

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

BRUKER SPATIAL BIOLOGY, INC.,
Petitioner

v.

PRESIDENT AND FELLOWS OF HARVARD COLLEGE and 10X
GENOMICS,
Patent Owner

Case IPR2024-00526
U.S. Patent No. 11,542,554

**DECLARATION OF JULIE L. DAVIS IN SUPPORT OF
PATENT OWNER RESPONSE**

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10x Genomics EX2026
Bruker v. Harvard
IPR2024-00526

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I, Julie L. Davis, hereby declare as follows:

I. INTRODUCTION

1. I am over the age of 18 and competent to make this declaration.
2. Although I am being compensated for my time in preparing this declaration, the positions articulated herein are my own, and I have no stake in the outcome of this proceeding or any related litigation or administrative proceedings.

II. PROFESSIONAL BACKGROUND AND EXPERIENCE

3. I have been providing audit and financial consulting services to attorneys and corporate clients for forty-six years. The early part of my career was devoted to directing and performing independent financial audits of private and publicly held companies ranging from manufacturing entities to financial institutions at Touche Ross & Co., which at the time was one of the Big 8 accounting firms. Drawing upon that background, I have spent the last thirty-six years consulting extensively with companies involved in business and intellectual property disputes. Prior to starting my own firm, Davis & Hosfield Consulting LLC, I served as the Partner-in-Charge of the National Intellectual Property Practice at KPMG LLP and prior to that served as the Co-Managing Partner of the Global Intellectual Asset Consulting Practice at Andersen LLP. Davis & Hosfield Consulting LLC was acquired by Stout Risius Ross, LLC (“Stout”) in August 2022. I am currently a Managing Director at Stout.

4. I have worked on numerous intellectual property cases during my career and have conducted complex studies of commercial success, damages, and other matters related thereto. These studies have included evaluations of sales, gross profits, incremental profits, manufacturing and marketing capacities, fixed and variable costs, consumer demand, product line profitability, price erosion, and reasonable royalties. I have testified in matters related to these studies.

5. In addition to intellectual property disputes, I have assisted companies in developing intellectual property strategies and managing their intellectual property portfolios. I have also conducted studies related to those portfolios including patent portfolio analyses, competitive assessments, licensing analyses, cost studies, and benchmarking studies. In addition, I have co-authored a book, *Edison in the Boardroom*, on the best practices used by leading companies in managing their intellectual property.

6. I graduated in 1978, *summa cum laude*, from Kansas State University with a Bachelor of Science degree in Business Administration and Accounting. In the same year, I earned the Gold Key in the State of Kansas for the highest score in the state on the CPA exam. I am a licensed CPA in California, Illinois, Kansas, Missouri, and Texas. I am a member of the American Institute of Certified Public Accountants, American Bar Association, and Licensing Executives Society. My *curriculum vitae*, which is attached as Exhibit 2016, describes in more detail my

professional credentials including other publications and prior testimony experience as required under Federal Rule of Civil Procedure 26(a)(2)(B).

III. OVERVIEW OF THE ASSIGNMENT

7. I understand that the above-referenced IPR of the 554 patent was filed by NanoString Technologies, Inc. (“NanoString”), now Bruker Spatial Biology, Inc., Bruker Nano, Inc., and Bruker Corp. (collectively, “Bruker” or “Petitioner”). I understand that President and Fellows of Harvard College (“Harvard”) is the sole legal owner of the 554 patent, and 10x Genomics, Inc. (“10x”) is the exclusive licensee.

8. Stout was retained by Sterne, Kessler, Goldstein & Fox PLLC (“Counsel”) on behalf of 10x in the above-referenced matter to provide analysis of the commercial success of 10x’s and NanoString’s products that practice the 554 patent. I understand that commercial success is related to secondary considerations (also called, objective indicia) of non-obviousness in connection with the patentability of the 554 patent.

IV. INFORMATION RELIED UPON

9. My opinions are based upon the documents cited herein (also listed in Appendix A).

10. I have reviewed the declaration submitted by Hari Shroff, Ph.D. (EX2024), technical expert retained on behalf of 10x.

11. My opinions are based on my skills, knowledge, experience, education, and training. It is usual and customary for experts to consider and/or rely upon sources of information such as those cited in this declaration in forming commercial success opinions.

V. BACKGROUND INFORMATION

A. NanoString (now a Bruker company)

12. NanoString was founded in 2003, and was acquired by Bruker for approximately \$392.6 million in cash and the assumption of certain liabilities.¹ NanoString (now a Bruker company) describes itself as striving “to create end-to-end solutions that are simpler, easier, faster and more relevant to today’s life science challenges,” and it “enables scientists across the globe to envision molecular interactions in three dimensions” through the use of its various products.²

13. NanoString currently offers three different systems including the nCounter[®] Analysis System (“nCounter”), the GeoMx[®] Digital Spatial Profiler

¹ EX2028 (<https://ir.bruker.com/press-releases/press-release-details/2024/Bruker-Completes-Asset-Acquisition-of-NanoString-Business/default.aspx>).

² EX2029 (<https://nanosttring.com/about-us/>), p. 1.

(“GeoMx), and the CosMx™ Spatial Molecular Imager Platform (also called “CosMx”).³

14. CosMx, NanoString’s third commercially available platform, is a spatial multiomics single-cell imaging platform that “provide[s] spatial multiomics . . . at cellular and subcellular resolution.”⁴ NanoString announced its first commercial shipment of CosMx on December 6, 2022.⁵

15. NanoString “derive[s] a substantial majority of [its] revenue from the sale of [its] products, which consist of [its] GeoMx, CosMx, and nCounter instruments and related proprietary consumables. [Its] instruments are designed to work only with [NanoString’s] consumable products.”⁶

³ EX2029.

⁴ EX2030 (<https://nanosttring.com/products/cosmx-spatial-molecular-imager/single-cell-imaging-overview/>), p. 1.

⁵ EX2031
(<https://www.businesswire.com/news/home/20221206005433/en/NanoString-Begins-Commercial-Shipments-of-CosMx-Spatial-Molecular-Imager-and-AtoMx-Spatial-Informatics-Platform>).

⁶ EX2032 (NanoString Technologies, Inc. Form 10-K for the fiscal year ended December 31, 2022), p. 55.

