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SILICON VALLEY FIRST CUP OF COFFEE SEMINAR SERIES

UPCOMING SEMINARS:

Artificial Intelligence (AI) Boot Camp

January 12	Computer-Implemented Inventions in Biotechnology and Healthcare, Patentability from European and US Perspective
January 13	M&A and Investment into AI Companies
January 19	AI in Healthcare, An Overview of Key FDA Policies and Developments
January 20	Patent and Trade Secret Protection for Inventions that Use AI
January 21	AI in Hiring and Recruiting
January 28	AI and Copyright

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SILICON VALLEY FIRST CUP OF COFFEE SEMINAR SERIES

UPCOMING SEMINARS:

Artificial Intelligence (AI) Boot Camp

February 2	The Ethics of Artificial Intelligence for the Legal Profession
February 3	AI and Data Privacy
February 4	Patents for Medtech AI: Opportunities and Pitfalls
February 9	IP Landscape of AI Hardware Startups
February 10	The Risks of Bias and Errors in AI-Enabled Decision-Making
February 11	AI in Digital Advisory Offerings: Regulatory Considerations
February 16	Bias Issues and AI

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COMPUTER-IMPLEMENTED INVENTIONS IN BIOTECHNOLOGY AND HEALTHCARE, PATENTABILITY FROM EUROPEAN AND US PERSPECTIVE

January 12, 2021

Presenters

Brett A. Lovejoy, Ph.D.

Andrew J. Gray IV

Morgan Lewis

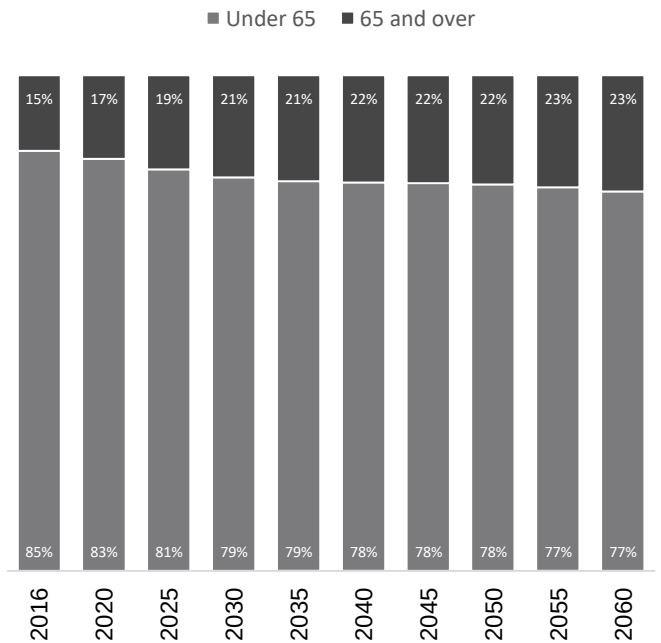
Trends in Adoption of AI in Healthcare

Morgan Lewis

Trends in Adoption of AI in Healthcare

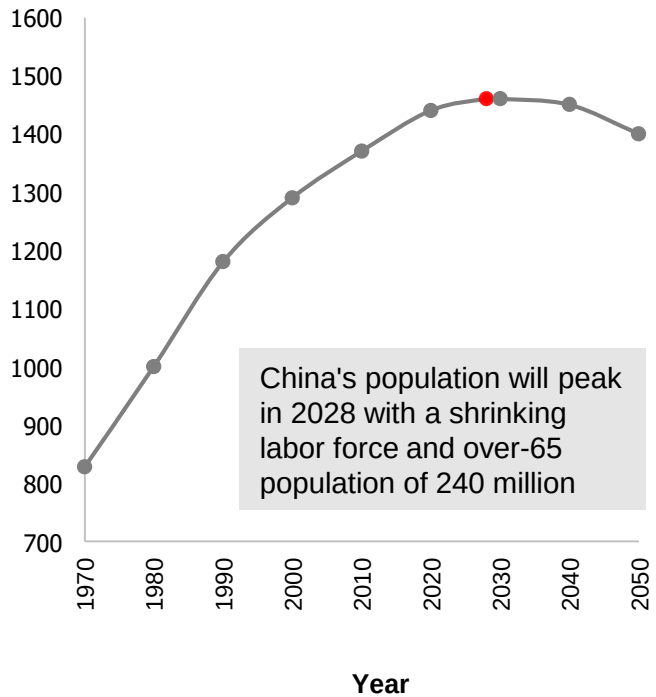
U.S. Population

Population Forecast by Age Group



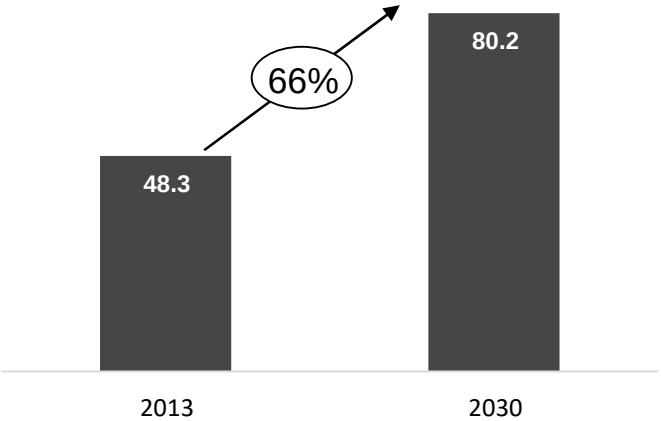
Chinese Population

Population Forecast (in M)



Global Healthcare Workforce

Estimated Health Worker Demand (in M)



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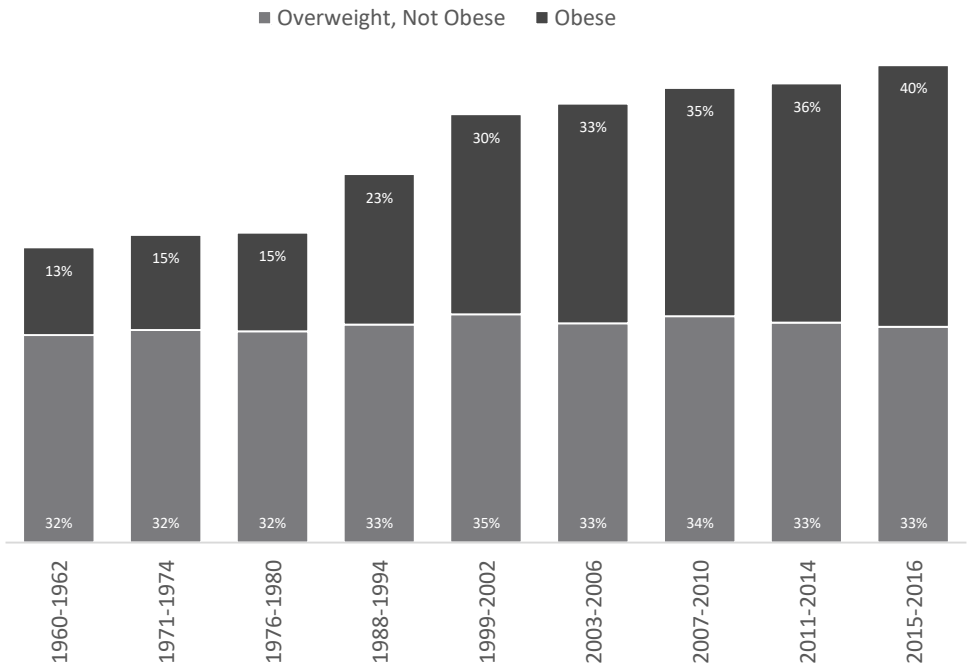
Sources – U.S. Census Bureau; World Population Review; World Health Organization

Trends in Adoption of AI in Healthcare

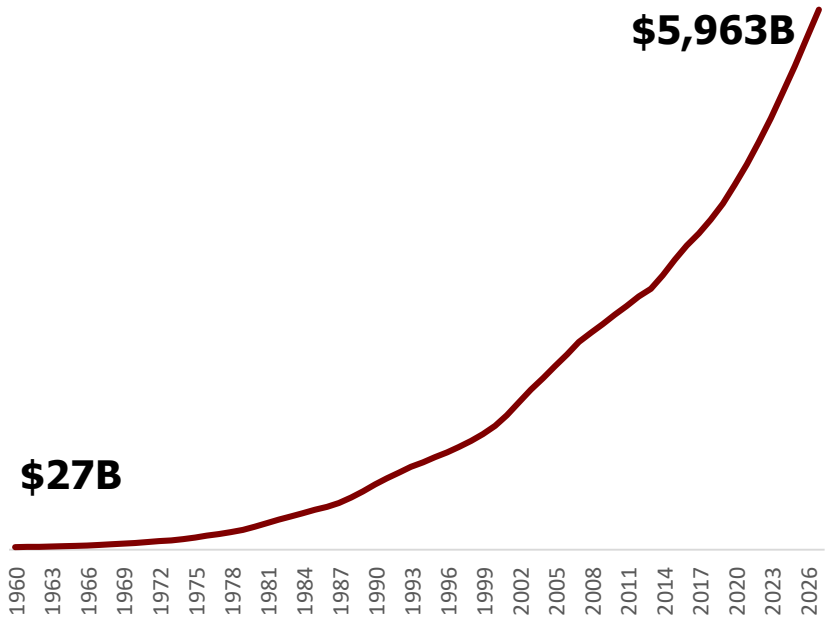
U.S. Obesity

Prevalence of Overweight and Obesity



U.S. Healthcare Spending

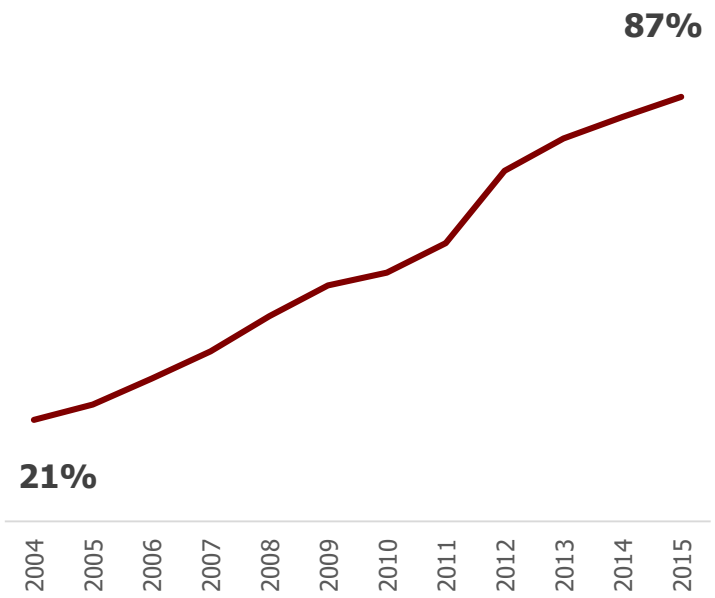
National Health Expenditure Forecast



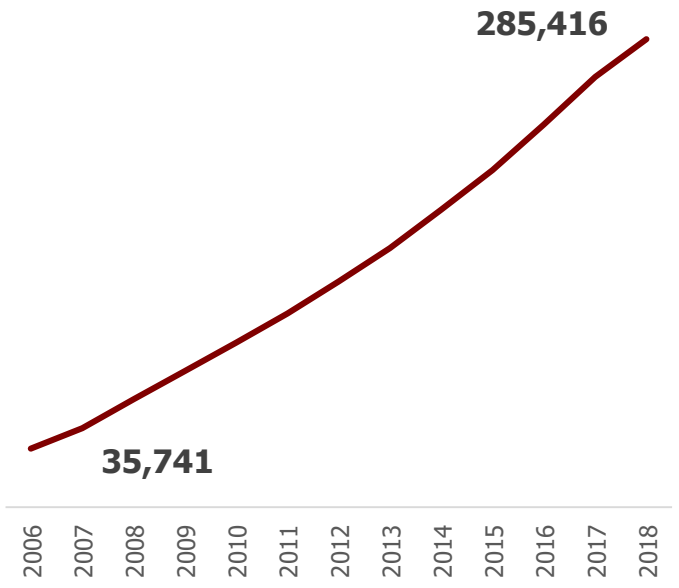
Sources – Milken Institute; CMS

Adoption + Data + Tech → Digital Health Growth

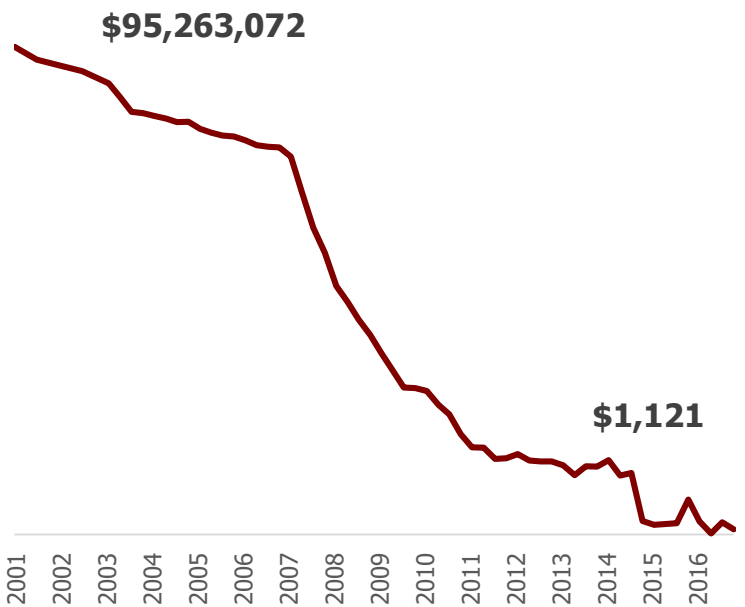
EHR Adoption
U.S. Physician EHR Adoption



Clinical Trials Growth
No. of Registered Studies



Technological Innovation
Cost to Sequence (p/Genome)



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Sources – ONC HIT Health IT Dashboard; U.S. National Library of Medicine (ClinicalTrials.gov); National Human Genome Research Institute

Adoption + Data + Tech → Digital Health Growth

Order Summary

30x Whole Genome Sequencing

We decode 100% of your DNA at 30x coverage using next-generation DNA sequencing technology (150bp paired-end reads), reconstruct your genome (using hg38 assembly) and identify all genetic variants. You get full access to all your DNA data including FASTQ, BAM and VCF files (> 100GB) which you can download anytime. **30x Whole Genome Sequencing offers the best value for money and is the best choice for most people.**

