, respiratory information can be periodically sensed during a treatment period and without synchronization to stimulation. In other words, in at least some instances, this periodic sensing is not related to and/or does not result in synchronizing stimulation to sensed respiratory information. Rather, such periodic sensing can be used to enhance and/or evaluate the effectiveness of the stimulation, among other uses for such periodically sensed respiratory information.

As shown at **504** in FIG. **15**B, if the duration of the sensed respiratory cycles (among a sample of respiratory cycles) is less variable from cycle-to-cycle than a duration variability criteria, then a stimulation protocol is adopted in which a repeating stimulation cycle is applied and which has a duration different than a duration of the reference respiratory cycle for this patient. This arrangement introduces an intentional stagger or offset between the duration of the stimulation cycle and the duration of respiratory cycle, which may ensure overlap of at least some stimulation periods (of the stimulation cycles) with the actual inspiratory phases of the respiratory cycles of the patient a majority of the time.

In some examples, the duration variability criteria establishes a measure of the variability of a duration of sensed respiratory cycles. The variability can be measured by a frequency of changes in the duration during an observation period and/or a magnitude of change in such durations during the observation period. Further details regarding the observation period are identified below.

In some examples, the duration variability criteria is based on several factors, including but not limited to, a duration of a typical stable respiratory period (e.g. 3-6 seconds, depending on the patient), the minimum duration of an apnea (e.g. 10 seconds), and/or an observation period (e.g. 5 minutes) following a change in stimulation parameters. In some examples, the observation period can more than 5 minutes while in some examples, the observation period can be less than 5 minutes, such as when some number (e.g. 3 apneas) of apneas are detected prior to reaching 5 minutes. In some examples, the duration variability criteria is further based on a standard deviation of respiratory periods of less than 1 second and a sample period of at least 4 minutes.

With further reference to **504** in FIG. **15**B, in some examples, this arrangement is implemented via stimulation protocol **210** in FIG. **3**B in which a respiratory waveform is represented via a series **202** of respiratory cycles **204**A-**204**H. Moreover, in this example, the duration of the stimulation cycle (4 stimulation periods plus 1 non-stimulation period) is less than a duration (R) of the reference respiratory cycles, such that the repeating stimulation cycle has a duration different than a duration (R) of the reference respiratory cycle.

This arrangement ensures that no matter when the stimulation protocol is generally activated, no more than a finite number (e.g. 2, 3, 4) of respiratory cycles would occur without a stimulation period significantly coinciding with an inspiratory phase **162** of the respective respiratory phases. This phenomenon occurs, at least in part, because of a sufficiently large difference between the duration of the stimulation cycle and the duration of the respiratory cycle, and in view of the relative proportion of the stimulation period to the non-stimulation period.

In some examples, other example stimulation protocols are used for implementation. For instance, example stimulation protocols **220**, **230** as described in association with at least FIGS. **3**C, **3**D can be used. It is noted that stimulation protocols **220**, **230** include stimulation cycles having a duration greater than a duration (R) of the reference respiratory cycle as shown in the respective legends **229**, **239** of FIGS. **3**C, **3**D, respectively.

As shown at **506** in FIG. **15**B, if the duration of the sensed respiratory cycle (of a sensed sample of respiratory cycles) is more variable than the duration variability criteria noted above, then a repeating stimulation cycle is applied and which has a duration generally matching a duration of a reference respiratory cycle. In this instance, the natural variability of the duration of the patient's respiratory cycle can be used to introduce a stagger or offset relative to the duration of the stimulation cycle, which may ensure an overlap of at least some stimulation periods relative to at least some of the inspiratory phases of the patient's live respiratory cycles at least a majority of the time.

In some examples, the reference respiratory cycle is defined by a patient-specific average respiratory cycle obtained at an earlier point in time. In some examples, the reference respiratory cycle is defined by a multi-patient specific average respiratory cycle obtained from a database.

In some examples, this arrangement is implemented via stimulation protocol **240** in FIG. **3**E in which a respiratory waveform is represented via a series **244** of respiratory cycles **245**A-**245**M. Accordingly, FIG. **3**E models the situation in which the duration (R**1**) of the respiratory cycles has

varied (relative to the duration R of its base/stable respiratory cycle) by more than a threshold. In some examples, the threshold includes R changing (increasing or decreasing) in duration by 5 percent. In this instance the duration R1 represents about an 8 percent change from the duration R because the respiratory cycles **245**A-**245**M have a duration R1 of 6½ time units whereas duration R is equal to 6 time units. It will be understood, of course, that other numeric values that are more or less than 5 percent can be used as the threshold.