B. 10x Genomics, Inc.

16. 10x “is a pioneering innovator of genomics and sequencing technologies” that delivers “powerful, reliable tools that fuel scientific discoveries and drive exponential progress to master biology to advance human health.”⁷ “10x has developed . . . award-winning products that give single cell and spatial views of complex biological systems,” which have helped enable new forms of research in life sciences including cancer research, neuroscience, immunology, infectious disease, and developmental biology.⁸ According to 10x’s website, the company has been cited in over 7,000 publications and has over 4,600 “[i]nstruments placed in top institutions worldwide.”⁹

17. 10x was founded in 2012, and today its product portfolio is comprised of three platforms for biological research, each including instruments, consumables, and software.¹⁰ 10x’s Xenium Platform (also called “Xenium”),

⁷ EX1063 (Second Amended Complaint, dated March 1, 2023), pp. 1-2; EX2033 (<https://www.10xgenomics.com/company>).

⁸ EX1063, p. 2.

⁹ EX2033, p. 3.

¹⁰ EX2034 (10x Genomics, Inc. Form 10-K for the fiscal year ended December 31, 2023), pp. 4 and 18.

launched in December 2022, is described as “the next generation of targeted spatial profiling of genes and proteins at subcellular resolution.”¹¹ It is “designed to give scientists the ability not only to locate and type cells in their tissue context, but also to address a variety of specific questions based on previous knowledge of their sample.”¹²

C. The 554 Patent

18. I understand that the 554 patent is a system patent entitled “Method and Apparatus for Volumetric Imaging” and lists Evan Daugharthy, Richard Terry, Je-Hyuk Lee, George Church, and Benjamin Pruitt as inventors and Harvard as the assignee.¹³

19. The Summary of the 554 patent states:

Aspects of the present disclosure further include an automated method and apparatus for volumetric imaging of in situ sequenced nucleic acids including an in situ

¹¹ EX2035 (<https://www.prnewswire.com/news-releases/10x-genomics-commercially-launches-xenium-platform-for-in-situ-analysis-301698748.html>), p.

1.

¹² EX2034, p. 4.

¹³ EX1001 (U.S. Patent No. 11,542,554 entitled “Method and Apparatus for Volumetric Imaging,” issued January 3, 2023), Face Page.

sequencing method or apparatus, a fluidics method or reagent delivery method or apparatus to regulate flow of reagents and deliver reagents and a volumetric imaging method or apparatus for imaging and/or detecting light signals from the in situ sequenced nucleic acids or other molecules or structures of interest.¹⁴

The 554 patent further explains:

The automated sequencing and three-dimensional imaging device uses biochemical methods to execute fluorescence- or optically-encoded nucleic acid sequencing, acquisition of image data, and optionally, data processing.¹⁵

D. 10x's Xenium Platform

20. 10x's Xenium Platform, which I understand embodies the claims of the 554 patent challenged in this IPR,¹⁶ provides “[h]igh-performance in situ from the single cell leader” and allows users to “[c]haracterize up to 5,000 genes in cells and tissues with ultra precise single cell spatial imaging.”¹⁷ It is “[b]uilt for rapid

¹⁴ EX1001, 2:18-26.

¹⁵ EX1001, 5:33-37.

¹⁶ EX2024 (Declaration of Dr. Shroff), ¶¶116-128.

¹⁷ EX2036 (<https://www.10xgenomics.com/platforms/xenium>), p. 1.

data exploration,” is a “state-of-the-art single cell spatial imaging platform,” and can “[t]arget the biology that matters.”¹⁸ 10x announced its first commercial shipments of its Xenium Platform on December 8, 2022.¹⁹

21. In its 2023 10-K, 10x explains that its

Xenium platform for in situ analysis is designed to give scientists the ability not only to locate and type cells in their tissue context, but also to address a variety of specific questions based on previous knowledge of their sample often discovered using [its] Chromium and Visium platforms. Xenium In Situ detects and preserves the cellular localization of hundreds of RNA targets directly in a fresh frozen or FFPE tissue section without the need for conventional sequencing, providing researchers with a detailed map of gene expression patterns without sacrificing resolution or target number.²⁰

22. 10x further describes its Xenium Platform as a “complete end-to-end solution including a robust instrument, consumables and software.”²¹ The “Xenium

¹⁸ EX2036, pp. 3-4.

¹⁹ EX2035, p. 1.

²⁰ EX2034, p. 4.

²¹ EX2034, p. 16.

consumables consist of a menu of curated, validated and fit-for-purpose gene panels along with the ability to design custom gene sets.”²² The Xenium Analyzer instrument allows customers to “easily transfer data from the instrument and perform visualization and further analysis with 10x-provided software or other tools of their choice.”²³ The Xenium Platform includes Xenium Explorer, “an easy-to-use desktop software tool for interactive exploration and data analysis” which “leverages the platform’s exploration-ready output to enable researchers to immediately see results at subcellular and tissue scale.”²⁴

23. On June 20, 2024, 10x announced that it had begun commercial shipments of Xenium Prime 5K Pan-Tissue and Pathways panel.²⁵ 10x’s press release noted that “[t]he new panel features an enhanced chemistry to increase plex by an order of magnitude while delivering excellent per-gene sensitivity, improved

²² EX2034, p. 16.

²³ EX2034, p. 16.

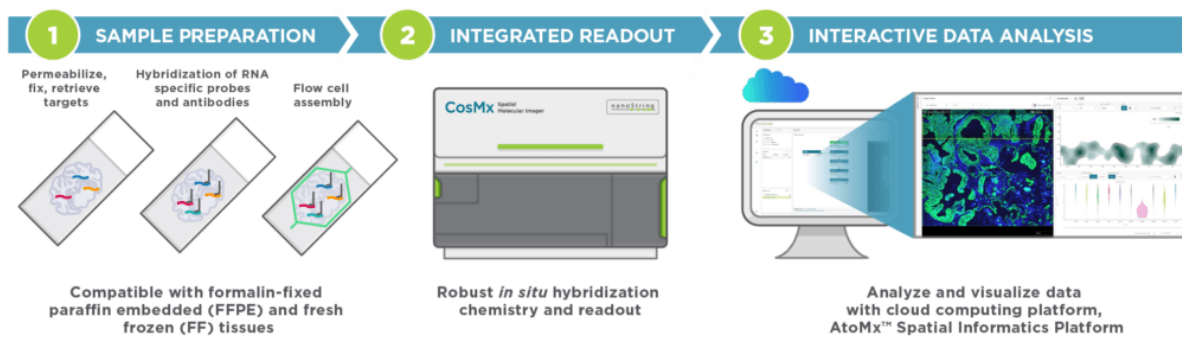
²⁴ EX2034, p. 16.