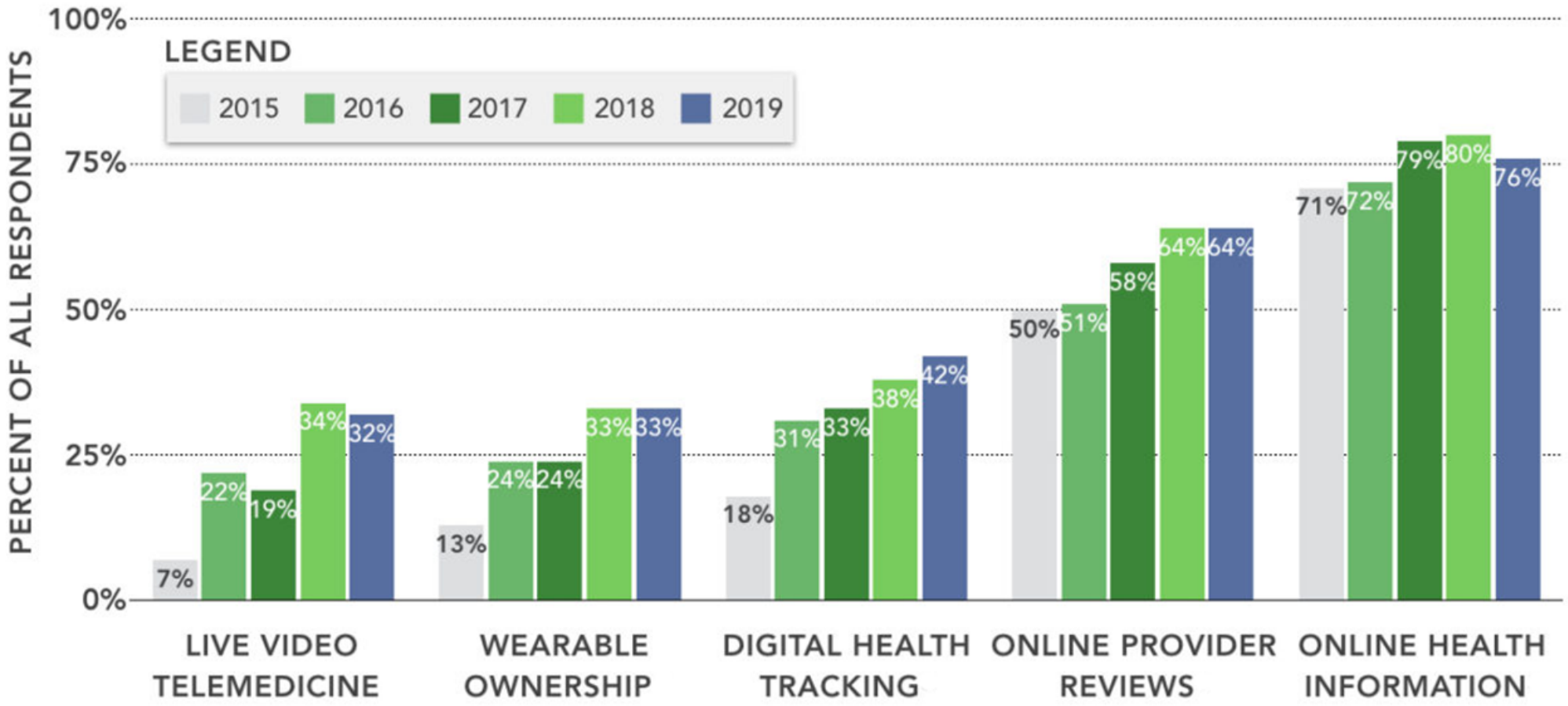
CAP ACCREDITED

QTY: 1

Was: ~~$1000~~

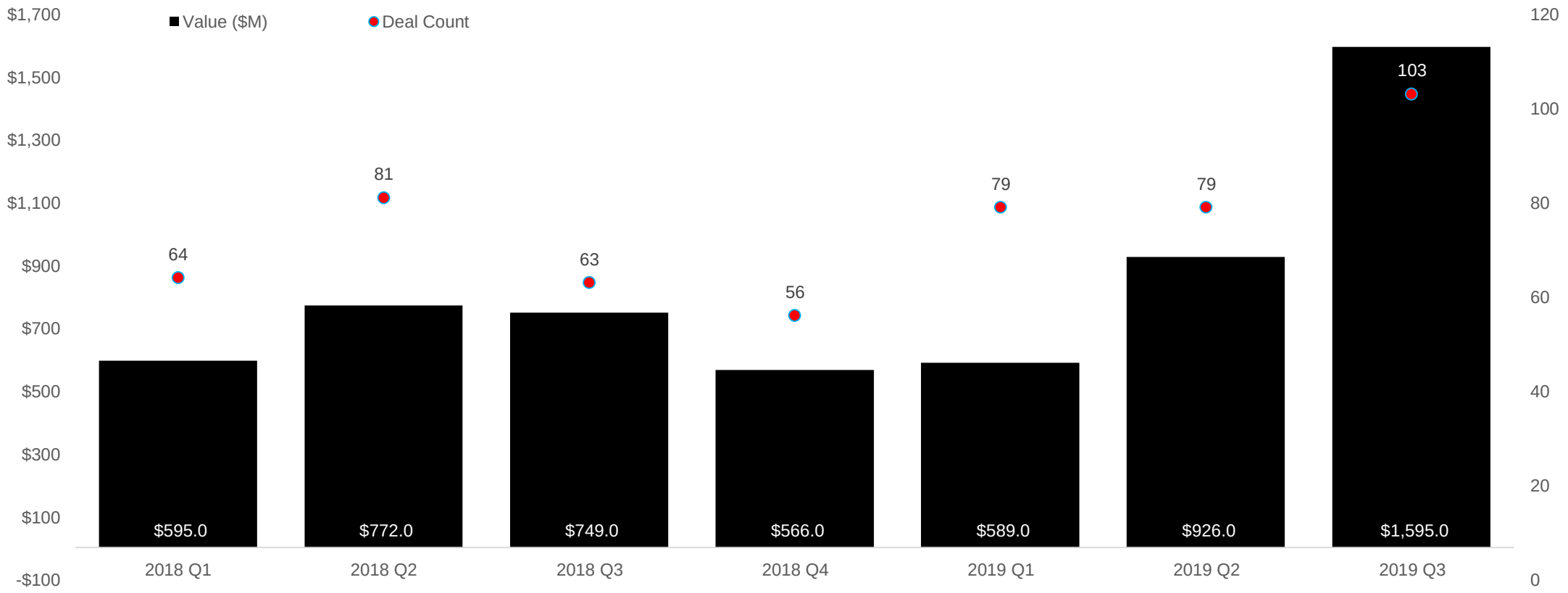
Now: $299

Trends in Adoption of AI in Healthcare



Sources – 2019 Rock Health Digital Health Consumer Adoption Report

Digital Health AI Funding Reaches New High in 2019



Source – CB Insights Global Healthcare Report Q3 2019

Recent Major Deals

10x GENOMICS®

IPO September ’19 (NASDAQ: TXG at $39/share)

Provides next generation sequencing (NGS) kits and tools for analyzing resulting NGS data using artificial intelligence

TEMPUS

Raised $200M in May ’19
Uses artificial intelligence to analyze xT data to match cancer patients with targeted therapies

Atomwise

Raised $123M in August ’20
Deciphering human disease using an AI-drug discovery portfolio

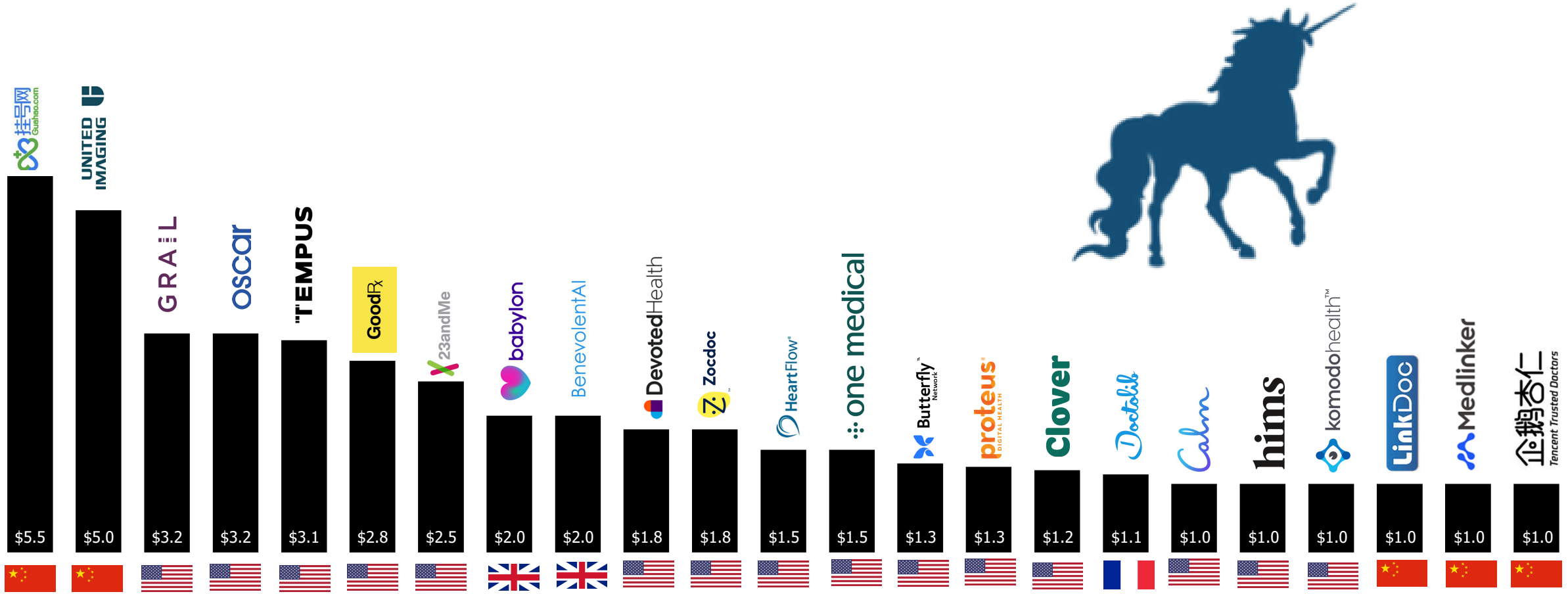
GRAIL

September ’20 Earlier stage cancer detection using machine learning, to be acquired by Illumina in 2021 for $8 billion

GENOMIND®

Raised $22M in October ’20
Mental health biotechnology and digital service company bringing innovative solutions to personalized mental healthcare and wellness through genetic testing

Digital Health Unicorns



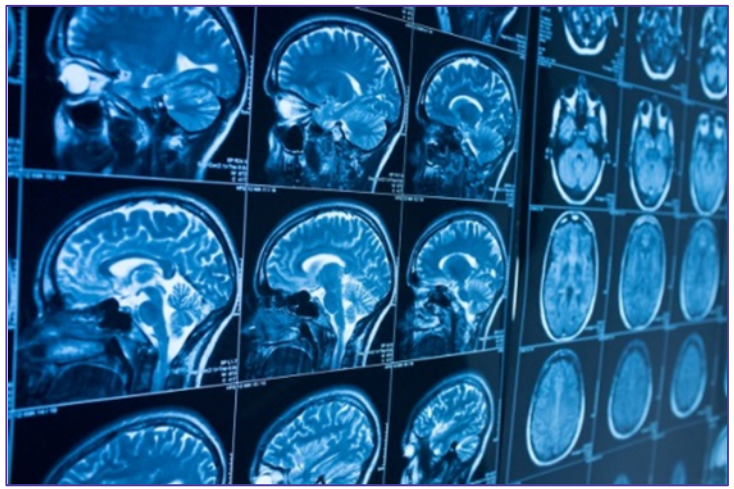
Major AI Categories in Healthcare

- **Medical Imaging and Diagnostics**
  - *"The FDA is greenlighting AI as a medical device."*
- **Advanced Healthcare Biometrics**
  - *"Using neural networks, researchers are starting to study and measure atypical risk factors that were previously difficult to quantify."*
- **Clinical Trial Enrollment**
  - *"One of the biggest bottlenecks in clinical trials is enrolling the right pool of patients. Apple might be able to solve the issue."*
- **Drug Discovery**
  - *"With AI biotech startups emerging, traditional pharma companies are looking to AI SaaS startups for innovative solutions to the long drug discovery cycle."*

Source: CBInsights

AI in Healthcare: U.S.

- 90% of U.S. Hospitals and Insurance companies will implement some type of AI System by 2025
  - **Examples of AI Systems**: Medical image analysis, digital image processing, pattern recognition solutions, machine learning platforms, automated patient guidance and engagement solutions
- Increased adoption of AI will depend on:
  - Innovators' ability to decrease cost an improve accuracy of technology such as natural language processing, big data and cognitive technologies
  - Trust and acceptance of AI tools from healthcare professionals and patients



U.S. LEGAL FRAMEWORK FOR PATENTABILITY OF AI

***Alice Corp. v. CLS Bank International*, 573 U.S. 208 (2014) a computer-implemented, electronic escrow service for facilitating financial transactions held ineligible under 35 U.S.C. § 101 because it covered abstract ideas ineligible for patent protection.**

***Mayo v. Prometheus*, 566 U.S. 66 (2012) Claims directed to a method of giving a drug to a patient, measuring metabolites of that drug, and with a known threshold for efficacy in mind, deciding whether to increase or decrease the dosage of the drug, were not patent-eligible subject matter.**

SYSTEMS AND METHODS FOR IDENTIFYING THERMODYNAMICALLY RELEVANT POLYMER CONFORMATIONS

U.S. Appl No.: 14/409,419

Filed: December 18, 2014

Claims finally rejected under 35 U.S.C. §101 on December 27, 2018

Appeal brief was filed October 28, 2019

Patent Board Decision rendered November 23, 2020

Status: Currently Pending

Publicly held biotechnology company based in Vancouver, British Columbia, that develops protein therapeutics for the treatment of cancer as well as for autoimmune and inflammatory diseases using artificial intelligence approaches

SYSTEMS AND METHODS FOR IDENTIFYING THERMODYNAMICALLY RELEVANT POLYMER CONFORMATIONS (continued)

Claims directed to evaluating an effect of a mutation on a protein.

The mutation is made *in silico* in an atomic protein structure.