While FIG. **3**E exhibits a duration R1 which remains constant at least for the illustrated series of respiratory cycles, it will be understood that duration R1 may have a different value (e.g. longer or shorter) in subsequent respiratory cycles and/or that duration R1 may have had different values (e.g. longer or shorter) in preceding respiratory cycles. Accordingly, at least with respect to the method of FIG. **15**B, duration R1 should not be viewed as being indefinitely static, but rather as having a particular value at one snapshot in time.

It will be further understood that variations in the duration of the respiratory cycle may be exhibited as decreases (instead of increases) and that variations in the duration of the respiratory cycle are not permanent but may last some finite number of respiratory cycles before reverting to a baseline or changing to yet another non-R duration.

In the example of FIG. **3**E, the duration of the stimulation cycle (4 stimulation periods plus 2 non-stimulation periods) is less than a duration (R1) of the respiratory cycles but with the duration of the stimulation cycles being equal to the duration (R) of the reference respiratory cycle (which is based on a historical baseline in at least some examples).

With this arrangement, because the duration (R1) of the sampled respiratory cycle (obtained via periodic sensing) has varied relative to a reference duration R, the therapy manager **16** utilizes a stimulation cycle having a duration to match the duration of the reference respiratory cycle, which in turn introduces the above-mentioned intentional stagger or offset.

This arrangement ensures that no matter when the stimulation protocol is generally activated, no more than a finite number of respiratory cycles would occur without a stimulation period significantly coinciding with an inspiratory phase of the respective respiratory phases. This phenomenon occurs, at least in part, because of a sufficiently large difference between the duration of the stimulation cycle and the duration of the respiratory cycle, and in view of the relative proportion of the stimulation period to the non-stimulation period.

Accordingly, as represented at block **506**, when the duration of the periodically sensed respiratory cycle varies more than a duration variability criteria, the therapy manager ensures an appropriate level of stimulation coinciding with the inspiratory phases of the respiratory cycles by intentionally not adjusting the duration of the stimulation cycle to match the modified duration R1 exhibited by the periodically sensed respiratory cycles.

While FIG. **3**E exhibits a duration R1 which remains constant at least for the illustrated series of respiratory cycles, it will be understood that duration R1 may have a different value (e.g. longer or shorter) in subsequent respiratory cycles and/or that duration R1 may have had different values (e.g. longer or shorter) in at least some preceding respiratory cycles. Accordingly, at least with respect to the method of FIG. **15**B, duration R1 should not be viewed as being indefinitely static, but rather as having a particular value at one snapshot in time.

FIG. **15**C is a block diagram schematically illustrating a stimulation protocol selector element **520**, according to one example of the present disclosure. In some examples, the stimulation protocol selector element **520** includes, and enables, selection between a first function **522** and a second function **524**. In some examples, a selection via element **520** between first function **520** and second function **522** can be implemented in association with the aspects of block **502** in FIG. **15**B. In some examples, first function **520** can be implemented via at least some of the aspects of stimulation selection as described in association with block **504** in FIG. **15**B while second function **522** can be implemented via at least some of the aspects of stimulation selection as described in association with block **506** in FIG. **15**B.

FIG. **15**D is a diagram **550** schematically illustrating a relationship between, and automatically selection between, the independent stimulation protocol **454** (FIG. **12**) and the respiration-dependent stimulation protocol **456** (FIG. **12**), according to one example of the present disclosure. In some examples, at least some aspects of stimulation protocol selection **551** in diagram **550** can be embodied as a method while in some examples, at least some aspects of stimulation protocol selection in diagram **550** can be embodied as operational aspects of a stimulation protocol manager of a therapy manager, as described in association with at least FIGS. **11**B-**13**.

In some examples, operation of the at least partially implantable stimulation system is implemented via providing cooperation or complementary deployment of the respective stimulation protocols **454**, **456** (at least FIGS. **11**B-**13**). Accordingly, as shown at **552** in FIG. **15**D, operation starts in a respiratory-dependent stimulation protocol.