²⁵ EX2037 (<https://www.prnewswire.com/news-releases/10x-genomics-begins-commercial-shipments-of-xenium-prime-5k-pan-tissue-and-pathways-panel-302177116.html>).

specificity and spatial fidelity, integrated multimodal cell segmentation and industry-leading speed and throughput.”²⁶

E. NanoString’s CosMx Platform

24. NanoString’s CosMx Platform includes the CosMx SMI instrument, CosMx RNA assays for FFPE and fresh frozen tissues, and related AtoMx Spatial Informatics Platform (“SIP”) data analysis software.²⁷ The image below depicts the high-level steps of the CosMx Platform.²⁸



25. CosMx “allows researchers to comprehensively map single cells in their native environment and extract deeper biological insights from a single

²⁶ EX2037, p. 1.

²⁷ EX2038 (<https://nanosttring.com/products/atomx-spatial-informatics-platform/cosmx-and-atomx-the-first-fully-integrated-single-cell-spatial-solution/>).

²⁸ EX2038.

experiment.”²⁹ “CosMx [] enables rapid quantification and visualization of up to 6,000 RNA and 64 validated protein analytes.”³⁰ The AtoMx SIP is a “cloud-based analysis solution” for secondary analysis, which then allows the user to “analyze and visualize CosMx single-cell spatial data with ease.”³¹

26. NanoString also “provides complete spatial molecular imaging service” through its CosMx SMI TAP.³² This program “enables researchers to visualize and quantify up to 6,000 RNAs’ expression directly in single cells with their spatial context preserved,” with NanoString’s “scientists provid[ing] support at every step of [the] project, including free consultations, real-time updates, and post data delivery assistance.”³³

27. NanoString announced the first commercial shipment of CosMx on December 6, 2022.³⁴

²⁹ EX2038, p. 1.

³⁰ [EX2030](#), p. 1.

³¹ EX2038, pp. 1-2.

³² EX2039 (<https://nanosttring.com/products/cosmx-spatial-molecular-imager/technology-access-program/>), p. 1.

³³ EX2039, p. 1.

³⁴ EX2031.

28. I understand from Dr. Shroff that CosMx embodies the claims of the 554 patent challenged in the IPR.³⁵

VI. SUMMARY OF OPINIONS

29. I understand that evidence of non-obviousness of a patent can be demonstrated by, among other things, the commercial success of the claimed invention.

30. Based on my analysis, I believe there is evidence of commercial success for the system covered by the 554 patent. In my opinion, the evidence related to commercial success supports a finding that the 554 patent is non-obvious.

VII. BASIS AND REASONING

31. In my determination of whether Xenium has been commercially successful, I have considered a number of factors that a reasonable businessperson would consider in determining commercial success and I understand are instructive in determining commercial success in an IPR. In particular, I have examined the following factors as evidence of commercial success:

- Sales and sales growth; and
- Profitability

³⁵ EX2024, ¶¶116-128.

32. I understand that a patent owner seeking to rely on evidence of commercial success to support a finding of non-obviousness must show a nexus between the claimed invention and the evidence of commercial success. I also understand that the successful product or method must embody the invention disclosed and claimed in the patent to satisfy nexus. I understand that 10x's Xenium embodies the claims of the 554 patent challenged in this IPR.³⁶

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

³⁶ EX2024, ¶¶116-128.

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

36. The technology covered by the 554 patent has been a significant driver of customer demand for Xenium. I understand that the 554 patent claims are directed to a system that integrates hardware and software components to implement in situ workflow.⁴¹ There is also evidence that Xenium has enjoyed recognition for the features that are the benefits of the 554 patent's claimed system over prior setups.⁴²

37. The commercial success of the 554 patent's claimed system is also illustrated through the rapid adoption of 10x's Xenium after launch.⁴³ For example, more than 250 Xenium Instruments were sold in the first year since launching, with researchers validating Xenium's sensitivity, specificity and high throughput.⁴⁴

⁴¹ EX2024, ¶¶56, 116-128.

⁴² EX2024, ¶¶130-131.

⁴³ EX2040 ("Accelerating the Mastery of Biology to Advance Human Health,"

42nd Annual J.P. Morgan Healthcare Conference, dated 2024

(https://s28.q4cdn.com/592666581/files/doc_presentations/2024/01/2024-TXG-JPM-Healthcare-Presentation-vF.pdf), pp. 5-8.

⁴⁴ EX2040, pp. 5-8.

Dr. Shroff further explained that without the patented technology, Xenium would not experience the same level of success.⁴⁵

38. I understand that the 554 patent is directed to a system that integrates hardware and software components to implement the in situ workflow.⁴⁶ As Dr. Shroff explained, the 554 patent is important to the way 10x implemented the technology in its Xenium platform.⁴⁷

39. Based on my understanding of the facts and circumstances surrounding this matter, my opinion is that the commercial success evidence supports a conclusion that the challenged claims of the 554 patent are non-obvious.

⁴⁵ EX2024, ¶129.

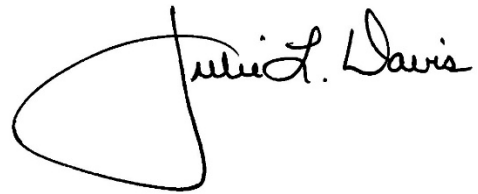
⁴⁶ EX2024, ¶¶56, 116-128.

⁴⁷ EX2024, ¶¶56, 116-128.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the U.S. Code.

I declare under penalty of perjury under the laws of the United States of America that the foregoing is true and correct.

Respectfully submitted,

A handwritten signature in black ink, reading "Julie L. Davis". The signature is written in a cursive style with a large, looped initial "J" that extends below the line of the text.