A subset of residues is randomly selected about the mutation, and the rotamers of this subset are altered.

Random residue subset selection and rotamer alteration is repeated a number of times to obtain several mutated structures of the protein.

The mutated structures are filtered for thermodynamic stability.

For each residue in the region of the mutation, the rotamers represented by the mutated structures are clustered (based on atomic coordinates).

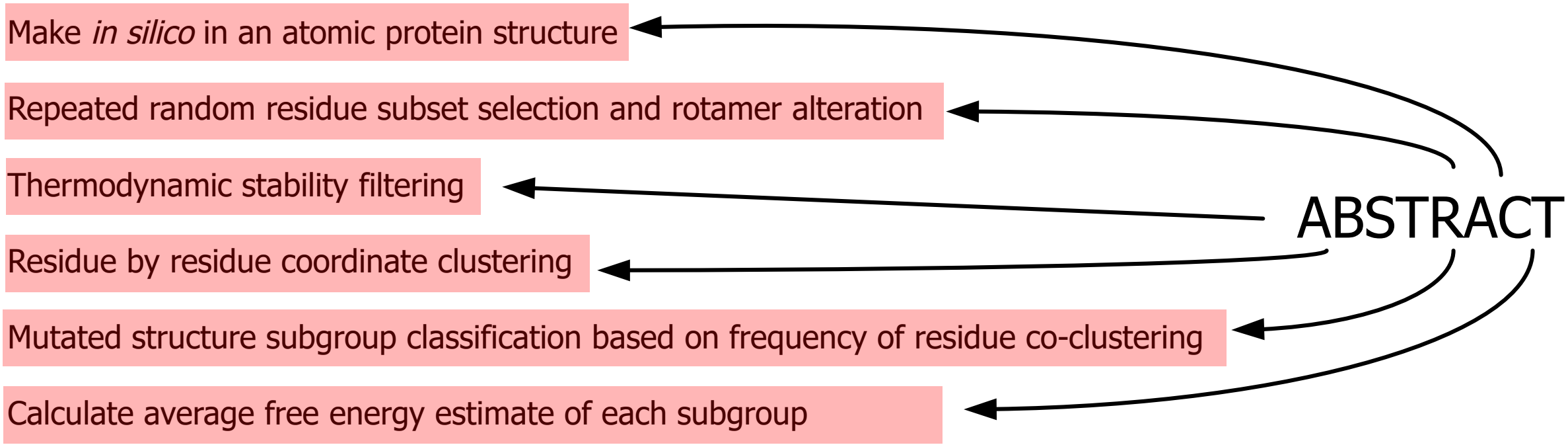
The mutated structures are classified into subgroups based on how often they clustered together (on the residue by residue basis).

A free energy estimate of each subgroup is determined to identify the effect the mutation has on the protein.

SYSTEMS AND METHODS FOR IDENTIFYING THERMODYNAMICALLY RELEVANT POLYMER CONFORMATIONS (continued)

The Examiner Argued:

Prong One (2A-1, are the claims directed to a judicial exception?): Yes. The claims are directed to a judicially recognized exception in the form of a mental process or mathematical concept



SYSTEMS AND METHODS FOR IDENTIFYING THERMODYNAMICALLY RELEVANT POLYMER CONFORMATIONS (continued)

The Examiner Argued:

Prong Two (2A-2, If 2A-1 is affirmative, has the judicial exception been integrated into a practical application?)

- No. There are no positive process limitations recited in the claim for actually using the information produced by the abstract idea outside of the computer.

Step 2B (Do the claims as a whole recite additional limitations such that the claims amount to significantly more than the abstract idea?)

- No. The claims do not improve the computer itself. The limitations as an ordered combination do not amount to a claim as a whole that is significantly more than the abstract idea.

SYSTEMS AND METHODS FOR IDENTIFYING THERMODYNAMICALLY RELEVANT POLYMER CONFORMATIONS (continued)

The Patent Board Adopted Applicant's Arguments and Overturned the Examiner:

An invention is patent-eligible if it claims a "new and useful process, machine, manufacture, or composition of matter." *35 U.S.C. § 101*

However, laws of nature, natural phenomena, and abstract ideas are not patentable (e.g., methods of organizing human activity, fundamental economic practices, mathematical concepts, mental processes). *Alice Corp. v. CLS Bank Int'l*, 573 U.S. 208, 216 (2014), and subsequent cases that rely on *Alice*.

To determine whether a claim falls into an excluded category, use the Supreme Court's two-part framework. *Alice, and Mayo Collaborative Servs. v. Promethius Labs, Inc.* 566 U.S. 66, 75-77 (2012).

- **(Step 2A, Prong 1)** First, determine what the claims are directed to.
- **(Step 2A, Prong 2)** Second, if the claims are directed to an abstract idea, examine the elements of the claims to determine if contains an inventive concept sufficient to transform the claimed abstract idea into a patent-eligible application.
- **(Step 2B, if directed to abstract idea and no transformation)** Are there specific limitations beyond the judicial exception that are not well-understood, routine or conventional?

SYSTEMS AND METHODS FOR IDENTIFYING THERMODYNAMICALLY RELEVANT POLYMER CONFORMATIONS (continued)

The Patent Board Adopted Applicant's Arguments and Overturned the Examiner:

(Step 2A, Prong 1; Determine what the claims are directed to)

- Directed to an abstract idea.

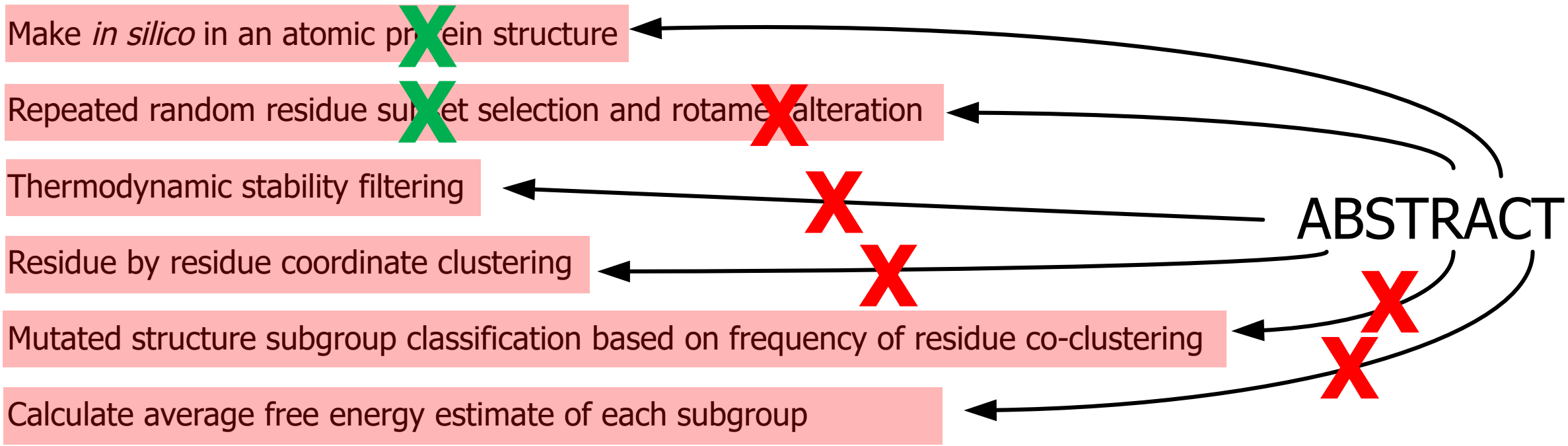
- The first parts of claim 1 are directed to an abstract idea because they can practically be performed in the human mind, and so the claim as a whole recites an abstract idea in the category of mental processes (even though the final parts of the claim including altering side chain rotamer conformations, *etc*. cannot be mentally performed).

- Contrary to the Examiner's assertions, the final elements of the claim do not recite a mathematical concepts. A claim does not fall into the mathematical concept exception if it is only based on or involves a mathematical idea. October 2019 Revised Patent Subject Matter Eligibility Guidance at 3.

SYSTEMS AND METHODS FOR IDENTIFYING THERMODYNAMICALLY RELEVANT POLYMER CONFORMATIONS (continued)

The Patent Board Adopted Applicant's Arguments and Overturned the Examiner:

(Step 2A, Prong 1; Determine what the claims are directed to)



SYSTEMS AND METHODS FOR IDENTIFYING THERMODYNAMICALLY RELEVANT POLYMER CONFORMATIONS (continued)

The Patent Board Adopted Applicant's Arguments and Overturned the Examiner:

(Step 2A, Prong 2; examine the elements of the claims to determine if contains an inventive concept sufficient to transform the claimed abstract idea into a patent-eligible application)

- In addition to the mental concepts of obtaining a protein structure and mutating it, the claims recite altering side-chain rotamers, generating sets of clusters, grouping the mutating structures, and determining a free energy estimate
- The specification states that these additional steps combine configurational sampling and structural clustering in novel ways and determines free energies close to the thermodynamic ground state.
- Thus, the claimed method, according to the specification, improves known methods of modeling the effect of mutations on the stability of proteins.
- Thus, the claimed method represents an improvement in the technical field of protein engineering and rational protein design.
- A physical step, such as actually making a mutant protein, is not required in order for the claimed method to constitute a practical application of the recited mental process. *McRO, Inc. v. Bandai Namco Games Amer. Inc.*, 837 F. 3d 1299, 1315 (Fed. Cir. 2016).
- One practical application of the recited claim is to rule out the manufacture of certain mutations that the modeling determines is not stable.

Synopsis

Make as many claim elements as possible incapable of being mentally performed

Provide basis in the specification for why the claim elements that cannot be mentally performed are novel, non-obvious, and integrated into a practical application

The more claim elements that are incapable of being mentally performed, the more you have to work with in terms of making the case under Prong Two (2A-2) that the abstract idea has been integrated into a practical application

U.S. LEGAL FRAMEWORK FOR PATENTABILITY OF AI

ADDITIONAL CASE STUDIES

CASE STUDY 2: SYSTEMS AND METHODS FOR OPTIMIZING MANAGEMENT OF PATIENTS WITH MEDICAL DEVICES AND MONITORING COMPLIANCE

- Mount Sinai US Application No.: 15/780,890, filed June 1, 2018

- Claims drawn to health care provider monitor compliance
  - First process:
    - Obtain data elements, each from an implanted medical device in a different subject
    - Determine condition of each of the medical device from the data elements
    - Record time-stamped medical codes based on the data elements
  - Second process:
    - For each **epoch in a plurality of epochs**, determine overall compliance for the plurality of subjects by checking to see if a code has been recorded for each subject
  - Third process:
    - Responsive to a compliance request, provide compliance information, provide suggested treatment options, provide list of subjects that appear not to be receiving required standard of care

- Rejected under 35 U.S.C. § 101 on February 14, 2019

CASE STUDY 2: SYSTEMS AND METHODS FOR OPTIMIZING MANAGEMENT OF PATIENTS WITH MEDICAL DEVICES AND MONITORING COMPLIANCE (continued)

In the February 14, 2019 Office Action, the Examiner Argued:

Prong One (2A-1, are the claims directed to a judicial exception?):

- Yes. The claims are directed to mathematical concepts, mental processes and/or methods of organizing human activity (*e.g.,* determining whether the first medical codes have been recorded in the medical record is a mental process because it can be performed in the human mind).

Prong Two (2A-2, If 2A-1 is affirmative, has the judicial exception been integrated into a practical application?)

- No. The additional claim elements add insignificant extra-solution activity to the abstract ideal They merely link the use of the judicial exception to a particular technological environment or field of use.

Step 2B (Do the claims as a whole recite additional limitations such that the claims amount to significantly more than the abstract idea?)

- No. The additional claim elements amount to no more than recitation of a generic computer or functions that are well understood or routine.

CASE STUDY 2: SYSTEMS AND METHODS FOR OPTIMIZING MANAGEMENT OF PATIENTS WITH MEDICAL DEVICES AND MONITORING COMPLIANCE (continued)

Applicant's June 11, 2019 Reply to the February 14, 2019 Office Action

- Amended the claims in view of USPTO's Analysis in June 2018 USPTO Memo "Recent Subject Matter Eligibility Decision: *Vanda Pharamaceuticals Inc. v. West-Ward Pharmaceuticals"* (Vanda Memo) to require providing a list of subjects and treatment options based on the compliance information thereby administrating a treatment for a subject based on subject's health conditions.

- Vanda Memo – Unlike the claim at issue in *Mayo*, the *Vanda* claims require administration of the drug to a subject. As a result, the Federal Circuit held the claims in *Vanda* patent eligible under the first step of the Alice/Mayo framework (step 2A) because the claims are directed to a method of using iloperidone to treat schizophrenia rather than being directed to a judicial exception.

CASE STUDY 2: SYSTEMS AND METHODS FOR OPTIMIZING MANAGEMENT OF PATIENTS WITH MEDICAL DEVICES AND MONITORING COMPLIANCE (continued)

June 25, 2019 Final Rejection (35 U.S.C. §101 rejection maintained)

- Applicant's "providing a list of subjects and treatment options based on the compliance information thereby administrating a treatment for the one or more subjects" do not amount to an actual administration of a therapy after data analysis.
- Claims are not solving a technical problem but rather attempt to solve problems rooted in a business process (managing compliance and treatment of subjects).

September 24, 2019 Applicant response

- Removed treatment option
- Made the device more specific "cardiac implantable electronic device"
- **Argued under Step 2A, Prong Two (2A-2, has the judicial exception been integrated into a practical application?) that it improves the field of cardiac health monitoring**
- Argued that the claim recites an ordered combination of specific rules to determine the compliance of a plurality of cardiac implantable electronic medical devices and to provide suggested treatment options for subjects based on the compliance information

CASE STUDY 2: SYSTEMS AND METHODS FOR OPTIMIZING MANAGEMENT OF PATIENTS WITH MEDICAL DEVICES AND MONITORING COMPLIANCE (continued)

October 21, 2019 Rejection

- The 35 U.S.C. § 101 rejection was maintained
- The claims recite several limitations that can be reasonably performed in the human mind and also recite methods of organizing human activity.

February 19, 2020 Response

(i) measuring ~~obtaining~~ the respective data element in the plurality of data elements from a wireless signal transmitted by the corresponding cardiac implantable electronic medical device ~~connected to~~ implanted within a corresponding subject in a first plurality of subjects, wherein the respective data element comprises (a) a medical device identifier and (b) a condition of the cardiac implantable electronic medical device or a medical device measurement.

