

REMARKS

In response to the Non Final Office Action mailed November 23, 2016, Applicants respectfully request consideration of the claims provided herein. With this response, claim 89 is canceled without prejudice or disclaimer.

Claims 49, 51, 53, 55-56, and 75-92 were pending prior to the entry of the above-mentioned amendments. Claim 89 is canceled.

Claims 49, 55 and 90 are amended. Support for amended claims 49 and 55 can be found at least in paragraphs [0003], [0031], [0037], [0039], [0041] and [00119] of the specification as published. Claim 49 has also been amended to correct typographical errors. Claim 90 has been amended to depend from claim 49.

No new matter has been added. Accordingly, claims 49, 51, 53, 55-56, and 75-88 and 90-92 are currently pending.

All amendments to the claims and any cancellations of claims are made without conceding the validity of the rejection; and Applicants reserve the right to pursue any canceled material in any future, related applications.

Claim Rejection-35 U.S.C. § 112 (pre-AIA), second paragraph

Former claim 89 was rejected under U.S.C. § 112 (pre-AIA), second paragraph. *See* Office Action, page 3. In response, without admission of the propriety of this rejection, claim 89 has been cancelled herein and claim 90 has been amended to depend from claim 49. In view of the present cancellation of claim 89, the rejection is rendered moot.

Claim Rejection-35 U.S.C. § 102

Former claims 49, 51, 53, 55, 56, 75-81, 84, 85 and 88-92 were rejected under pre-AIA USC 102(b) as being anticipated by U.S. Patent Application Publication No. 2003/0148544 to Nie et. al. *See* Office Action at p. 5. Claim 89 has been canceled herein.

The Office asserts, *inter alia*, that the capability of “non-degenerately detecting the presence or absence of at least seven analytes in a single sample volume...” as previously recited was interpreted as an “intended use that does not differentiate the recitations of the claims from the prior art”.

In response, without admitting the propriety of the rejection and solely in the interest of advancing prosecution, Applicants have canceled claim 89 and amended independent claims 49 and 55 to recite that the claimed methods are carried out without a step of “immobilization of said analytes, physical separation of said analytes, or mass spectrometry”, and has replaced the expression “capable of detecting” with “detects”. Applicants respectfully submit that the present amendments to independent claims 49 and 55 render the present rejection moot. However, in the event that a corresponding rejection is raised against any of the presently amended claims, Applicants respectfully traverse such rejection and submit the following argument.

Applicants submit that Nie does not anticipate presently amended independent claims 49 and 55 for at least the following reasons.

Applicant submits that none of the passages of Nie pointed to in the Office Action specifically discloses a method having each and every element of the presently claimed solution. Put another way, none of the cited passages discloses the identical composition “in as complete detail as is contained in the ... claim.” *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989); MPEP 2131. Accordingly, Applicants submit that the present amendments to independent claims 49 and 55 fully address the rejection raised in the Office Action under 35 USC § 102(a)(1).

In particular, Nie fails to teach a method of non-degenerately detecting the presence or absence of at least six (or at least seven) analytes in a single sample volume without immobilization of said analytes, physical separation of said analytes, or mass spectrometry.

Applicants respectfully submit that it is evident from the teaching of Nie that the coding methods taught by Nie do not address the issue of degeneracy. Rather, Nie suggests that physical separation of analytes in order to distinguish between identically coded (i.e. degenerately coded) analytes. For example, at paragraph [0084], Nie suggests a method of detecting multiple analytes by flowing conjugates through a microchannel or by spreading on a substrate surface, each of which requires physical separation to allow for resolution of multiple analytes when employing a redundant coding scheme such as that taught by Nie.

In particular, Applicants submit that Nie explicitly teaches that codes can be formed with *every possible RGB combination*, which, if performed as described in Nie, will necessarily result in a redundancy when attempting to detect six or seven analytes in a single volume, without physical separation, melting curve analysis, or mass spectrometry. For example, based on a review of the potential combinations shown in Figure 1 of Nie, a person of ordinary skill in the art would understand that the codes shown were selected from the set of RGB combinations where the levels for each color channel range, at minimum, from 0 to 10 (hence, 11 values each). Thus, in the embodiment described and depicted in Figure 1, $11 \times 11 \times 11 = 1331$ codes are possible. This is consistent with the following statements set forth in Nie at paragraph [0046]:

Each color (i.e., wavelength) of the QD can be embedded in the bead at a predetermined intensity, thereby forming a multicolor QD-tagged bead. For each color, the use of 10 intensity levels (0, 1, 2, . . . 9) gives 9 unique codes ($10^1 - 1$), because level "0" cannot be differentiated from the background. The number of codes increases exponentially for each intensity and each color used. For example, a three color and 10 intensity scheme yields 999 codes ($10^3 - 1$), while a six color and 10 intensity scheme has a theoretical coding capacity of about 1 million ($10^6 - 1$). In general, n intensity levels with m colors generate $(n^m - 1)$ unique codes. However, the actual coding capabilities are likely to be substantially lower because of spectral overlapping, fluorescence intensity variations, and signal-to-noise requirements. In general, it is more advantageous to use more colors rather than more intensity levels, in order to increase the number of usable codes. The number of intensities is preferably from 0 to 20, more preferably 1-10, more preferably 2-8, more preferably 3-7, more preferably 4-6, more preferably 5-6, and most preferably 6. The number of colors is preferably 1-10 (e.g., 2-8), more preferably, 3-7, and most preferably 5-6. The term "multicolor QD", is meant that the more than one color of luminescent quantum dots are embedded in the bead. Although preferably more than one color of quantum dot is incorporated in the bead, instances wherein one or more colors' intensity is zero, such as a bead with the red:green:blue code of 1:0:0, is also encompassed by the present invention.

For illustrative purposes, three codes selected from this set are as follows:

- Target 1 label is (R=1,G=1,B=1);
- Target 2 label is (R=2, G=2, B=2); and
- Target 3 label is (R=3, G=3, B=3).

With this set, if target 1 is present in isolation, the intensity readout would come from contributions from the Target 1 label only, and would be (1,1,1). Similarly, if target 2 is present in isolation, the readout would be (2,2,2). Likewise, if Target 3 is present in isolation, the readout would be (3,3,3).

However, if targets 1 and 2 are both present in a measurement, the readout would be (3,3,3): **the same readout for target 3 in isolation**, and it would be impossible to distinguish between a “target 3 only” signal (3,3,3) and a “target 1 and target 2 both present” signal (1,1,1 and 2,2,2 = 3,3,3). This happens because the codes specified are **degenerate**. Thus, the true combinations of targets cannot be discriminated using the method specified in Nie. Accordingly, Nie does not address this issue of degeneracy, and certainly does not teach or suggest a method that “non-degenerately detects the presence or absence of at least [six or seven] analytes in a single sample volume” as recited by the presently amended independent claims. With respect to the independent claims, these claims all depend from independent claim 49 or 55, and are not anticipated by Nie for at least the same reasons.

For the foregoing reasons, Applicants respectfully request withdrawal of the rejection of claims 49, 51, 53, 55, 56, 75-81, 84, 85, 88 and 90-92, as amended, under pre-AIA 35 U.S.C. 102(b).

Claim Rejection-35 U.S.C. § 103

Former claims 49, 51, 53, 55, 56, 75-81, 84, 85, and 88-92 were rejected under pre-AIA USC 103(a) as being purportedly obvious over Nie further in view Craig, *Nucleic Acids Research*, vol. 18, 1990, pp. 2653-2660, alone or in combination with International Patent Application Publication No. WO/2010/128206 to Orpana et al. See Office Action at pp. 9 and 10. Claim 89 has been canceled herein.

No *Prima Facie* Case of Obviousness Established - Not All Limitations Shown

Applicant respectfully traverses the rejection. As discussed above, Nie does not teach or suggest all of the limitations of independent claims 49 or 55, as amended, nor any claim dependent thereon. Further, the teachings of Craig and Orpana, either taken alone or in combination, do not teach or suggest the elements not taught by Nie, for example, these references do not teach a method of non-degenerately detecting the presence or absence of at least six (or at least seven) analytes in a single sample volume without immobilization of said analytes, physical separation of said analytes, or mass spectrometry. Further, there is no motivation to modify the teachings of Nie, either alone or in combination, to arrive at the subject

matter of instant claims. Finally, none of Nie, Craig, nor Orpana, enable the methods recited in the presently amended claims.

Relevant Law

MPEP 2143, states that a *prima facie* case of obviousness may be established only when three basic criteria have been met. “*First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.*”

In Applicants’ respectful submission, there is no suggestion or motivation in the teachings of Nie, Craig, or Orpana, either taken alone or in combination, to **non-degenerately detect** the presence or absence of at least six or seven analytes in a single sample volume without immobilization of said analytes, physical separation of said analytes, or mass spectrometry, as recited in independent claims 49 and 55, as amended. Indeed, with reference to the discussion of Nie above regarding the rejections raised under §102, Nie teaches a redundant method, and fails to even address the issue of degeneracy.