Julie L. Davis

Date: December 10, 2024

APPENDIX A

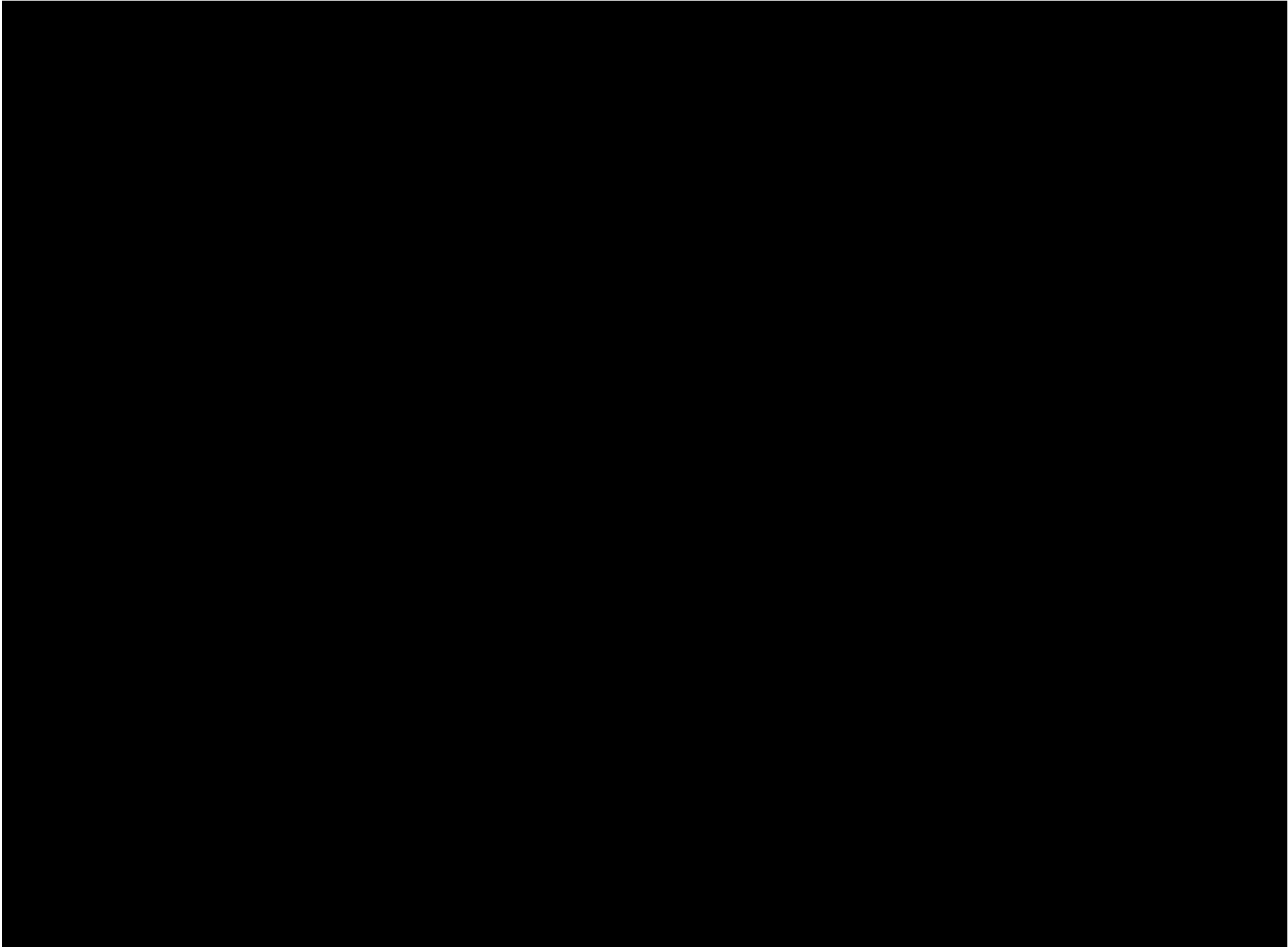
LIST OF MATERIALS RELIED UPON

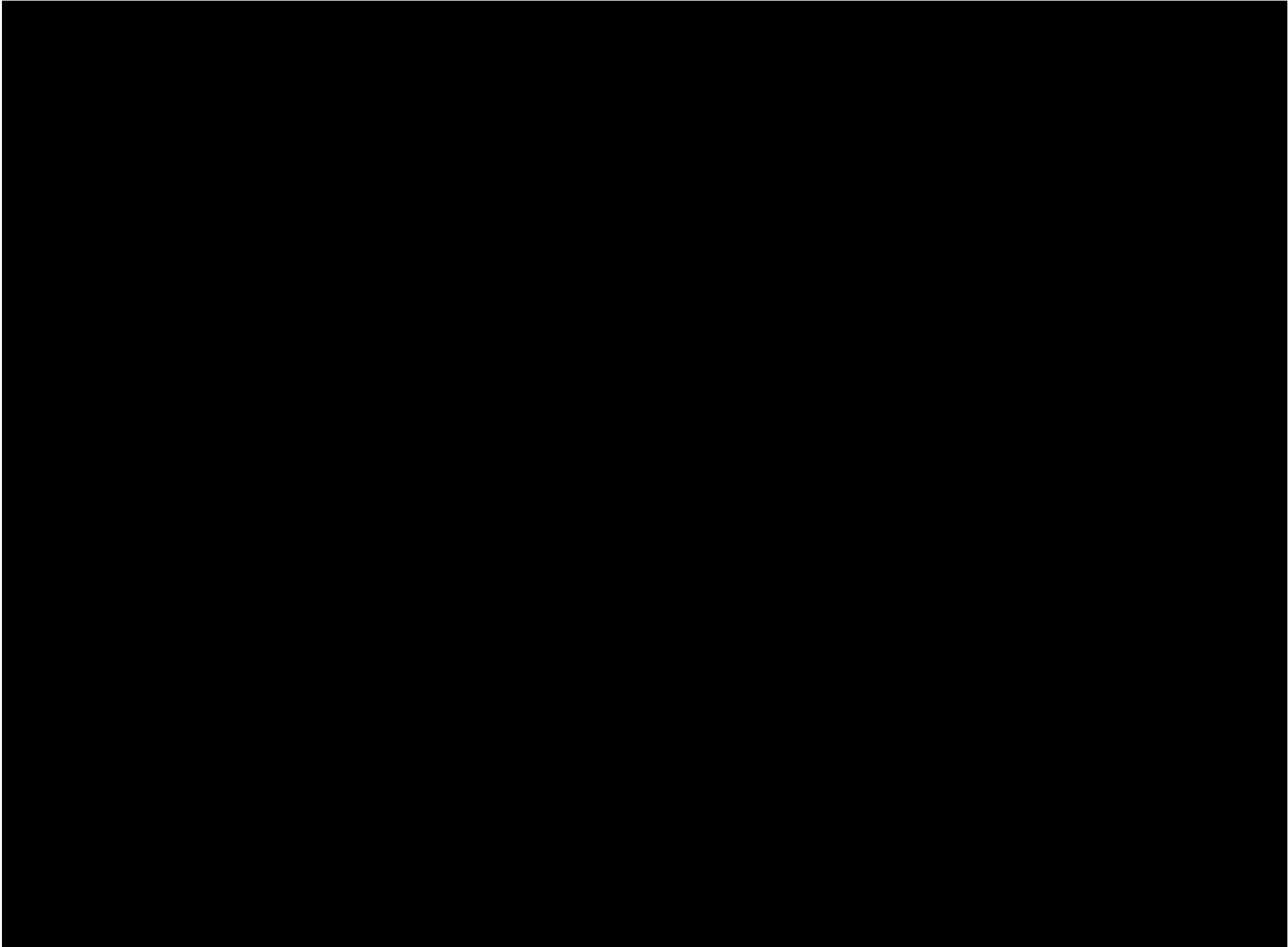
Exhibit No.	Description
1001	U.S. Patent No. 11,542,554 (“the ’554 Patent”)
1063	Plaintiffs, 10x Genomics, Inc. and President and Fellows of Harvard College’s Second Amended Complaint, <i>10x Genomics, Inc. and President And Fellows of Harvard College v. Nanostring Technologies Inc.</i> , C.A. No. 22-261-MFK (March 1, 2023 D. Del.) (No. 92)
2024	Declaration of Hari Shroff, Ph.D., in Support of Patent Owner’s Response
2027	<i>Curriculum Vitae</i> of Julie L. Davis
2028	“Bruker Completes Asset Acquisition of NanoString Business,” Bruker Corporation Press Release, May 6, 2024 (accessible at https://ir.bruker.com/press-releases/press-release-details/2024/Bruker-Completes-Asset-Acquisition-of-NanoString-Business/default.aspx , last accessed December 9, 2024)
2029	“Who We Are,” NanoString Technologies, Inc. (accessible at https://nanostring.com/about-us/ , last accessed December 9, 2024)
2030	“CosMx™ SMI for Single-Cell Imaging,” NanoString Technologies, Inc. (accessible at https://nanostring.com/products/cosmx-spatial-molecular-imager/single-cell-imaging-overview/ , last accessed December 9, 2024)
2031	“NanoString Begins Commercial Shipments of CosMx Spatial Molecular Imager and AtoMx Spatial Informatics Platform,” BusinessWire, December 6, 2022 (accessible at https://www.businesswire.com/news/home/20221206005433/en/NanoString-Begins-Commercial-Shipments-of-CosMx-Spatial-Molecular-Imager-and-AtoMx-Spatial-Informatics-Platform , last accessed December 9, 2024)