- February 19, 2020 Examiner interview: the Examiner indicated that the proposed claim amendment would be sufficient to establish that the claim is not directed to an abstract idea because the wireless signal cannot be received by the human mind.

CASE STUDY 2: SYSTEMS AND METHODS FOR OPTIMIZING MANAGEMENT OF PATIENTS WITH MEDICAL DEVICES AND MONITORING COMPLIANCE (continued)

March 5, 2020 Final Rejection (35 U.S.C. § 101 rejection maintained)

- Applicant's "providing a list of subjects and treatment options based on the compliance information thereby administrating a treatment for the one or more subjects" can be a mental process because this limitation can be performed in the human mind and is a method of organizing human activity.
- The active of wirelessly measuring in merely extra-solution activity used t provide a list of subjects and suggested treatments.

June 20, 2020 Interview

- Examiners: Applicant needs to amend the claims to emphasize how the data analysis is used to alter the operation of the implanted device or the computer itself

- Applicants: Proposed to amend claims to specify that the claimed data analysis is used to adaptively change the length of the epoch period (poor compliance, shorter epoch).

September 3, 2020 Case allowed

Synopsis

Consider addressing 35 U.S.C. § 101 under *Vanda* by treating subject with a drug.

Interview cases that have been rejected under 35 U.S.C. § 101 each time the rejection is maintained and request the supervising examiner to participate in second and subsequent interviews

In arguing that the claim elements, as an ordered combination, integrate an abstract idea into a practical application under Step 2A, Prong Two, emphasize some novel change to the environment that arises due to the ordered combination (*e.g.*, change in epoch period)

CASE STUDY 3: SYSTEMS AND METHODS FOR FACILITATING PATIENT SELF-SELECTION (continued)

Astra Zeneca Patent No. 10,325,678, filed January 22, 2018

Claims directed to a method of lowering cholesterol with over the counter statin:

- Subject is asked sex, age, total cholesterol level, pregnant, *etc*., in a survey
- Survey results run against a first set of filters
- The subject is not authorized if subject fails any filter in the first set of filters (*e.g*., pregnancy)
- Survey results run against a second set of filters
- If subject fails any filter in the second set (*e.g*., total cholesterol), the subject is authorized, provided that they acknowledge that they have discussed the risk factor with their physician
- Electronic fulfilment process proceeds if the first and second set of filters are satisfied

CASE STUDY 3: SYSTEMS AND METHODS FOR FACILITATING PATIENT SELF-SELECTION (continued)

May 30, 2018 Office Action - claims rejected under 35 U.S.C. § 101, the Examiner Argued:

Prong One (2A-1, are the claims directed to a judicial exception?):

- Yes. The claims are directed to obtaining an information set from a human, and running the information set against a plurality of filters. The identified abstract idea is analogized to collecting information, analyzing it, and displaying certain results.

Prong Two (2A-2, If 2A-1 is affirmative, has the judicial exception been integrated into a practical application?)

- No. The additional verbiage and limitations recited in the claims all describe the abstract idea or do not amount to significantly more.

Step 2B (Do the claims as a whole recite additional limitations such that the claims amount to significantly more than the abstract idea?)

- No. Essentially, the Applicant is attempting to claim the mental process a physician would perform when deciding whether a statin should be provided to a patient.

CASE STUDY 3: SYSTEMS AND METHODS FOR FACILITATING PATIENT SELF-SELECTION (continued)

Applicant's November 30, 2018 Reply to the May 30, 2018 Office Action

- Amended the claims in view of *Vanda* to require "administering, upon authorization of the provision (of the statin)"

February 6, 2019 Notice of Allowance

- With respect to 35 U.S.C. §101 "The claims recite a method for lowering cholesterol in a human with an over the counter drug by comparing patient survey information to statin safety information and obtaining confirmation of receiving and reading drug information and subsequently administering the statin pharmaceutical composition to a human."

- Therefore, Prong Two (2A-2, If 2A-1 is affirmative, has the judicial exception been integrated into a practical application?), the claims include an additional element that applies or used a judicial exception to effect a particular treatment and so the claims are not "directed to" the judicial exception

CASE STUDY 4: MICROBIAL STRAIN IMPROVEMENT BY A HTP GENOMIC ENGINEERING PLATFORM

Zymergen Patent No. 10,647,980, filed July 1, 2019

Claims directed to a method (using a computer) for engineering a host cell to have improved phenotypic performance comprising:

a) accessing a training dataset with genetic alteration input variables (that have been introduced into a host cell) and measured phenotypic performance variables (associated with the genetic alterations);

b) "developing a predictive machine learning model that is populated with the training data set";

c) generating, *in silico*, design candidate host cells incorporating the genetic alterations;

d) using the predictive machine learning model to predict the expected phenotypic performance of each of the candidate host cells, where

i) at least one design candidate host cell comprises "a consolidated combination" of genetic alterations from the training set, and

ii) the expected phenotypic performance predicted by the machine learning model is based on the introduced genetic alterations and their associated performance measurements in a); and

e) providing some of the design candidate host cells to create engineered host calls.

CASE STUDY 4: MICROBIAL STRAIN IMPROVEMENT BY A HTP GENOMIC ENGINEERING PLATFORM (continued)

Examiner Brusca "The rejection of claims 1-9 under 35 U.S.C. 101 because the claimed invention is directed to an abstract idea without significantly more in the Office action […] **is withdrawn** in view of the arguments presented in the response filed […] that the claims require use of machine learning that is too complex to be a mental process."

a) accessing a training dataset with genetic alteration input variables (that have been introduced into a host cell) and measured phenotypic performance variables (associated with the genetic alterations);

b) "developing a predictive machine learning model that is populated with the training data set";

c) generating, *in silico*, design candidate host cells incorporating the genetic alterations;

d) using the predictive machine learning model to predict the expected phenotypic performance of each of the candidate host cells, where

i) at least one design candidate host cell comprises "a consolidated combination" of genetic alterations from the training set, and

ii) the expected phenotypic performance predicted by the machine learning model is based on the introduced genetic alterations and their associated performance measurements in a); and

e) providing some of the design candidate host cells to create engineered host calls.

CASE STUDY 4: MICROBIAL STRAIN IMPROVEMENT BY A HTP GENOMIC ENGINEERING PLATFORM (continued)

The claim requires both training the model ***and*** application of the model. The claim therefore has a divided infringement issue. From the file history, model training is not required for patentablity. Proposed broadening continuation claim:

A method (using a computer) for engineering a host cell to have improved phenotypic performance comprising:

a) accessing ~~a training dataset with~~ genetic alteration input variables ~~(that have been introduced into a host cell) and measured phenotypic performance variables (associated with the genetic alterations)~~;

~~b) "developing a predictive machine learning model that is populated with the training data set";~~

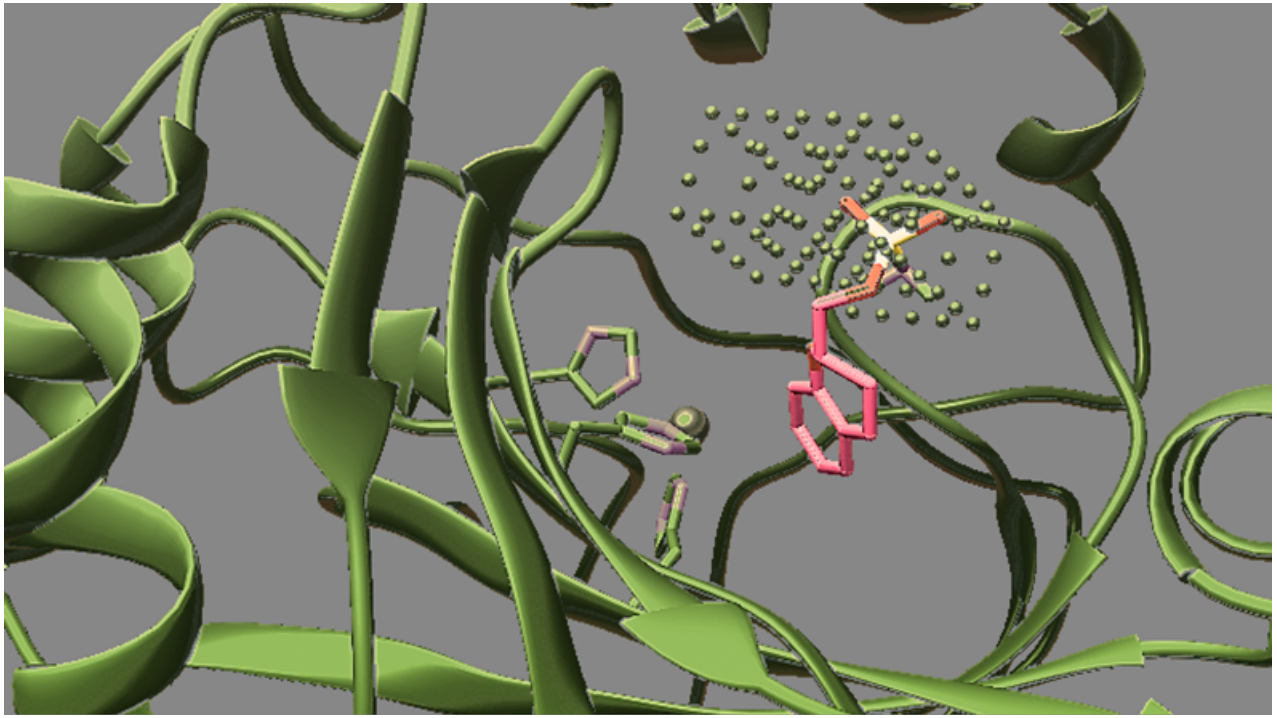
c) generating, *in silico*, design candidate host cells incorporating the genetic alterations;

d) using ~~the~~ a predictive machine learning model to predict the expected phenotypic performance of each of the candidate host cells, where

i) at least one design candidate host cell comprises "a consolidated combination" of genetic alterations from the genetic alteration input variables ~~training set~~, and

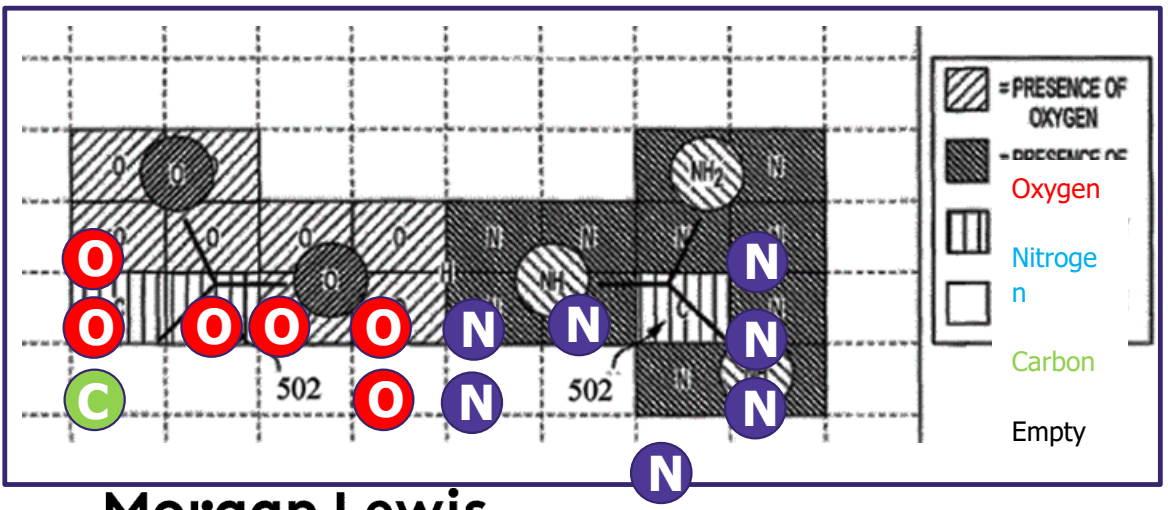
ii) the expected phenotypic performance predicted by the machine learning model is based on ~~the~~ introduced genetic alterations and their associated performance measurements of training data ~~in a~~); and

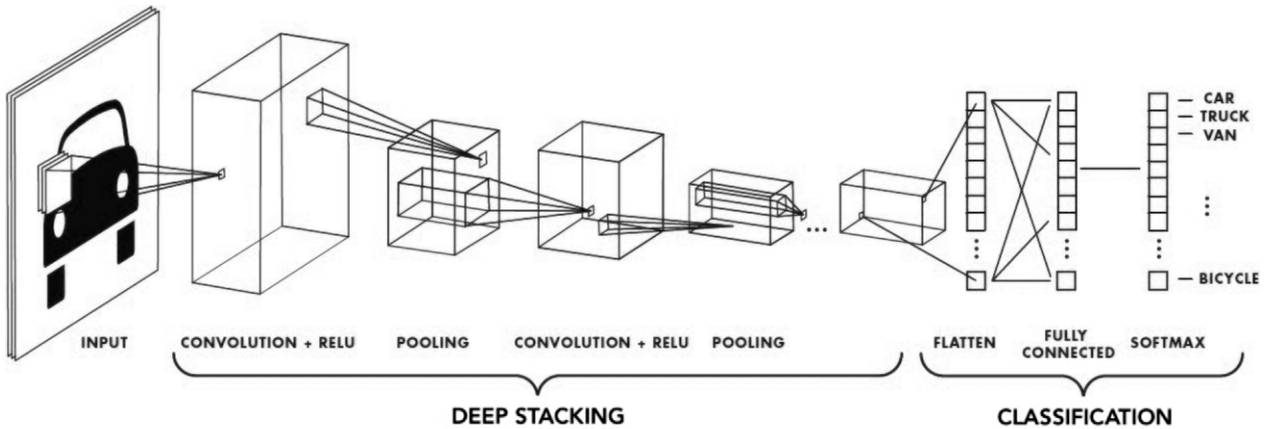
e) providing some of the design candidate host cells to create engineered host calls.