With further reference to FIG. **15**D, based on monitoring of the sensed respiratory waveform, at repeating intervals, at **554** it is queried whether the respiratory waveform is sufficiently stable to support continued operation of respiratory-dependent stimulation at **552**. If the answer to the query at **554** is YES, then pathway **556** affirms continued operation of respiratory-dependent stimulation at **552**. However, if the answer to the query at **554** is NO, then pathway **557** directs initiation of operation of independent stimulation at **558** of FIG. **15**D for at least a predetermined period of time. The first predetermined period of time is defined in substantially the same manner as previously described in association with at least FIG. **14**, and the operation of the independent stimulation function at **558** is not a test mode. Rather, the independent stimulation (at **558**) operates for at least the predetermined period of time to apply therapeutic stimulation to achieve a stable respiratory behavior and a stable respiratory waveform.

Upon operation of independent stimulation at **558** for at least the predetermined period of time, the query at **554** is periodically implemented via pathway **559**. If the answer to the query (at **554**) is YES, then operation in independent stimulation at **558** in FIG. **15**D is terminated as operation is returned via pathway **556** to respiratory-dependent stimulation at **552** in FIG. **15**D. For at least the current example, it will be understood that, in the event that no stable respiratory waveform is established, the operation would remain in the independent stimulation at **558** without reverting operation into respiratory-dependent stimulation at **552**.

In some examples, the query at **554** is performed by monitoring parameters indicative of respiratory signal sensing quality (i.e. sensor signal quality criteria), such as but not limited to, peak to peak amplitude, inspiratory duty cycle, respiratory rate, etc.

FIG. **16**A is diagram **640** schematically illustrating a nerve stimulation protocol **641**, according to one example of the present disclosure.

In one aspect, diagram **640** omits a representative respiratory waveform relative to the stimulation protocol because, in at least some examples, operation according to independent stimulation function **14** (FIG. **1**A) occurs regardless of whether a sensed respiratory waveform is available or reasonably stable. Accordingly, diagram **640** illustrates stimulation periods relative to predetermined time periods instead of relative to inspiratory and expiratory phases of a normal respiratory pattern, as further described and illustrated below.

As shown in FIG. **16**A, a nerve stimulation protocol **641** comprises stimulation segments **642** and non-stimulation segments **648**, **649** (i.e. rest periods), which may occur within a time frame (T). In this arrangement, the time frame T comprises a series of eight time units with each time unit having a duration t, as shown in FIG. **16**A. In some examples, a combination of two consecutive time units have a duration R that generally corresponds to a duration of a respiratory cycle. In one aspect, the duration of one time unit (t) comprises one-half of duration R.

As shown in diagram **640**, stimulation protocol **641** includes a repeating sequence of continuous stimulation segments **642** and non-stimulation segments **648**, **649**. Each stimulation segment **642** has a duration of 3 time units (t), each non-stimulation segment **648** has a duration of two time units, and each non-stimulation segment **649** has a duration of one time unit. This pattern is represented by legend **645** as 3:SK2:3:SK1, where SK represents "skip" to indicate skipping stimulation.

As further shown by diagram **640**, as this stimulation cycle pattern (3:SK 2:3:SK 1) is repeated through a series of time frames T (with each time frame T including 8 time units), one can identify the number of stimulation time units that occurs within each time frame T. For example, the first time frame includes 6 stimulation time units out of 8 total time units, followed by three time frames T including 5 stimulation time units out of 8 total time units, followed by two "six stimulation time unit" time frames T, and then three "five stimulation time unit" time frames T. With this in mind, one can express a pattern of the stimulation time units for the first twelve consecutive time frames as 6:5:5:5:6:6:5:5:5.

Via the stimulation protocol **641**, a therapeutic nerve stimulation regimen is applied in which no period of four consecutive respiratory cycles will transpire without a stimulation period coinciding with an expected inspiratory phase of a respiratory cycle. In this stimulation protocol, the duration of stimulation periods exceeds the duration of non-stimulation periods.

FIG. **16**B is a diagram **651** schematically illustrating a stimulation protocol **650**, according to one example of the present disclosure. In some examples, protocol **650** exhibits at least some of substantially the same features and attributes as the stimulation protocols, as previously described in association with at least FIGS. **3**B-**3**E. In general terms, via stimulation protocol **650**, via stimulation element **12** (FIG. **1**A) and/or therapy manager **16** (FIG. **1**B) the independent stimulation function **14** implements asynchronous nerve stimulation which to promote stable respiration despite potential sleep disordered breathing.