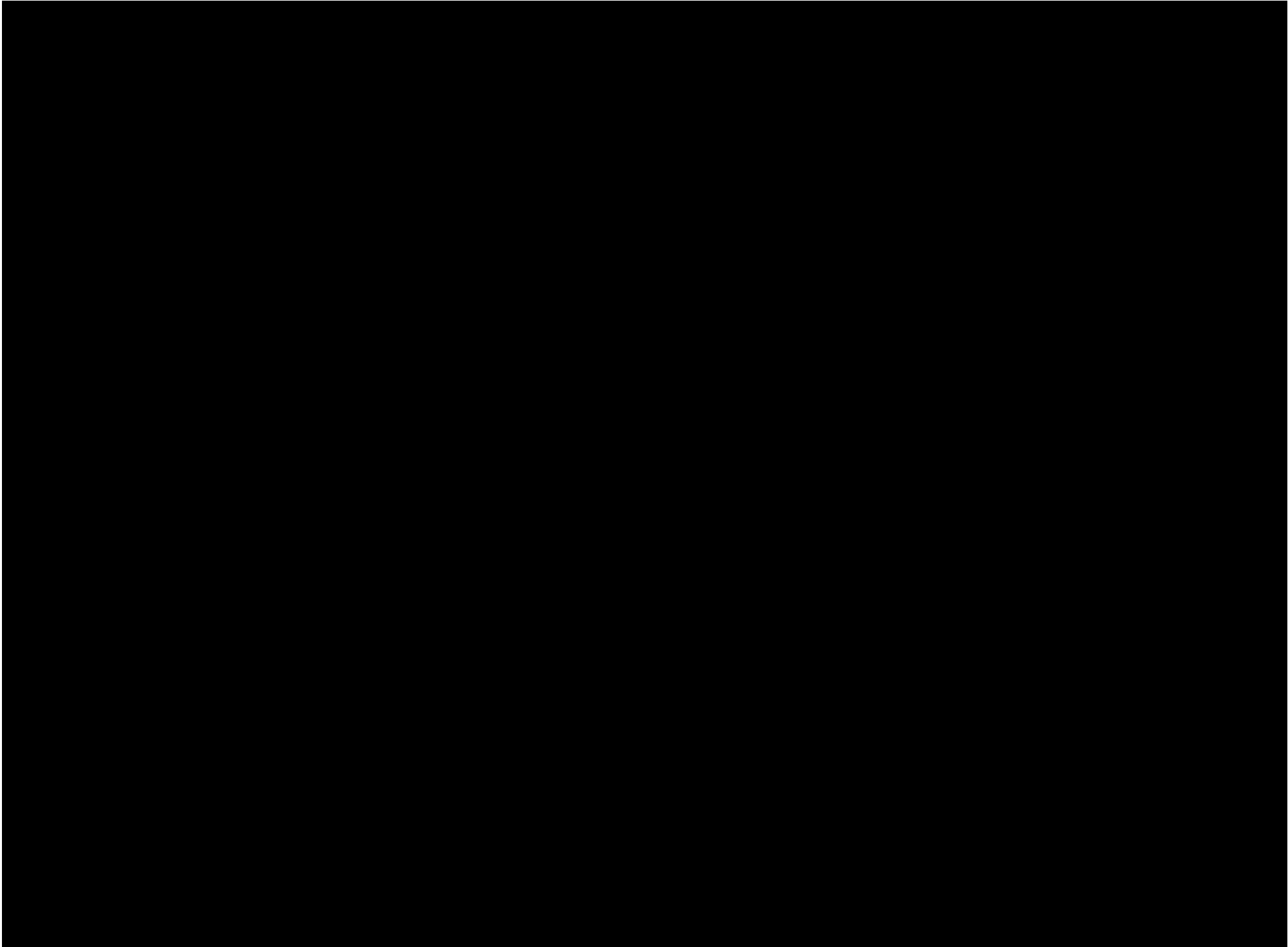
Exhibit No.	Description
2032	NanoString Technologies, Inc. Form 10-K for the fiscal year ended December 31, 2022
2033	“Our mission,” 10x Genomics, Inc. (accessible at https://www.10xgenomics.com/company , last accessed December 9, 2024)
2034	10x Genomics, Inc. Form 10-K for the fiscal year ended December 31, 2023
2035	“10x Genomics Commercially Launches Xenium Platform for In Situ Analysis,” PR Newswire, December 8, 2022 (accessible at https://www.prnewswire.com/news-releases/10x-genomics-commercially-launches-xenium-platform-for-in-situ-analysis-301698748.html , last accessed December 9, 2024)
2036	“Xenium In Situ,” 10x Genomics, Inc. (accessible at https://www.10xgenomics.com/platforms/xenium , last accessed December 9, 2024)
2037	“10x Genomics Begins Commercial Shipments of Xenium Prime 5K Pan-Tissue and Pathways Panel,” PR Newswire, June 20, 2024 (accessible at https://www.prnewswire.com/news-releases/10x-genomics-begins-commercial-shipments-of-xenium-prime-5k-pan-tissue-and-pathways-panel-302177116.html , last accessed December 9, 2024)
2038	“The First Fully Integrated Single-Cell Spatial Solution,” NanoString Technologies, Inc. (accessible at https://nanosttring.com/products/atomx-spatial-informatics-platform/cosmx-and-atomx-the-first-fully-integrated-single-cell-spatial-solution/ , last accessed December 9, 2024)
2039	“CosMx™ SMI Technology Access Program,” NanoString Technologies, Inc. (accessible at https://nanosttring.com/products/cosmx-spatial-molecular-imager/technology-access-program/ , last accessed December 9, 2024)