Atomwise

- Founded in 2012
- Based in San Francisco, CA
- ~50 employees
- Annual revenue: USD $2M
- Patented use of deep neural networks for structure-based drug design
- CEO: Abraham Heifets, Ph.D.
  - Formerly at the University of Toronto
  - Created SCRIPDB database and LigAlign protein analysis tool
- 17 investors (ex: B Capital Group, Monsanto Growth Ventures, Y Combinator, Khosla Ventures, DFJ)
- 200 academic collaborations (e.g., Dana Farber Cancer Institute, Tulane, and Duke University)





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10,002,312 Issued 06-19-18 to Atomwise
Systems and Methods for Applying a Convolutional Neural Network to Spatial Data

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

(10) **Patent No.: US 10,002,312 B2**
(45) **Date of Patent: *Jun. 19, 2018**

(54) **SYSTEMS AND METHODS FOR APPLYING A CONVOLUTIONAL NETWORK TO SPATIAL DATA**

(71) Applicant: **Atomwise Inc.**, San Francisco, CA (US)

(72) Inventors: **Abraham Samuel Heifets**, San Francisco, CA (US); **Izhar Wallach**, Tel-Mond (IL); **Michael Dzamba**, San Francisco, CA (US)

(73) Assignee: **Atomwise Inc.**, San Francisco, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 186 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **15/187,018**

(22) Filed: **Jun. 20, 2016**

(65) **Prior Publication Data**

US 2016/0300127 A1 Oct. 13, 2016

Related U.S. Application Data

(63) Continuation of application No. 15/050,983, filed on Feb. 23, 2016, now Pat. No. 9,373,059, which is a
(Continued)

(51) **Int. Cl.**
G06K 9/62 (2006.01)
G06K 9/66 (2006.01)
(Continued)

(52) **U.S. Cl.**
CPC ***G06K 9/66*** (2013.01); ***G06F 19/16*** (2013.01); ***G06F 19/18*** (2013.01); ***G06F 19/24*** (2013.01);
(Continued)

(58) **Field of Classification Search**
None
See application file for complete search history.

(56) **References Cited**

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9,190,053 B2 11/2015 Penn et al.
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(Continued)

FOREIGN PATENT DOCUMENTS

WO WO 2015/168774 A1 11/2015

OTHER PUBLICATIONS

Chae, Myong-Ho, et al. "Predicting protein complex geometries with a neural network." Proteins: Structure, Function, and Bioinformatics 78.4 (2010): 1026-1039. 14 pages.*
(Continued)

Primary Examiner — Ryan P Potts
(74) *Attorney, Agent, or Firm* — Morgan, Lewis & Bockius LLP

(57) **ABSTRACT**

Systems and methods for test object classification are provided in which the test object is docked with a target object in a plurality of different poses to form voxel maps. The maps are vectorized and fed into a convolutional neural network comprising an input layer, a plurality of individually weighted convolutional layers, and an output scorer. The convolutional layers include initial and final layers. Responsive to vectorized input, the input layer feeds values into the initial convolutional layer. Each respective convolutional layer, other than the final convolutional layer, feeds intermediate values as a function of the weights and input values of the respective layer into another of the convolutional layers. The final convolutional layer feeds values into one or more fully connected layers as a function of the final layer weights and input values. The one or more full
(Continued)

1. A computer system for characterization of a test object using spatial data, the computer system comprising:

at least one processor: and

memory addressable by the at least one processor, the memory storing at least one program for execution by the at least one processor, the at least program comprising instructions for:

[...]

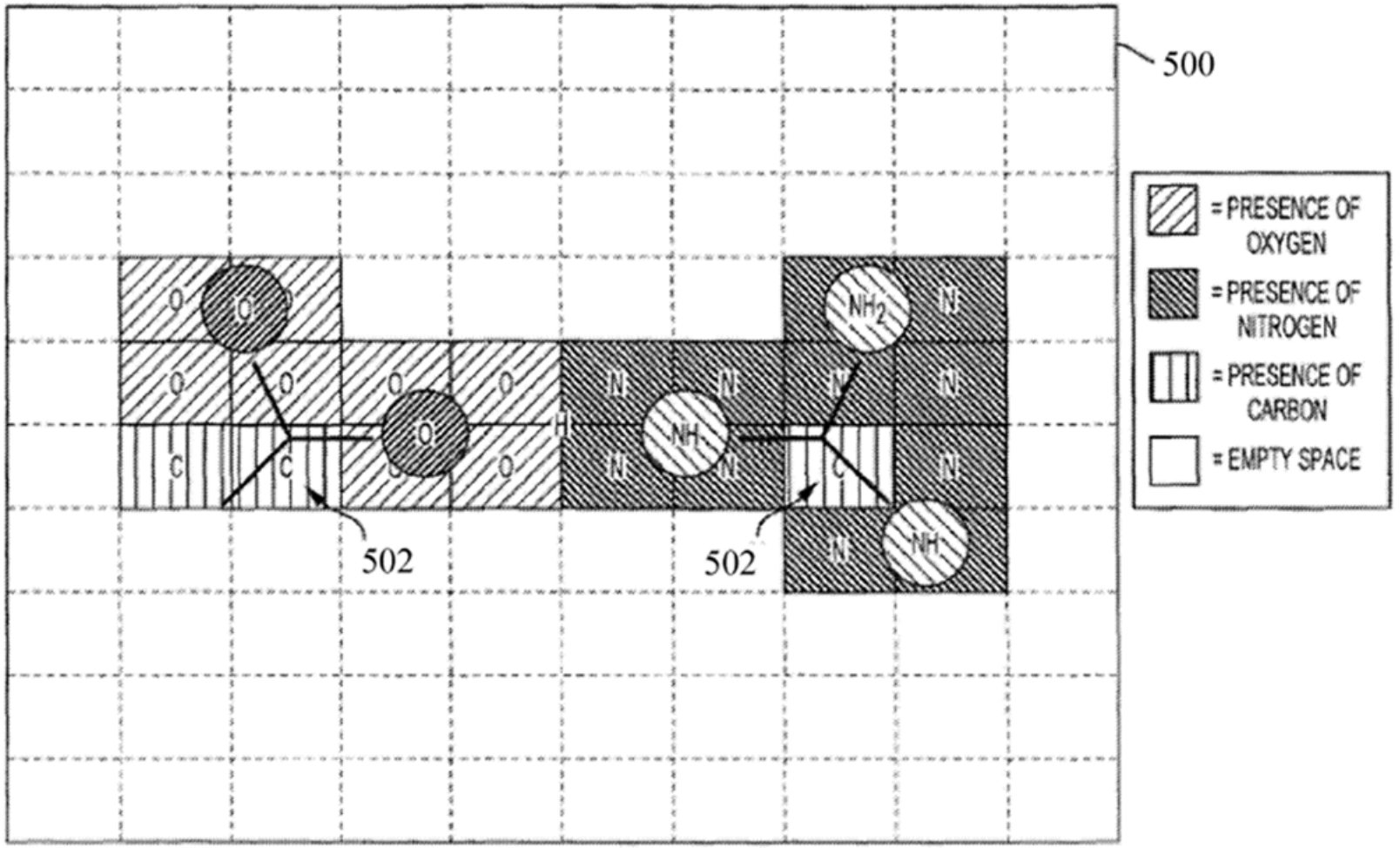
(D) inputting [a] plurality of vectors to a network architecture that includes an input layer for sequentially receiving the plurality of vectors, a plurality of convolutional layers, and a scorer

[...]

(F) using the plurality of scores to characterize [a] test object

10,002,312 - continued

- Sample a test compound after it has been docked to the macromolecular target by encoding, as a plurality of vectors, a three-dimensional matrix representation of the test compound docked to the macromolecular target.



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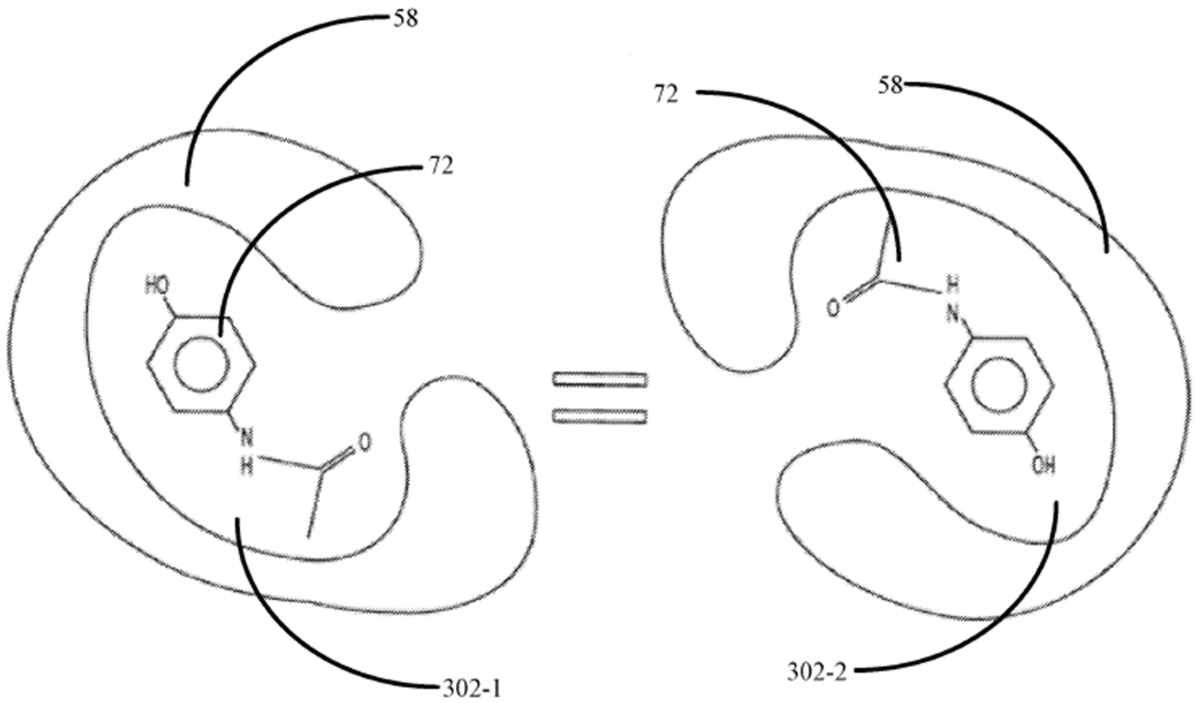
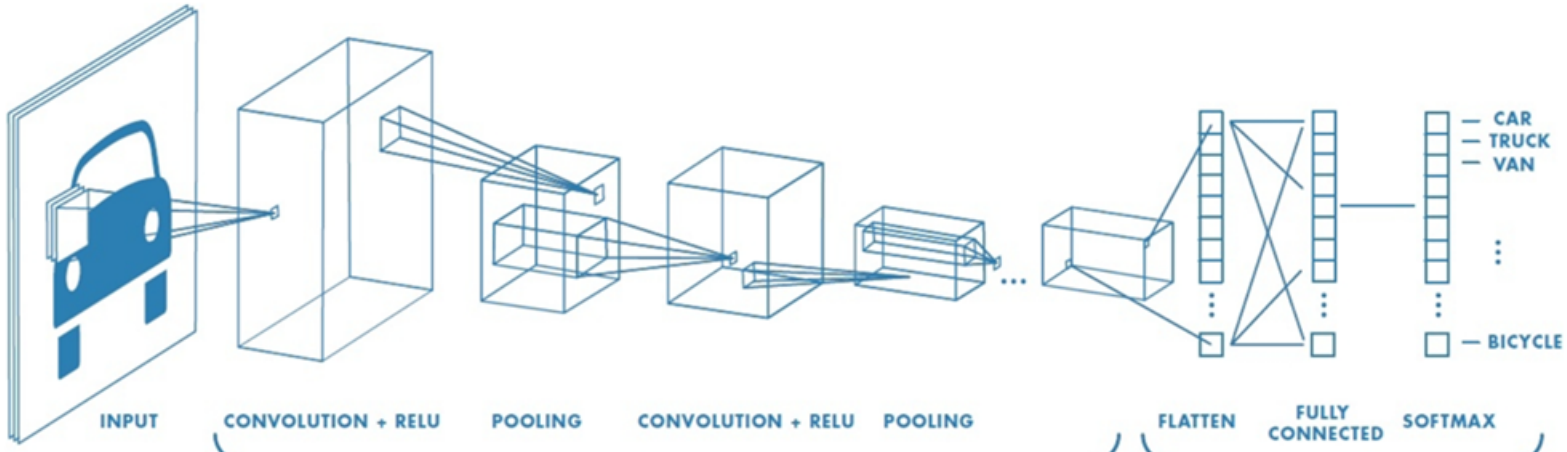
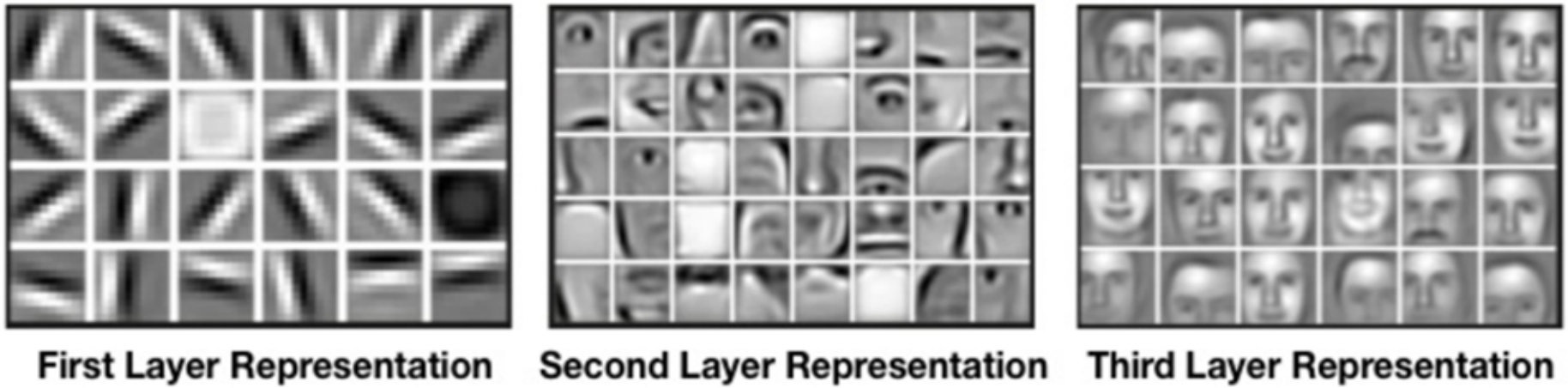