As illustrated in FIG. **16**B, the stimulation protocol **650** operates according to stimulation cycles in which the duration (D) of each stimulation cycle is less than the duration (R) of the reference respiratory cycles **654**A, **654**B. Moreover, in some examples, the stimulation cycle has a duration (D) which is significantly less (at least half or less) than the duration (R) of the reference respiratory cycles **654**A, **654**B. In one of these examples, a duration (D) of the stimulation cycle is less than 30 percent of the duration (R) of the reference respiratory cycles **654**A, **654**B. In one of these examples, a duration (D) of the stimulation cycle is less than 20 percent of the duration (R) of the reference respiratory cycle **654**A, **654**B. In one such instance, as illustrated in FIG. **16**B, the duration (D) of the stimulation cycle is about 1 second, whereas the duration (R) of the reference respiratory cycle is about 6 seconds.

In some examples of implementing stimulation protocol **650**, within a given stimulation cycle the stimulation period (e.g. **652**A, **652**B, etc.) and the non-stimulation period (e.g. **658**A, **658**B, etc.) are in a proportion of 4 to 1 to yield a stimulation duty cycle of 80 percent (for each stimulation cycle). In such examples, each stimulation cycle lasts about 1 time unit (t), including a continuous stimulation period of 4"⅕" time units followed by a non-stimulation period of a single "⅕" time unit, with this stimulation cycle being repeated continuously when nerve stimulation via stimulation protocol **650** is implemented. Accordingly, in some examples, the duration of the entire stimulation cycle (e.g. 4"⅕" time units of stimulation and a single "⅕" time unit of non-stimulation) is 1 time unit (t), which is significantly less than the duration R of the respiratory cycle, which is 6 time units in this example.

However, it will be understood that in some examples, the duration of the stimulation period need not coincide with a discrete number (e.g. 4) of fractional time units (e.g. "⅕" time units) and the duration of the non-stimulation period need not coincide with a discrete number (e.g. 1) of fractional time units (e.g. "⅕" time units).

In some examples, the duration (R) of the reference respiratory cycles (e.g. **654**A, **654**B, etc.) can be selected to be more or less than 6 time units (t), as shown in FIG. **16**B. In some examples, the duration (D) of each stimulation cycle (including a stimulation period, such as **652**A and a non-stimulation period, such as **658**A) can be selected to be more or less than one time unit (t).

In FIG. **16**B, the first end **653** of stimulation period **652**A is shown as coinciding with the beginning of an inspiratory phase **162** of the respiratory cycle **654**A. However, it will be understood that the beginning **653** of the stimulation period **652**A is not synchronized relative to the inspiratory phase **162**. Rather, the beginning **653** of stimulation period **652**A is shown as coinciding with the beginning of inspiratory phase **162** for illustrative simplicity in juxtaposing the stimulation protocol **650** relative to the reference respiratory cycles **654**A, **654**B, etc. Accordingly, it will be understood that when stimulation (according to stimulation protocol **650**) is initiated during a treatment period, the beginning of the stimulation period **652**A may coincide with a different portion of the reference respiratory cycle (e.g. **654**A) than shown in FIG. **16**B.

As further shown in FIG. **16**B, in one aspect, each respective non-stimulation period (e.g. **658**A, **658**B, etc.) has a duration significantly less than (e.g. at least less than half) a duration of each respective stimulation period (e.g. **652**A, **652**B, etc.). In one aspect, the duration of each stimulation period (e.g. **652**A, **652**B, etc.) is also significantly less than (e.g. at least less than 30%) a duration (R) of the respective reference respiratory cycles (e.g. **654**A, **654**B, etc.). In some examples, in stimulation protocol **650**, the duration (D) of each stimulation period (e.g. **652**A, **652**B, etc.) is significantly less than a duration (I) of the inspiratory phase **162** of an individual respiratory cycle (e.g.

654A) such that multiple, different stimulation periods occur during a single inspiratory phase **162**. Accordingly, with this arrangement, several stimulation cycles will be repeated within a single reference respiratory cycle.