Neither Orpana nor Craig cure the defects of Nie. Indeed, neither Orpana nor Craig address the issue of redundancy in a coding scheme as recited in the presently amended claims.

Regarding the methods taught by Craig, these methods require spotting analytes onto nylon membranes. *See* Craig at p. 2654, first column. Accordingly, the method taught by Craig does not teach detection of the “presence or absence of at least six [or seven] analytes in a **single sample volume... without immobilization of said analytes or physical separation** of said analytes”. Indeed, the methods taught by Craig clearly require both immobilization and physical separation (on the nylon membranes), in order to allow for resolution and combination of the results obtained for each of the various probes. *See, e.g.*, Craig, Fig. 2.

Regarding the methods taught by Orpana, these methods fail to provide any teaching or suggestion of any method of coding, nor do they address the issue of coding or degeneracy. In particular, Orpana fails to cure the defects of Nie and Craig discussed above, and fails to teach or suggest any method of encoding and non-degenerately detecting the presence or absence of at

least six or seven analytes in a single sample volume without immobilization of said analytes, physical separation of said analytes, or mass spectrometry, as recited in the amended independent claims 49 and 55.

Conclusion

Accordingly, Applicants submits that the test set out at MPEP 2143 is not met in the present case, that the cited references, either taken alone or in combination, fail to render obvious the subject matter claimed by independent claims 49 and 55, as amended, and that a *prima facie* case of obviousness has not been established in the present case for those independent claims or the claims that depend therefrom. Favorable consideration of the amended claims is respectfully requested.

Claim Rejection-35 U.S.C. § 101

The Office had rejected former claims 49, 51, 53, 55, 56, 75-81 and 83-92 as being allegedly directed to a judicial exception “without significantly more”. *See* Office Action at page 4. The Office went on to allege that the rejected claims were “directed to the abstract idea of encoding signals in a manner that reduces or eliminates degeneracy,” and that the claims did “not include additional elements that [were] sufficient to amount to significantly more than the judicial exception... because providing samples, performing assays, and determin[ing] presence/absence patterns of analytes is routine and conventional in the prior art”. *Id.*

In response, without admitting the propriety of the rejection and solely in the interest of advancing prosecution, Applicants have canceled claim 89 and amended independent claims 49 and 55 to recite that the claimed methods do not require “immobilization of said analytes, physical separation of said analytes, or mass spectrometry”. Applicants respectfully submit that the present amendments to independent claims 49 and 55 render the present rejection moot. However, in the event that a corresponding rejection is raised against any of the presently amended claims, Applicants respectfully traverse such rejection and submit the following argument.

A. The Present Rejection Fails to Account for the Specific Requirements of the Claims

In the *Alice* decision, the Supreme Court applied a two-step framework for determination of patent eligibility under Section 101. First, one must “determine whether the claims at issue are directed to a patent-eligible concept.” *Alice* at 2355. Second, one “must examine the elements of the claims to determine whether it contains an inventive concept sufficient to transform the claimed abstract idea into a patent-eligible application.” *Id.* at 2357. In the second step, the claim elements must be analyzed separately and as an “ordered combination.” *Id.* at 2359.

On November 2, 2016, the Robert W. Bahr, the Deputy Commissioner for Patent Examination Policy, issued a memorandum regarding “Recent Subject Matter Eligibility Decisions” (hereinafter “Nov. 2016 Eligibility Memo”). The Nov. 2016 Eligibility Memo is intended provide guidance to examiners “about finding eligibility for software claims.” The Nov. 2016 Eligibility Memo at page 1. Here, the Nov. 2016 Eligibility Memo “provides a discussion of two of the recent decisions identifying eligible subject matter, namely *McRO, Inc. dba Planet Blue v. Bandai Namco Games America Inc.*, 120 USPQ2d 1091 (Fed. Cir. 2016) and *BASCOM Global Internet Services v. AT&T Mobility LLC*, 827 F.3d 1341 (Fed. Cir. 2016). *Id.* Specifically, the Nov. 2016 Eligibility Memo noted:

- “The *McRO* court cautioned that courts ‘**must be careful to avoid oversimplifying the claims**’ by looking at them generally and **failing to account for the specific requirements of the claims**.” *Id.* at page 2 (emphasis added).
- Following the section titled “Notable Points from *McRO*,” the Nov. 2016 Eligibility Memo stated how “[e]xaminers should consider the claim **as a whole** under Step 2A of the USPTO’s SME guidance, and **should not overgeneralize the claim or simplify it into its “gist” or core principles**, when identifying a concept as a judicial exception.” *Id.* (emphasis added).
- Notwithstanding the claims having “additional elements [that] were generic computer, network, and Internet components that did not amount to significantly more when considered individually,” the *BASCOM* court still “recognize[d] that **when combined, an inventive concept may be found in the non-conventional and non-generic arrangement**.” *Id.* at page 3.

- Following the section titled “Notable Points from *BASCOM*,” the Nov. 2016 Eligibility Memo stated how “examiners should – when analyzing Step 2B of the USPTO’s SME guidance – consider the additional elements in **combination**, as well as individually, when determining whether a claim as a whole amounts to significantly more, as this may be found in the non-convention and non-generic arrangement of known, conventional elements.” *Id.* (emphasis in original).

As set out above, the Office alleges that the rejected claims were “directed to the abstract idea of encoding signals in a manner that reduces or eliminates degeneracy,” and that the claims did “not include additional elements that [were] sufficient to amount to significantly more than the judicial exception... because **providing samples, performing assays, and determin[ing] presence/absence patterns of analytes is routine and conventional in the prior art**”. Office Action at p. 4 [emphasis added].

However, in so doing, the Office fails to account for the claims’ **specific** requirements – a failure the Nov. 2016 Eligibility Memo specifically warns against. *See* the Nov. 2016 Eligibility Memo at 2.

By way of example, claim 49 recites:

A method of detecting the presence or absence of each analyte of a plurality of analytes, comprising:

- a. encoding each of said analytes as a first value of a signal, thereby generating a coding scheme, wherein each of said analytes is represented in said coding scheme by one of said first values, wherein said encoding is performed in a manner that reduces or eliminates degeneracy;
- b. **providing a sample comprising, or potentially comprising, at least one of said analytes;**
- c. **contacting said sample with analyte-specific reagents** that generate said first values, as represented in said coding scheme, when each of said analytes is present;
- d. **cumulatively measuring said first values of said signal within said sample, thereby providing a cumulative measurement;** and
- e. determining whether each of said analytes is present or absent based on said cumulative measurement and said coding scheme;
wherein said method is non-degenerately detects the presence or absence of at least seven analytes in a single sample volume, in any combination of presence or absence, without immobilization of said analytes, physical separation of said analytes, or mass spectrometry. [Emphasis to exemplary specific elements added].

Rather than addressing the specific elements recited in the claim, as presently amended, including the exemplary specific elements highlighted above, the Office generalizes the entire claim with a broad description. In doing so, the Office simplifies the claim to its “gist” or core principles. This is improper. The Nov. 2016 Eligibility Memo specifically prohibits this. The Nov. 2016 Eligibility Memo at page 2 (“Examiners should consider the claim as a whole under Step 2A of the USPTO’s SME guidance, and should not overgeneralize the claim or simplify it into its ‘gist’ or core principles, when identifying a concept as a judicial exception.”).

To summarize, the Office oversimplifies the claims, and fails to address the specific elements recited in the claims. By generalizing the claims (rather than accounting for the specific requirements of the claims), the Office fails to adhere to its own guidelines in the Nov. 2016 Eligibility Memo. For at least these reasons, Applicant disagrees that the Office has properly satisfied the first step and respectfully requests that the Office withdraw the present rejection.

B. The Claims Recite an Inventive Concept

Even assuming, *arguendo*, that independent claims 49 and 55 are directed to an abstract idea, which is traversed in Sections II.A and II.B, *supra*, the claims recite “significantly more” than an abstract idea itself.

The Nov. 2016 Eligibility Memo provides guidance on how examiners should apply the second step. *See* the Nov. 2016 Eligibility Memo at page 3. Specifically, the Nov. 2016 Eligibility Memo explicated the *BASCOM* case, highlighting how the *BASCOM* court found an inventive concept in the “claimed system for filtering content retrieve from an Internet computer network” may be found notwithstanding additional elements being “generic computer, network, and Internet components.” *Id.*

A closer examination of *BASCOM* provides further guidance on how to apply the second step. In *BASCOM*, the lower court applied the second step by looking at each limitation individually and collectively and finding that there was no inventive concept because “the limitations, ‘considered individually, or as an ordered combination, are no more than routine additional steps involving generic computer components and the Internet, which interact in well-known ways to accomplish the abstract idea of filtering Internet content.’” *BASCOM*, 827 F.3d at 1349.