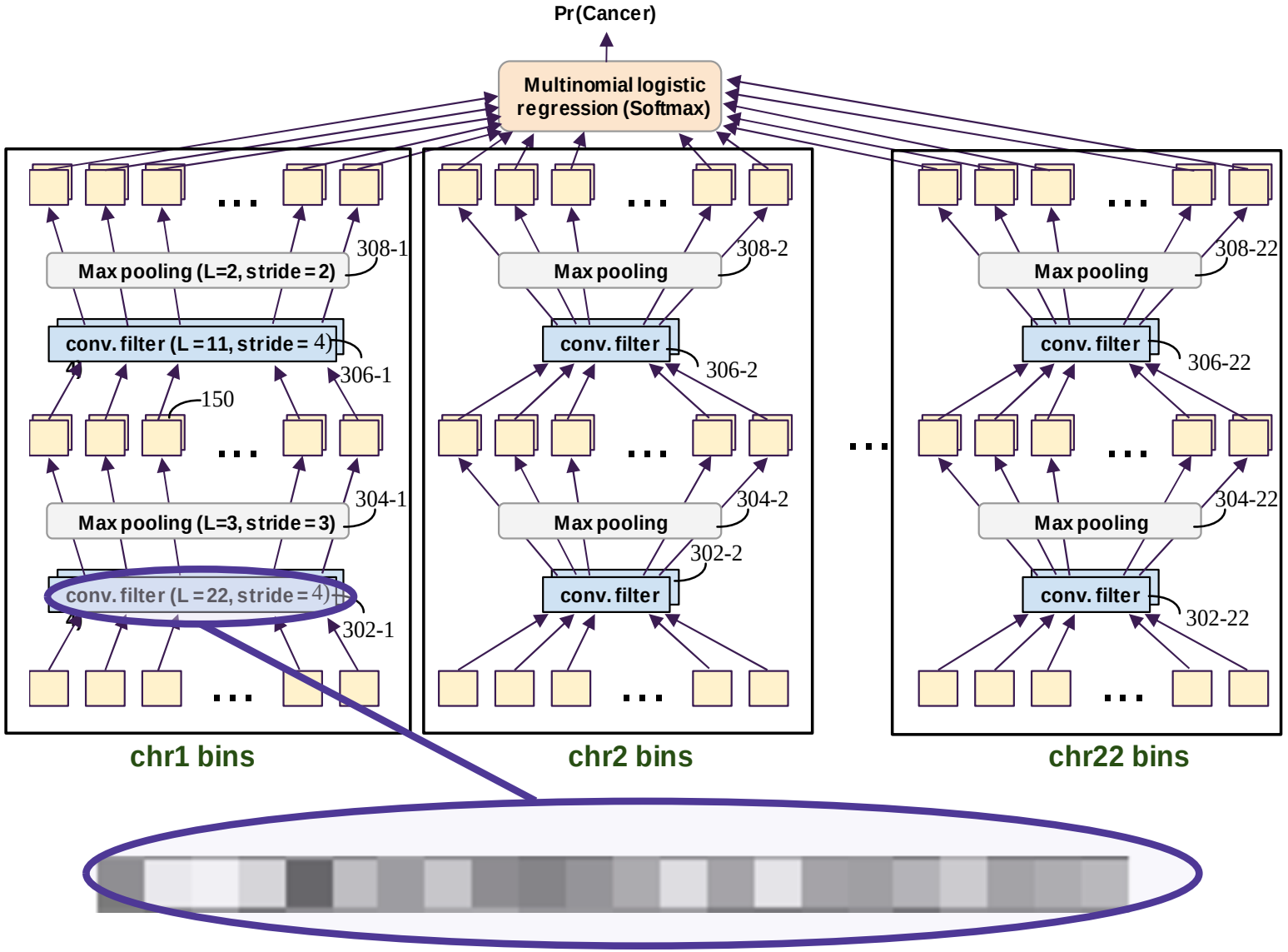
10,002,312 - continued

- Feed the plurality of vectors, which collectively represent the test compound after it has been docked to the macromolecular target, into the same form of convolutional neural network that classically has been trained to recognize objects, such as cars in images, or perform facial recognition.





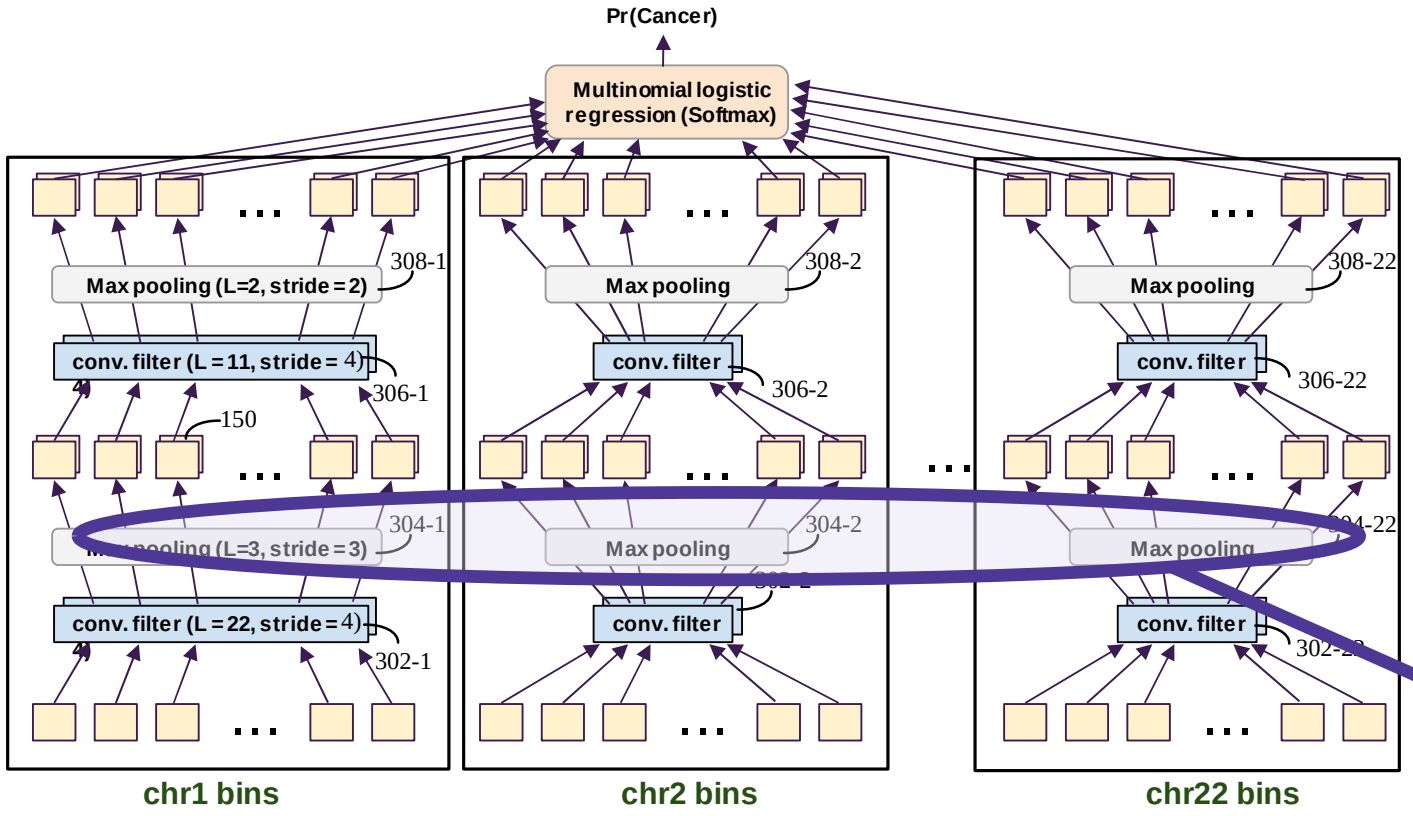
First Layer Representation | Second Layer Representation | Third Layer Representation

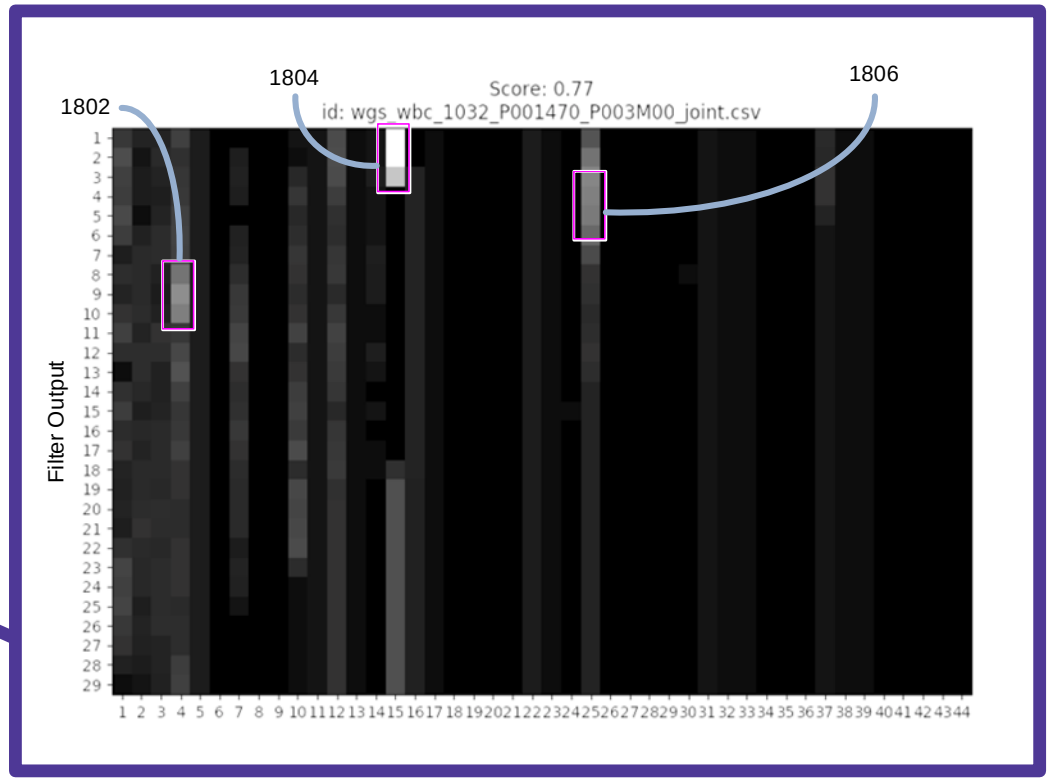


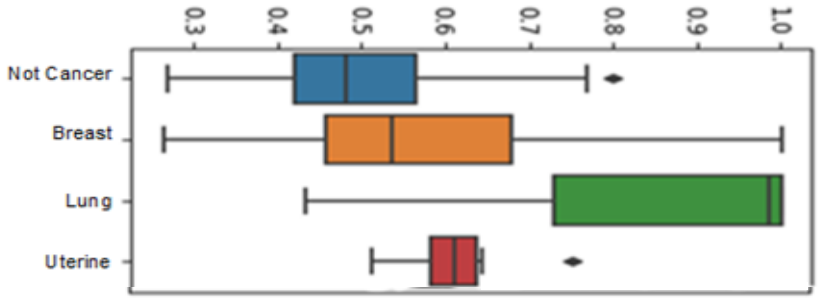
GRAIL

- Founded in 2015
- Based in Palo Alto, CA
- ~500 employees
- Valuation: USD $8B
- Privately held spin out of Illumina
- Focus on use of early cancer detection and tissue of origin determination using patent pending artificial intelligence analysis of cell-free nucleic acid from liquid biopsies
- CEO: Hans Bishop
  - 30+ years experience in biotech
  - Executive Chair of Sana Board and Director at Celgene and Agilent Technologies
  - Former CEO of Juno Therapeutics

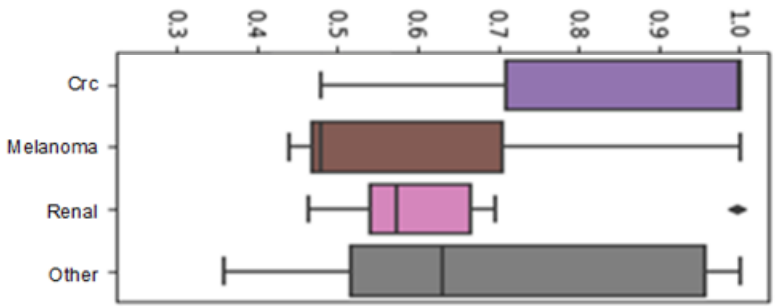
GRAIL







True Positive Rate



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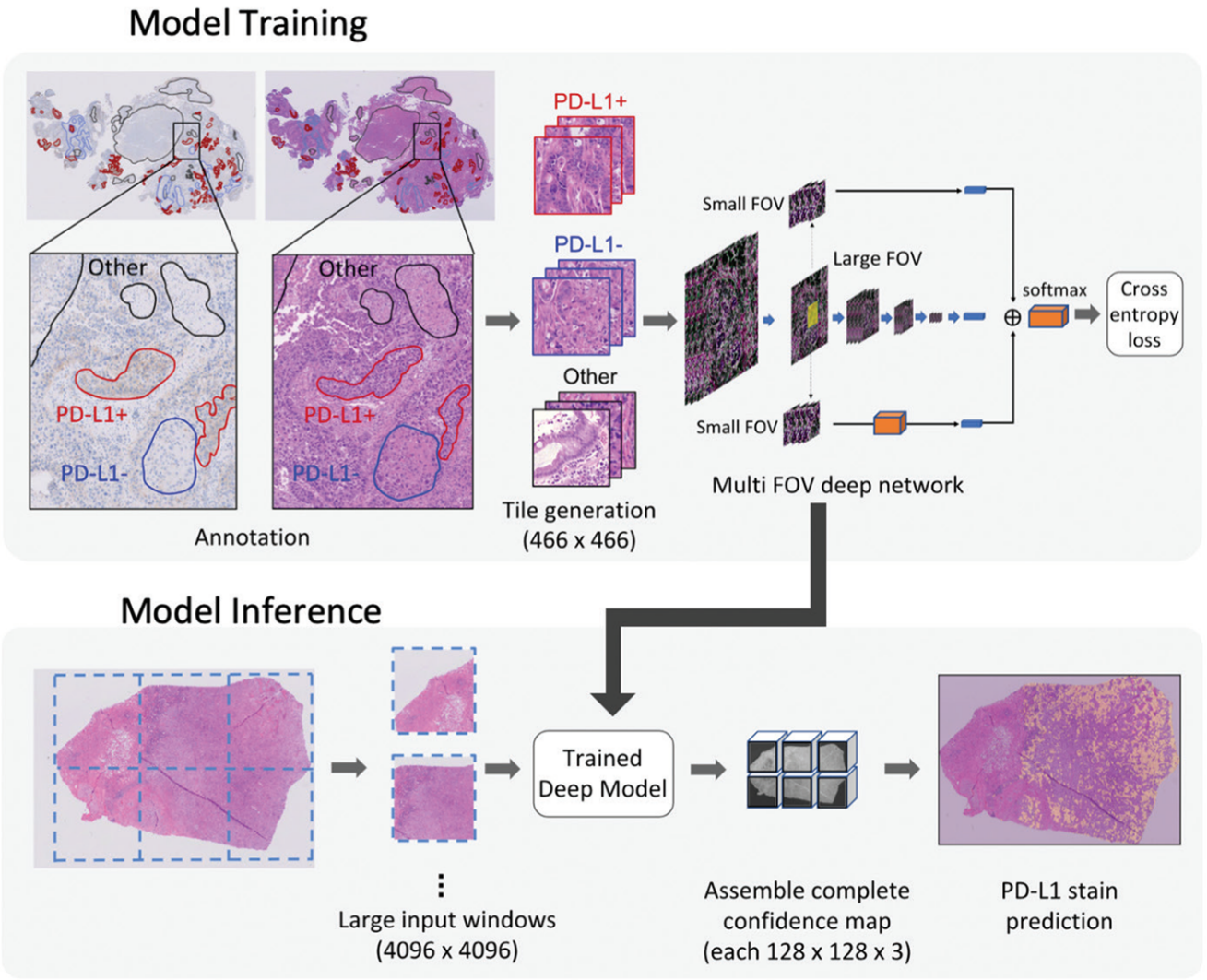
TEMPUS