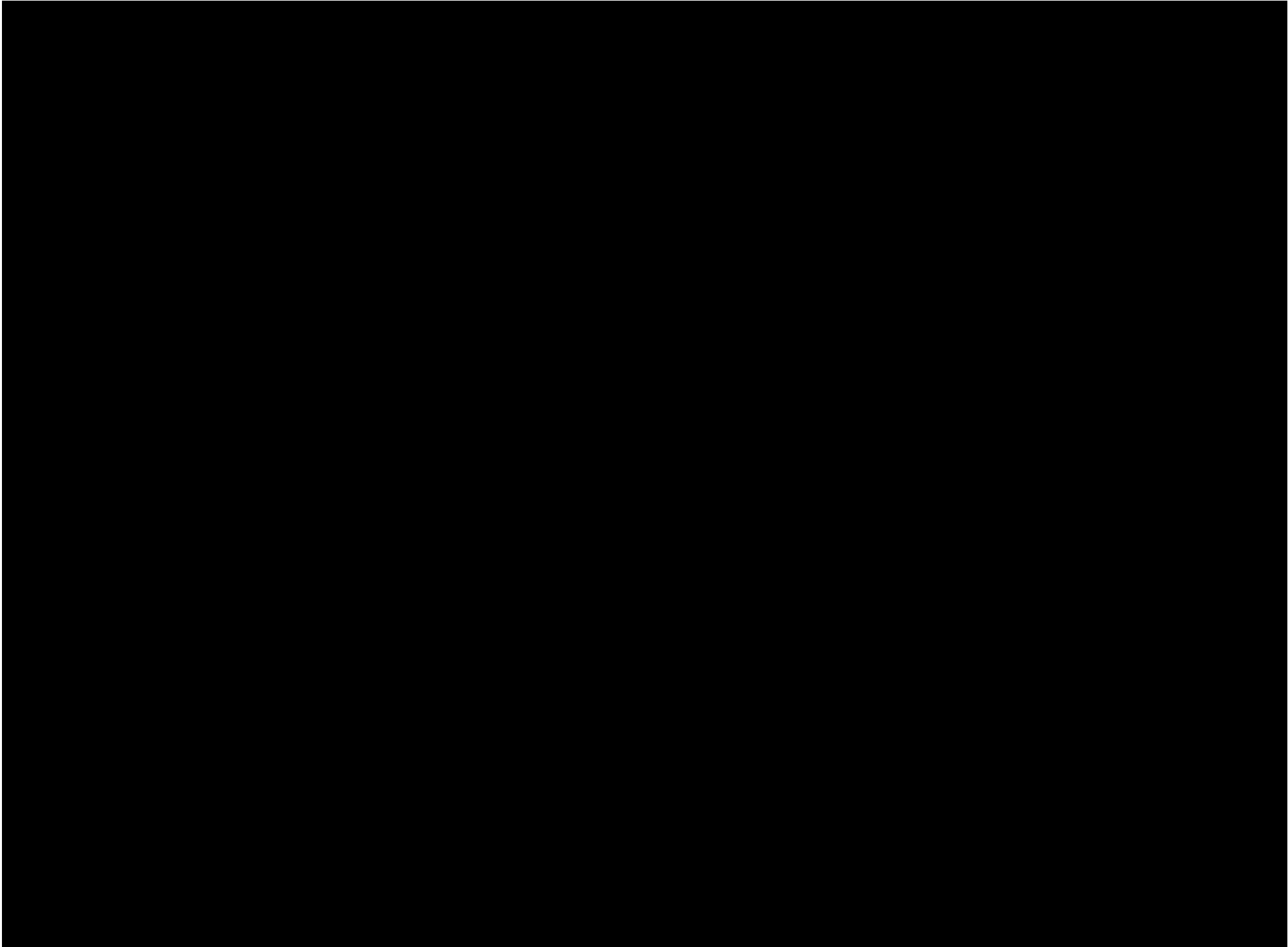
Exhibit No.	Description
2040	“Accelerating the Mastery of Biology to Advance Human Health,” 42 nd Annual J.P. Morgan Healthcare Conference, dated 2024 (accessible at https://s28.q4cdn.com/592666581/files/doc_presentations/2024/01/2024-TXG-JPM-Healthcare-Presentation-vF.pdf , last accessed December 9, 2024)