The Federal Circuit held the lower court erred in its analysis – in particular its conclusion about the lack of inventive concept as it pertained to “the ordered combination of limitations.” *Id.* The Federal Circuit emphasized that the “inventive concept inquiry requires more than recognizing that each claim element, by itself, was known in the art” and noted how the lower court’s analysis improperly “looked similar to an obviousness analysis under 35 U.S.C. § 103, except lacking an explanation of a reason to combine the limitations as claimed.” *Id.* at 1350. The Federal Circuit then proceeded to describe the inventive concept of the relevant patent by pointing to specific parts of the specification and ultimately found that the “specific method of filtering Internet content cannot be said, as a matter of law, to have been conventional or generic”:

The inventive concept described and claimed in the [] patent is the installation of a filtering tool at a specific location, remote from the end-users, with customizable filtering features specific to each end user. This design gives the filtering tool both the benefits of a filter on a local computer and the benefits of a filter on the ISP server. BASCOM explains that the inventive concept rests on taking advantage of the ability of at least some ISPs to identify individual accounts that communicate with the ISP server and to associate a request for Internet content with a specific individual account. According to BASCOM, the inventive concept harnesses this technical feature of networking technology in a filtering system by associating individual accounts with their own filtering scheme and elements while locating the filtering system on an ISP server.

Id. (internal citations to patent specification and oral arguments omitted).

The facts and holding in *BASCOM* are analogous to the present situation.

First, like the overturned lower court in *BASCOM*, the Office erred in its analysis by arguing how the recitation of “providing samples, performing assays, and determin[ing] presence/absence patterns of analytes is routine and conventional in the prior art.” Office Action at p. 4. Thus, the Office’s argument amounts to an obviousness analysis under 35 U.S.C. § 103 without the explanation of a reason to combine the limitations as claimed – an argument the Federal Circuit in *BASCOM* specifically held was improper in the second step. *BASCOM*, 827 F.3d at 1350.

Next, like the specific method of filtering Internet content in *BASCOM*, a very specific system, namely analytes in a sample volume, and method of detecting the presence or absence of those analytes in that single sample volume (**without immobilization of said analytes, physical separation of said analytes, or mass spectrometry**) exists in the presently claimed methods. In other words, the present claims have specific applications in the marketplace, which “are not likely to be so abstract that they override the statutory language and framework of the Patent Act.” *See Res. Corp. Techs. v. Microsoft Corp.*, 627 F.3d 859, 869 (Fed. Cir. 2010).

Finally, the claims in *BASCOM* sought to overcome the technical challenges associated with networking technology with a filtering system by associating individual accounts with their own filtering scheme and elements while locating the filtering system on an ISP server. *See BASCOM*, 827 F.3d at 1350. Similarly, the claims at issue seek to overcome the technical challenges associated with detecting the presence or absence of six or seven analytes in a single volume namely difficulties associated with detection of such analytes in that single sample volume without immobilization of said analytes, physical separation of said analytes, or mass spectrometry, as discussed further above with respect to the rejections under 35 USC §§ 102 and 103.

In sum, the second step analysis, when conducted in a manner consistent with the governing caselaw and the Nov. 2016 Eligibility Memo, should arrive at a conclusion that the presently amended claims recite an inventive concept that renders the claims patent eligible under Section 101. Under *BASCOM* and the Office’s own guidelines set forth in the Nov. 2016 Eligibility Memo, the independent claims 49 and 55 in the pending application recite an inventive concept and satisfy the second step. For at least these reasons, Applicants submit that the second step is satisfied and respectfully request the Office to consider the claims as being patent eligible under Section 101, and to withdraw the rejection.

CONCLUSION

Applicants believe that the application is in condition for allowance and respectfully solicit the Examiner to expedite prosecution of this patent application to issuance. Should the Examiner have any questions, the Examiner is encouraged to telephone the undersigned.

The Commissioner is authorized to charge any additional fees which may be required, including petition fees and extension of time fees, to Deposit Account No. 23-2415 (Docket No. 38075-716.301).

Respectfully submitted,

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