- Founded in 2015
- Based in Chicago, IL
- ~900 employees
- Valuation: USD $3B
- Developed xT platform that includes (i) analytics of patient's structured clinical data, (ii) molecular data from tumor/normal matched DNA sequencing, (iii) whole-transcriptome RNA sequencing and (iv) immunological biomarker measurements
- Used artificial intelligence to analyze xT data to match cancer patients with targeted therapies
- CEO: Eric Lefkofsky
  - American billionaire businessman
  - Founder of Tempus and Groupon
  - Managing director of Lightbank
- Has raised USD $520 million in venture capital (*e.g.*, Franklin Templeton, New Enterprise Associates)

(12) **United States Patent**
Chaisson

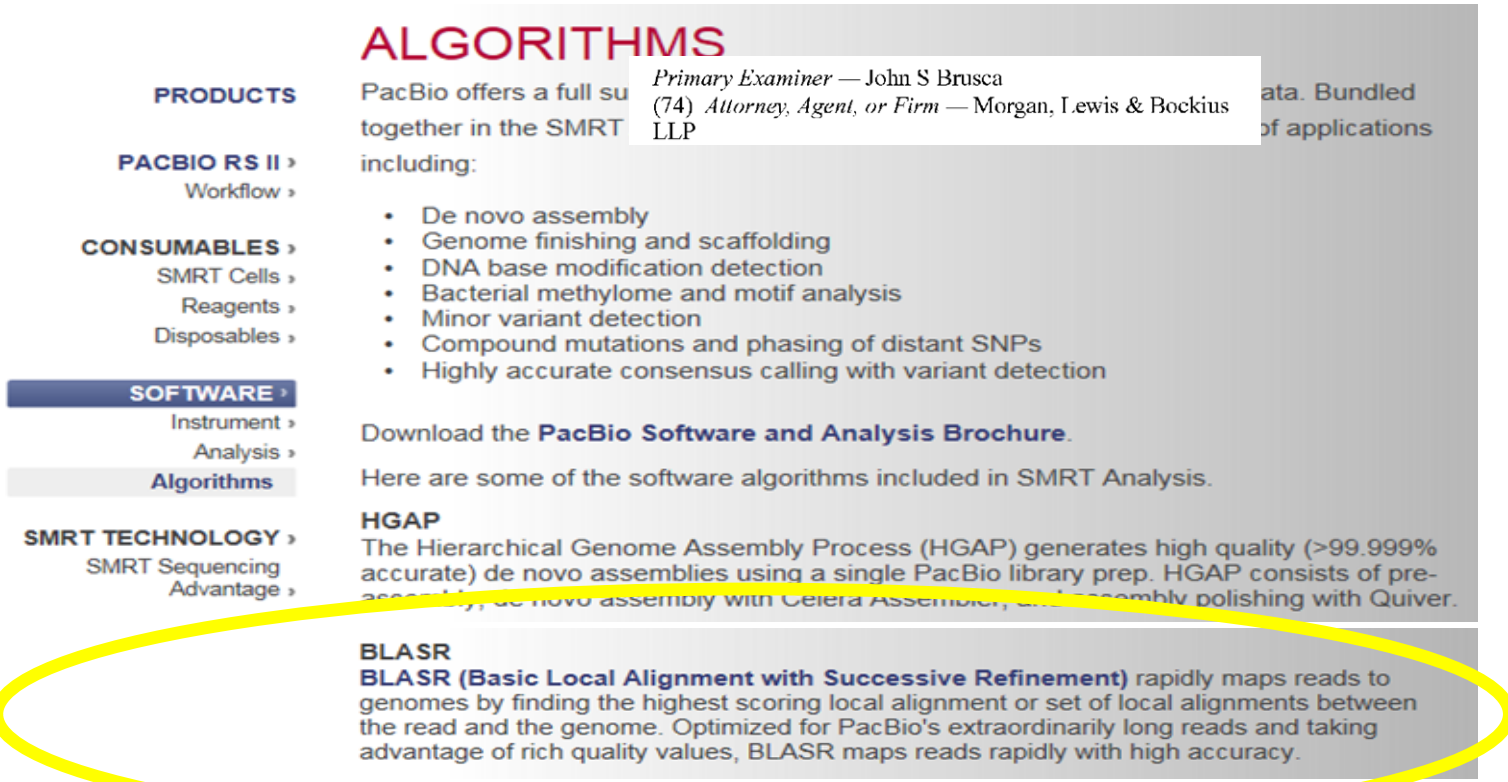
(10) **Patent No.: US 9,165,109 B2**
(45) **Date of Patent: Oct. 20, 2015**

(54) **SEQUENCE ASSEMBLY AND CONSENSUS SEQUENCE DETERMINATION**

(75) Inventor: **Mark Chaisson**, San Francisco, CA (US)

(73) Assignee: **Pacific Biosciences of California, Inc.**, Menlo Park, CA (US)

Primary Examiner — John S Brusca
(74) *Attorney, Agent, or Firm* — Morgan, Lewis & Bockius LLP



PACBIO®

- Founded in 2004
- Based in Menlo Park, California
- ~440 employees
- Applies patented artificial intelligence techniques to analyzing sequence read data
- Presently in contract to be acquired by Illumina for $1.2B
- 2018 Revenue: $78.6M
- CEO: Michael Hunkapiller, Ph.D.
  - 30 year career at Applied Biosystems (acquired by Thermo Fisher Scientific Inc.)

What is claimed is:

1. A method of aligning a sequence read r to a reference sequence g using a minimum match length of k nucleotides, comprising:

a) obtaining the sequence read r of a target nucleic acid by performing a single molecule sequencing assay, wherein the sequence read r has an insertion-deletion error rate of over 5%;

- Founded in 2012
- Based in Pleasanton, California
- ~425 employees
- IPO September 2019 (NASDAQ: TXG at $39/share)
- Now at $51-$56/share (market cap $5B)
- Expected 2019 revenue: $240M
- Provides next generation sequencing (NGS) kits and tools for analyzing resulting NGS data using artificial intelligence
- CEO: Serge Saxonov
  - Founding architect and director of R&D at 23andMe

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

(10) **Patent No.: US 10,347,365 B2**
(45) **Date of Patent: Jul. 9, 2019**

(54) **SYSTEMS AND METHODS FOR VISUALIZING A PATTERN IN A DATASET**

(71) Applicant: **10X Genomics, Inc.**, Pleasanton, CA (US)

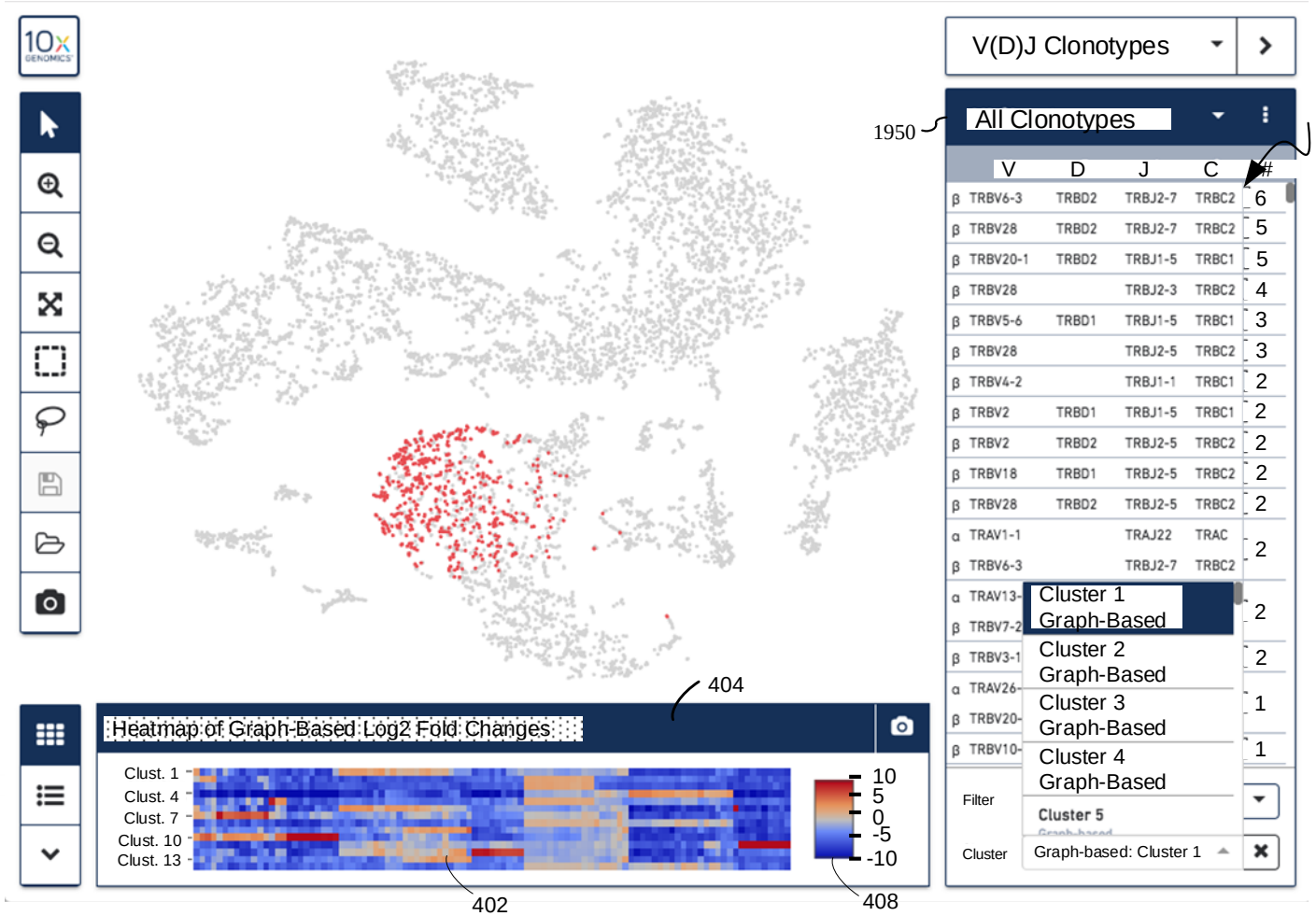
(73) Assignee: **10X GENOMICS, INC.**, Pleasanton, CA (US)

(21) Appl. No.: **15/891,607**

(22) Filed: **Feb. 8, 2018**

(58) **Field of Classification Search**
None
See application file for complete search history.

(74) *Attorney, Agent, or Firm* — Morgan, Lewis & Bockius LLP



RECURSION
pharmaceuticals

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

(10) **Patent No.: US 10,281,456 B1**
(45) **Date of Patent: *May 7, 2019**

(54) **SYSTEMS AND METHODS FOR DISCRIMINATING EFFECTS ON TARGETS**

(71) Applicant: **Recursion Pharmaceuticals, Inc.**, Salt Lake City, UT (US)

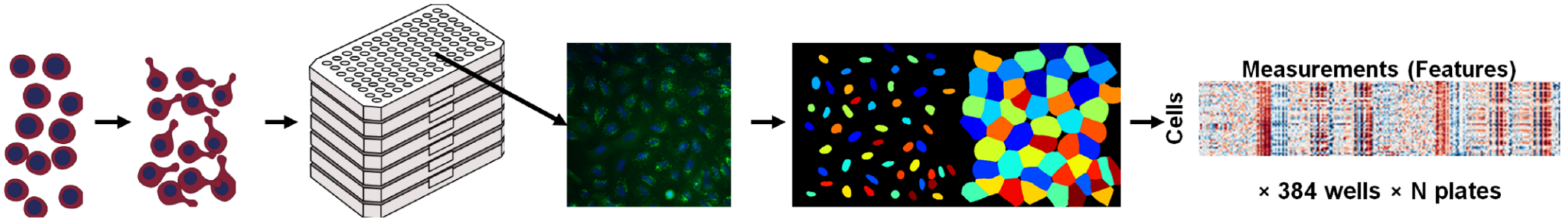
(21) Appl. No.: **15/995,835**

(22) Filed: **Jun. 1, 2018**

Buenrostro et al., 2013, "Transposition of native chromatin for fast and sensitive epigenomic profiling of open chromatin, DNA-binding proteins and nucleosome position," Nature Methods 10, 1213-1218.

Primary Examiner — Russell S Negin
(74) *Attorney, Agent, or Firm* — Morgan, Lewis & Bockius LLP

- Founded in 2013
- Based in Salt Lake City, Utah
- ~165 employees
- Applies patented artificial intelligence techniques to morphological profiles derived by cell painting to identify and develop drugs for over 30 diseases
- **CEO**: Chris Gibson, Ph.D.
  2013 Ph.D. graduate of University of Utah
- **Total VC investment to date:** USD $200M
- **Notable 2019 events:**
  - *"Recursion Pharmaceuticals, which uses automated, experimental biology with artificial intelligence to reveal new drug targets and develop drug candidates, raised $121 million (led by investment fund Baillie Gifford) in a Series C round to further develop its in-house pipeline of small molecules and the technology."*
  - *"…new therapeutic candidates identified for over a half a dozen diseases within its AI-driven collaboration with Takeda Pharmaceuticals, started in 2017. This year Takeda has exercised its option for drug candidates in two rare diseases, and the companies extended collaboration*



EUROPEAN LEGAL FRAMEWORK FOR PATENTABILITY OF AI

Morgan Lewis

Europe: What is a computer-implemented invention (CII)?