In some examples, the relatively short duration of the stimulation cycle causes a successive stimulation period (e.g. **652**B) to begin at a different place within the inspiratory phase **162** of the reference respiratory cycle than prior stimulation period (e.g. **652**A), such that the stimulation pattern is considered to be independent of (i.e. not synchronized relative to) the characteristics of the respiratory cycle. Rather, the asynchronous nature of stimulation protocol **650** is further exhibited via the stimulation periods **652**C-**652**F occurring during the expiratory phase **170** of respiratory cycle **654**A because the same stimulation cycle is repeated regardless of where the stimulation periods falls relative to different portions of the reference respiratory cycle.

Accordingly, even though the stimulation is not synchronized relative to a characteristic (e.g. inspiration) of the respiratory waveform, no matter where the stimulation protocol **650** is started relative to a series of respiratory cycles, the short duration (D) of the stimulation cycle (relative to the longer duration R of the respiratory cycle) ensures that at least a portion of two stimulation periods (e.g. **652**A, **652**B) will significantly overlap (at least a majority) the inspiratory phase **162** of the respective reference respiratory cycles throughout the portion of the treatment period during which stimulation protocol **650** is applied.

In some examples, via therapy manager **16** (FIG. **1**B) a clinician can set a criteria how many respiratory cycles through which the stimulation protocol **650** will be applied before stimulation terminates and/or before a different stimulation protocol is implemented. In some examples, the criteria are based on a predetermined amount of time and/or a predetermined number of respiratory cycles for a particular patient.

It will be understood that each inspiratory phase **162** of each respiratory cycle (**204**A-**204**H) is shown in its ideal form in FIG. **3**B, and that in some instances where the inspiratory phase **162** at least partially coincides with one of the respective non-stimulation periods (e.g. **218**D), the inspiratory phase may sometimes have an irregular shape compared to the idealized shape shown in FIG. **3**B.

Accordingly, via stimulation protocol **650**, the independent stimulation function **14** of therapy manager **16** (FIG. **1**B) employs asynchronous nerve stimulation to achieve stable respiration despite potential sleep disordered breathing.

In some examples, the stimulation protocol **650** (and similar protocols described above) is implemented via the "other" function **496** (FIG. **15**A) of override function **492** to help overcome the type of persistent sleep-disordered breathing that does not become controlled via less intensive stimulation protocols. Accordingly, stimulation protocol **650** provides stimulation, which is not continuous but which has an intensity substantially greater than implemented via the stimulation protocols of one of the independent stimulation function **454** (FIG. **12**) or the respiratory-dependent function **456** (FIG. **12**), as previously illustrated in association with at least FIGS. **3**B-**3**E.

However, unlike a continuous stimulation pattern such as provided via continuous function **494** (FIG. **15**A) of override function **492**, stimulation protocol **650** regularly provides non-stimulation periods to enable the targeted nerve and/or muscle to rest somewhat among the stimulation periods, while still achieving an overall 80% stimulation duty cycle. In this arrangement, multiple stimulation periods can occur during each inspiratory phase of the repeating reference respiratory cycles such that no inspiratory phase occurs without stimulation occurring during at least a majority of any given inspiratory phase. In one aspect, such an arrangement may contribute to more favorable patient comfort or tolerance for the implementation of the "other" override function and/or contribute to diminishing any potential nerve or muscle fatigue.

In some examples, variations of stimulation protocol **650** are implemented in which the duration (D) of the stimulation cycle is significantly less than the duration (R) of the reference respiratory cycle, and the stimulation duty cycle is about 60 percent or 70 percent (instead of 80 percent). In such an arrangement, multiple stimulation periods can still occur during each inspiratory phase of the repeating reference respiratory cycles such that no inspiratory phase occurs without stimulation occurring during at least a majority of any given inspiratory phase, but with more non-stimulation available. In one aspect, such an arrangement may provide more comfort for some patients and/or potentially less muscle fatigue, as compared to the illustrated example stimulation protocol **650** having an 80% stimulation duty cycle (with relatively short duration stimulation cycles).

As with the other example stimulation protocols described herein, stimulation protocol **650** can be modified by an operator via the various parameters, functions, and components as previously described in association with at least FIGS. **4**-**5** can be selected and/or adjusted via a control portion (**56** in FIG. **2**C; **360** in FIG. **9**; **380** in FIG. **10**) in association with user interface (**396** in FIG. **11**A; **400** in FIG. **11**B).