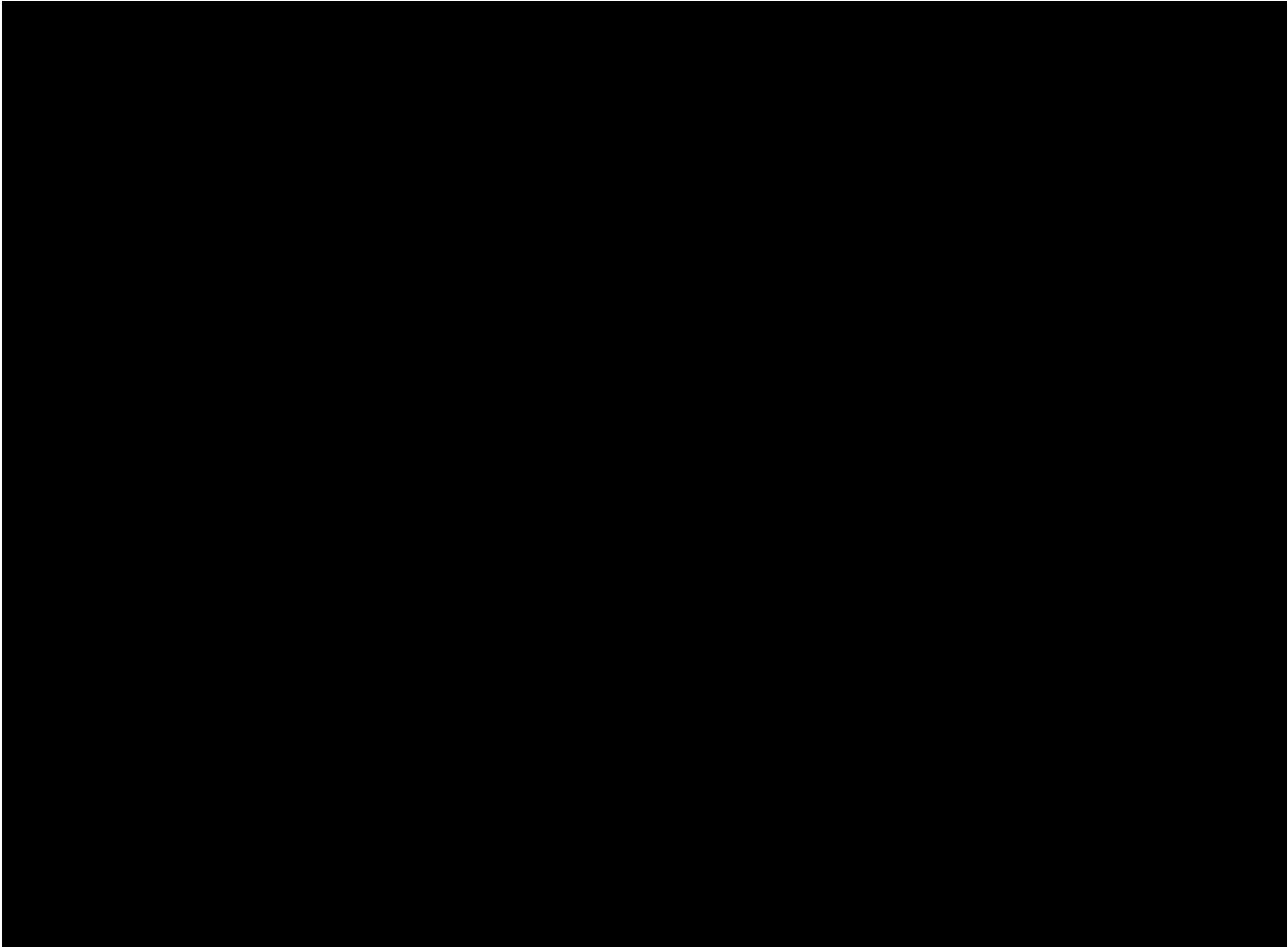
APPENDIX B

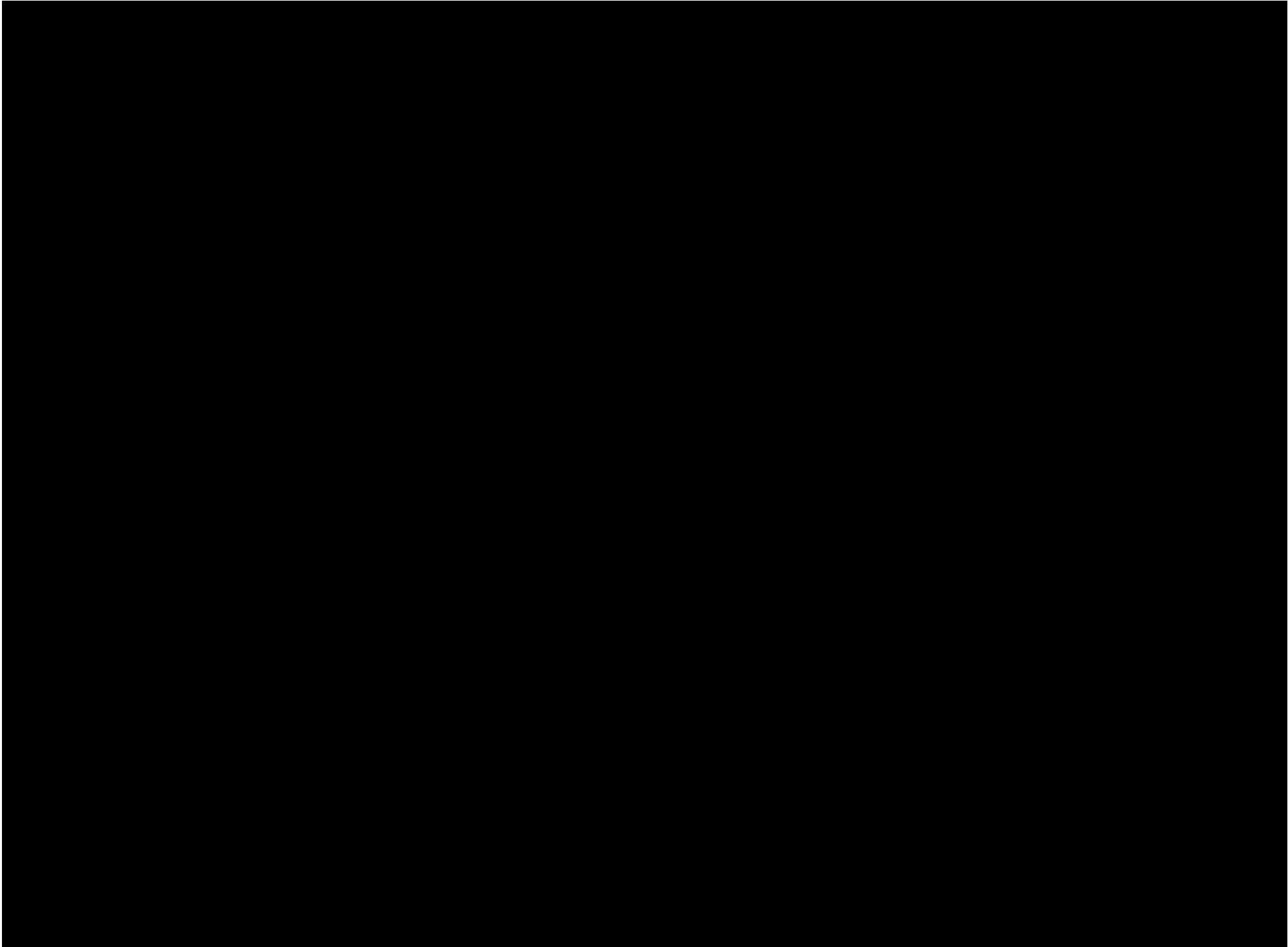