FIG. **17**A is a flow diagram **700** of a method **701** of nerve stimulation to treat sleep disordered breathing, according to one example of the present disclosure. In some examples, method **701** is performed using the components, elements, systems, etc. previously described and illustrated in association with FIGS. **1**-**16**B. In some examples, method **701** is performed using components, elements, systems, etc. other than those previously described and illustrated in association with FIGS. **1**-**16**B.

As shown in FIG. **17**A, at **705** method **701** includes asynchronously stimulating an airway-patency-related nerve, according to a first stimulation protocol of stimulation cycles including a stimulation period and a non-stimulation period.

FIG. **17**B is a flow diagram **720** of a method **721** of nerve stimulation to treat sleep disordered breathing, according to one example of the present disclosure. In some examples, method **721** is performed using the components, elements, systems, etc. previously described and illustrated in association with FIGS. **1**-**16**B. In some examples, method **721** is performed using components, elements, systems, etc. other than those previously described and illustrated in association with FIGS. **1**-**16**B.

As shown in FIG. **17**B, in cooperation with the method **701** of FIG. **17**A, method **721** includes performing nerve stimulation via the therapy manager providing automatic convertible operation between the independent stimulation mode/function of FIG. **17**A and a second stimulation mode of stimulating the airway-patency-related nerve synchronous with a characteristic of the sensed respiratory waveform, as shown at **724**. With this arrangement, the therapy manager causes operation in the first mode for at least a first predetermined period of time (**726**) and converts operation into the second mode upon at least one parameter of the sensed respiratory waveform meeting a sensor signal quality criteria (**728**). Upon the at least one parameter of the sensed

respiratory waveform failing to meet the sensor signal quality criteria (**730**), operation reverts into the first mode for at least the first predetermined period of time In this example, the first mode acts as the default mode of operation.

In some examples, the sensor signal quality criteria is indicative of the system's ability to actually deliver stimulation at the targeted portion of the respiratory period with a high degree of confidence. In some examples the system may define an obstructive event (e.g. apnea/hypopnea) as lasting at least 10 seconds, then the above-mentioned high degree of confidence would correspond to not missing the target portion of the respiratory period twice in consecutive respiratory cycles.

In some examples, the sensor signal quality criteria can be indicative of a patient's real-time condition either in the absence of or in the presence of stimulation. In some examples, the sensor signal quality criteria can be indicative of sensor noise, thereby indicating how well the sensor signal correlates with the patient's real-time condition.

However, in some examples, the second mode can act as the default mode of operation. Accordingly, as shown in FIG. **17**C, in cooperation with the method **701** of FIG. **17**A, method **771** includes performing nerve stimulation via the therapy manager providing convertible operation between the independent stimulation mode/function of FIG. **17**A and a second stimulation mode of stimulating the airway-patency-related nerve synchronous with a characteristic of the sensed respiratory waveform, as shown at **774**. With this arrangement, the therapy manager causes operation in the second mode (**776**), and upon at least one parameter of the sensed respiratory waveform failing to meet a sensor signal quality criteria, operation converts into the first mode for at least a first predetermined period of time (**778**). At **780**, upon the at least one parameter of the sensed respiratory waveform meeting the sensor signal quality criteria, operation reverts back into the second mode.

In some examples, with respect to at least FIGS. **17**B and **17**C, the conversion between the first stimulation mode and the second stimulation mode is automatic.

With respect to selection of the first mode or the second mode in association with FIGS. **17**B and **17**C, in some examples a therapy manager **800** includes a default mode selector function **802** (as shown in FIG. **18**) to enable user selection of either the first mode or the second mode as a default mode. In some examples, the therapy manager **800** also comprises at least some of the features and attributes as therapy manager **16** (FIG. **1**B) and other examples of a therapy manager, as previously described in association with at least FIGS. **1**-**17**C.

With respect to selection of the first mode or the second mode in association with FIGS. **17**B and **17**C, in some examples a therapy manager **850** includes a manual conversion function **852** (as shown in FIG. **19**) to selectively cause conversion between the two different stimulation modes. In one aspect, such selective conversion can be implemented during operator titration of the therapeutic treatment as the operator adjusts parameters of the stimulation protocols for a particular patient. In some examples, the therapy manager **850** also comprises at least some of the features and attributes as therapy manager **16** (FIG. **1**B) and other examples of a therapy manager, as previously described in association with at least FIGS. **1**-**17**C. Accordingly, at least some examples of the present disclosure provide for a robust scheme to increase the effectiveness of nerve stimulation to treat sleep disordered breathing.

Although specific examples have been illustrated and described herein, it will be appreciated by those of ordinary skill in the art that a variety of alternate and/or equivalent implementations may be substituted for the specific examples shown and described without departing from the scope of the present disclosure. This application is intended to cover any adaptations or variations of the specific examples discussed herein.

What is claimed is:

1. A device for treating obstructive sleep apnea, comprising:

a non-cardiac stimulation element to engage and to stimulate an upper-airway-patency-related nerve, according to a first stimulation therapy protocol not synchronized relative to actively-sensed respiratory information, wherein the first stimulation therapy protocol comprises a series of repeating stimulation cycles in which each stimulation cycle includes a stimulation period and a non-stimulation period,

wherein each stimulation period includes continuous stimulation and has a minimum duration equal to or greater than an inspiratory reference of a reference respiratory cycle, wherein the inspiratory reference corresponds to a duration of an inspiratory phase of the reference respiratory cycle, and wherein the reference respiratory cycle comprises at least one of:

a historical patient-specific average respiratory cycle for stable respiration; and

a multi-patient average respiratory cycle for stable respiration, and

wherein each stimulation period of each respective stimulation cycle has a duration greater than a duration of the inspiratory reference of the reference respiratory cycle and the stimulation period is followed by the non-stimulation period of the respective stimulation cycle comprising a duration less than the duration of the stimulation period.

2. The device of claim **1**, wherein the non-cardiac stimulation element comprises an implantable electrode and a pulse generator electrically connected to the implantable electrode.

3. The device of claim **2**,

wherein the implantable electrode comprises a cuff electrode including at least one operative contact group through which the stimulation is deliverable non-selectively to the upper-airway-patency-related nerve.

4. The device of claim **1**, wherein a total duration of stimulation via the first stimulation protocol during a treatment period is greater than 30 percent of the total duration of the treatment period.

5. The device of claim **1**, wherein the duration of the stimulation period comprises

at least 50 percent of a duration of the stimulation cycle.

6. The device of claim **1**, wherein the duration of the stimulation period comprises

at least 50 percent of a duration of the reference respiratory cycle.

7. The device of claim **1**, wherein the duration of each respective stimulation cycle is less than the duration of the reference respiratory cycle, and a duration of the stimulation period exceeds the duration of the non-stimulation period by a factor of at least 3.

8. The device of claim **1**, wherein the duration of each respective stimulation cycle is greater than the duration of the reference respiratory cycle.

9. The device of claim 8, wherein the stimulation period and the non-stimulation period are in a proportion of at least 1.5 to 1.

10. The device of claim 8, wherein the duration of the stimulation cycle is less than a duration of two consecutive reference respiratory cycles.

11. The device of claim 1, wherein the duration of each respective stimulation cycle is equal to the duration of the reference respiratory cycle, and wherein the duration of the reference respiratory cycle differs from a duration of a real time respiratory cycle from actively-sensed respiration information by an amount exceeding a duration variability criteria.

12. The device of claim 1, comprising:

a processor; and

a non-volatile computer readable medium storing instructions, executable on the processor, to implement the non-cardiac stimulation element and to perform the first stimulation therapy protocol.

13. The device of claim 1, comprising:

a sensing element to at least periodically actively sense respiratory information to obtain the actively-sensed respiratory information unrelated to stimulation synchronization,

wherein the non-cardiac stimulation element is activated for stimulation upon the sensing element identifying, via at least the actively-sensed respiratory information, obstructive sleep apnea behavior which meets or exceeds a severity threshold and wherein the non-cardiac stimulation element is deactivated upon the sensing element identifying, via at least the actively-sensed respiratory information, that the obstructive sleep apnea behavior is less than the severity threshold.

14. The device of claim 1, comprising:

a sensing element to obtain the actively-sensed respiratory information; and

a control portion including:

a processor; and

a non-volatile memory storing instructions, executable via the processor, to:

provide convertible operation via a therapy manager between:

a first stimulation mode implementing the first stimulation therapy protocol; and

a second stimulation mode of stimulating the upper-airway-patency-related nerve synchronous with a characteristic of the actively-sensed respiratory information.

15. The device of claim 1, wherein the stimulation period and the non-stimulation period are in a proportion of at least 1.5 to 1.

* * * * *