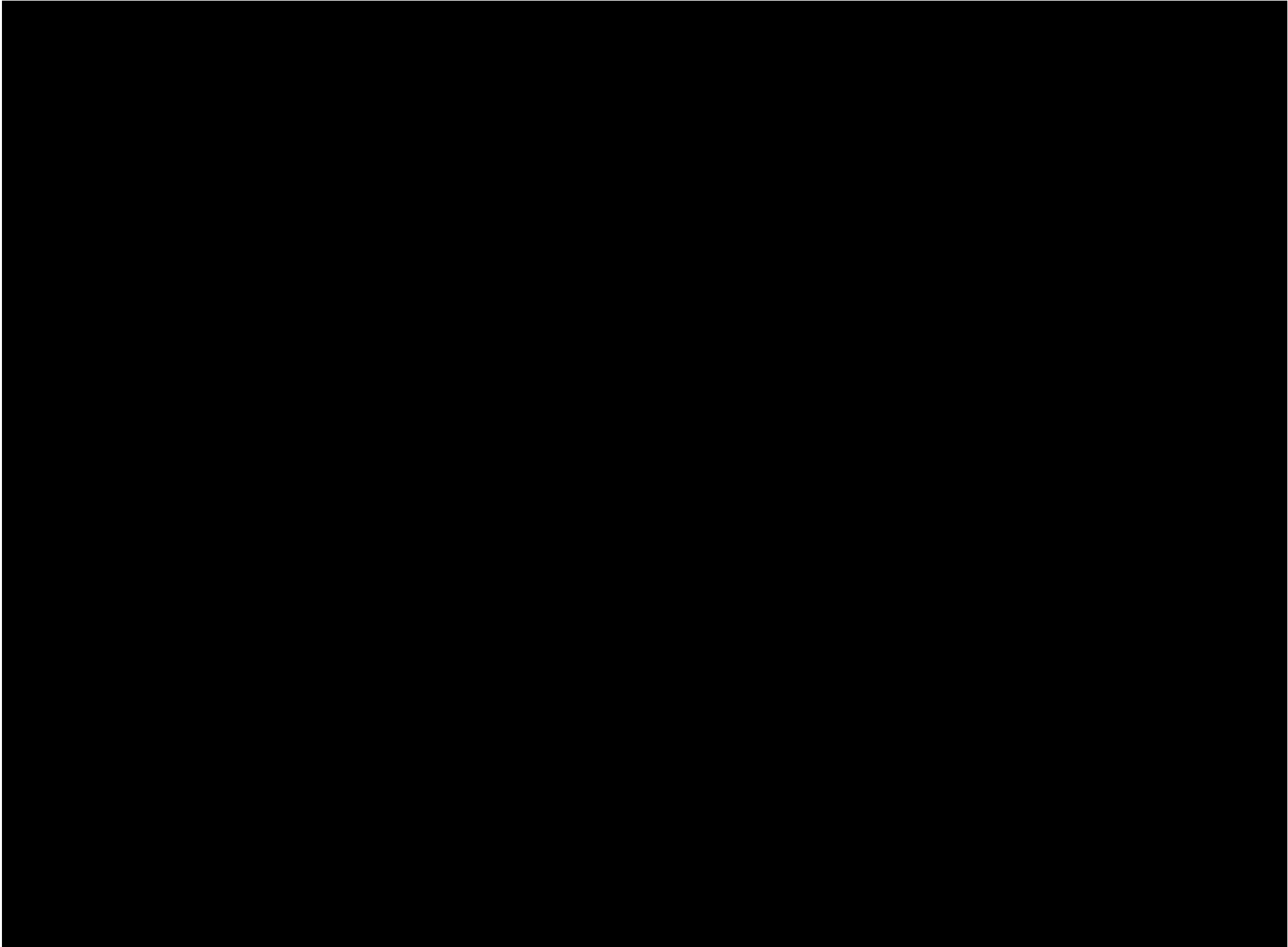












APPENDIX C