A computer-implemented invention is an invention whose implementation involves the use of a **computer**, **computer network** or other **programmable apparatus**, wherein one or more features of the invention are realised wholly or partly by means of a **computer program**.

Such inventions, which involve technical features as well as algorithmic or mathematical steps and/or presentations of information, are treated as **"mixed type"** inventions for which special considerations with respect to the assessment of **exclusion from patentability** (eligibility) and **inventive step** apply.

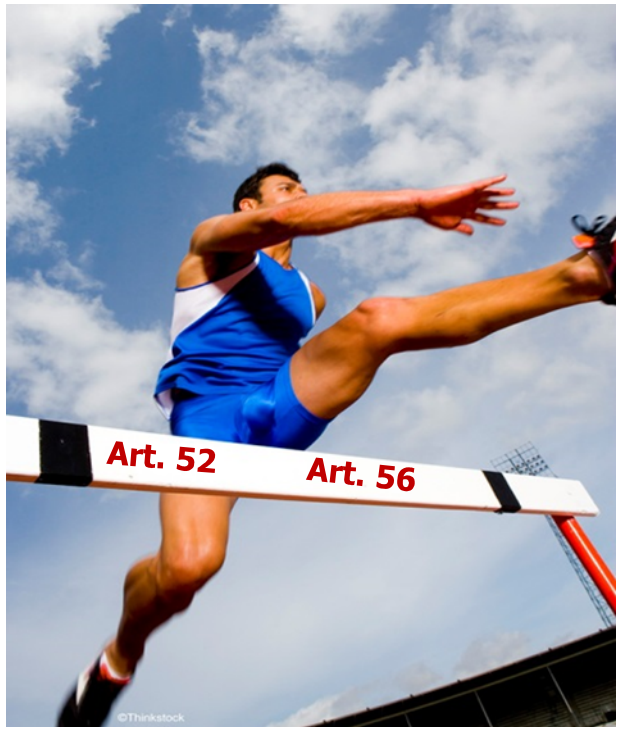
How to obtain a patent for CII at the EPO

Two (main) hurdles:

- First hurdle:
  Exclusion from Patentability (Art. 52 EPC)

- Second hurdle:
  Inventive step (Art. 56 EPC)

- Pitfalls: Insufficient detail
  - in the claims
  - in the original application



Europe: The first hurdle - Exclusion from patentability (eligibility)

Excluded from patentability:

Inventions which are **not in a technical field**

a) discoveries, scientific theories and **mathematical methods**

b) aesthetic creations

c) schemes, rules and methods for performing mental acts, playing games or doing business, and programs for computers

d) **presentations of information**

Art. 52(2) EPC

Europe: Claim example (first hurdle)

A **computer-implemented** method for clustering data curves comprising mathematical steps a) ... , b)... and c)...., *wherein the data curves represent DNA melting curves*

Non-technical features when taken in isolation

Technical features

Any involvement of a physical step or technical entity (e.g. a computer) is sufficient to overcome an exclusion from patentability

Claim is **not** excluded from patentability (Art. 52(2) EPC) – first hurdle is cleared!

Europe: The second hurdle: substantive requirements

- As with all applications, claims to computer-implemented inventions also have to fulfil the requirements of Novelty (Art. 54 EPC) and Inventive Step (Art. 56 EPC) vis-à-vis the prior art
- For the assessment of novelty, all features – whether technical or non-technical – are taken into account
- Inventive step is assessed by the so-called "**problem-solution approach**"
- For computer-implemented inventions, special considerations with respect to the features to be considered in the problem-solution approach apply

Europe: The second hurdle - Inventive step

- When assessing the inventive step of mixed type inventions, all **features that contribute to the technical character of the invention are taken into account.**

- These also include the features that, when taken in isolation, are non-technical, but do, **in the context of the invention**, contribute to producing a **technical effect** serving a **technical purpose**, thereby contributing to the technical character of the invention.

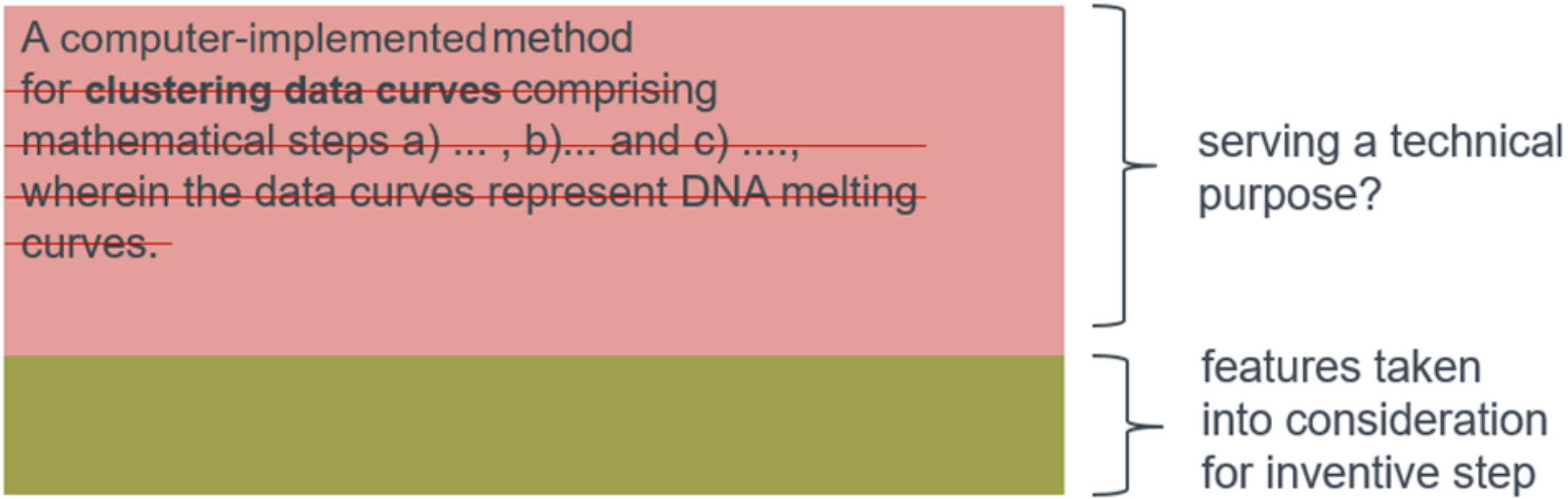
Guidelines, G-VII, 5.4

Europe: The second hurdle - Inventive Step

This means that even if the only differing feature versus the prior art lies in a **mathematical element** or in a particular **presentation of information**, this element **may render your claim inventive** as long as it serves, in the context of the claim, **a technical purpose**.

Whether a technical purpose is served is primarily determined by the **direct technical relevance of the results**, e.g. by its application to **solve a specific problem** in a field of technology.

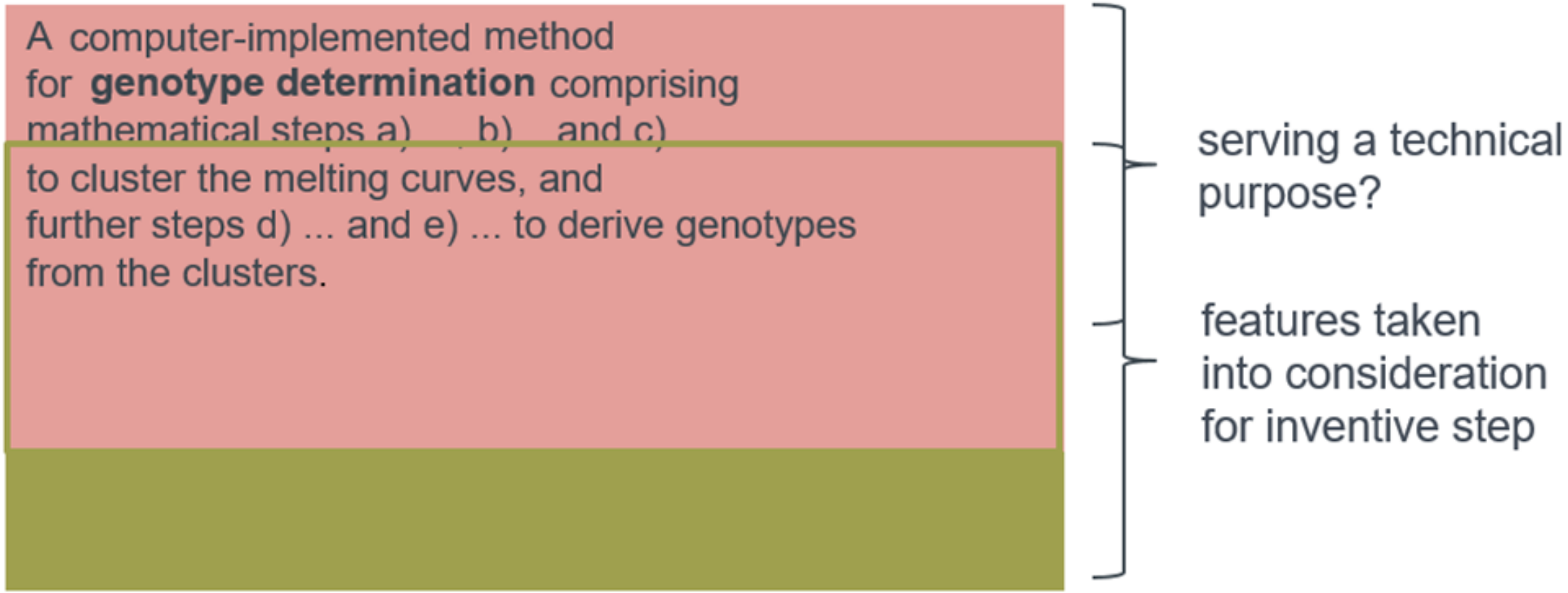
Claim example 1



Weak position for 2nd hurdle:

Only one feature ("computer-implemented") is assessed with regard to prior art

Claim example 2



Strong position for 2nd hurdle:

All features are assessed with regard to prior art

Claim example 3

A computer-implemented method to determine a fetal genetic abnormality which is a chromosomal aneuploidy, comprising

(a) obtaining sequence information of multiple polynucleotide fragments from a sample, ...

(b) assigning said fragments to chromosomes based on said sequence information by comparing said fragments to the reference unique reads of the same size for each of said chromosomes ...;

(c) determining coverage depth and GC content of a chromosome ...;

(d) determining fitted coverage depth of said chromosome using said GC content of said chromosome and established relationship between coverage depth and GC content for said chromosome in the absence of aneuploidy ...; and

(e) comparing said fitted coverage depth to the coverage depth of said chromosome determined in step (c), wherein a difference between them indicates fetal chromosomal aneuploidy.

Claim Example 4

A computer-implemented statistical genetics analysis system for performing a statistical genetics analysis with a collection of multi-loci genotype data of individuals, the statistical genetics analysis system comprising

- a means for generating multi-loci data, which is genotype data of possible multiple loci including two specific loci, based on the multi-loci genotype data of individuals;
- a means for performing a process for computing maximum likelihood estimates of haplotype frequencies of the multiple loci including the two specific loci with the multi-loci data for each of the possible multiple loci including the two specific loci; and
- a means for estimating haplotype frequencies between the two specific loci based on the two-loci haplotype frequencies stored for each of the possible multiple loci including the two specific loci.

EUROPEAN LEGAL FRAMEWORK FOR PATENTABILITY OF AI – CASE STUDY

Morgan Lewis

NOVO NORDISK European Patent No. 3479267 (Filed June 22, 2017)

REGIMEN ADHERENCE MEASURE FOR INSULIN TREATMENT BASED ON GLUCOSE MEASUREMENTS AND INSULIN PEN DATA

Claims directed to a method of adjusting a standing insulin regimen for a subject:

- Obtain a 1st dataset comprising autonomous time-stamped glucose measurements
- Obtain a 2nd dataset from an insulin pen used to apply the insulin, that included timestamped injection events (including amount injected)
- Identify fasting events using the 1st dataset
- Characterize each fasting event as basal regimen adherent (when the 2nd data set includes records that establish, on a temporal and quantitative basis, adherence with the standing basal insulin dosage regimen during the respective fasting event) or not adherent
- adjust insulin medicine dosage in the basal insulin medicine dosage regimen based upon glucose measurements that are contemporaneous with the fasting events that are basal regimen adherent and by excluding glucose measurements that are contemporaneous with fasting events that are basal regimen nonadherent

REGIMEN ADHERENCE MEASURE FOR INSULIN TREATMENT BASED ON GLUCOSE MEASUREMENTS AND INSULIN PEN DATA (CONT.)

International Search Report – the problems to be solved by the present invention may be regarded as:

- How to systematically allow tracking and recording of adherence to a basal insulin regimen based on automatically generated event-dependent reference points in time
- How to flexibly adjust regimen dosage base on a correlation between medication injection events and metabolic (fasting) events of a patient
- How to adjust a standing regimen dosage by additionally discarding/excluding non-compliant adherence data from consideration

Coronavirus COVID-19 Resources

We have formed a multidisciplinary **Coronavirus/COVID-19 Task Force** to help guide clients through the broad scope of legal issues brought on by this public health challenge.

To help keep you on top of developments as they unfold, we also have launched a resource page on our website at **www.morganlewis.com/topics/coronavirus-covid-19**

If you would like to receive a daily digest of all new updates to the page, please visit the resource page to **subscribe** using the purple "Stay Up to Date" button.

Morgan Lewis

Biography

Brett A. Lovejoy, Ph.D.
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+1.415.442.1211
brett.lovejoy@morganlewis.com

Brett Lovejoy writes and prosecutes, on a worldwide basis, patents directed to computer-implemented technologies, including life science applications making use of machine learning or artificial intelligence. He also has significant experience securing intellectual property protection for software, bioinformatics, diagnostics, digital health, quantum computing algorithms and hardware, medical and consumer devices, as well as chemistry, biochemistry, and renewable energy applications. When beneficial, Brett makes use of design patent law to protect client's intellectual property, including fashion, sporting equipment, and devices (e.g., device casings).

Biography

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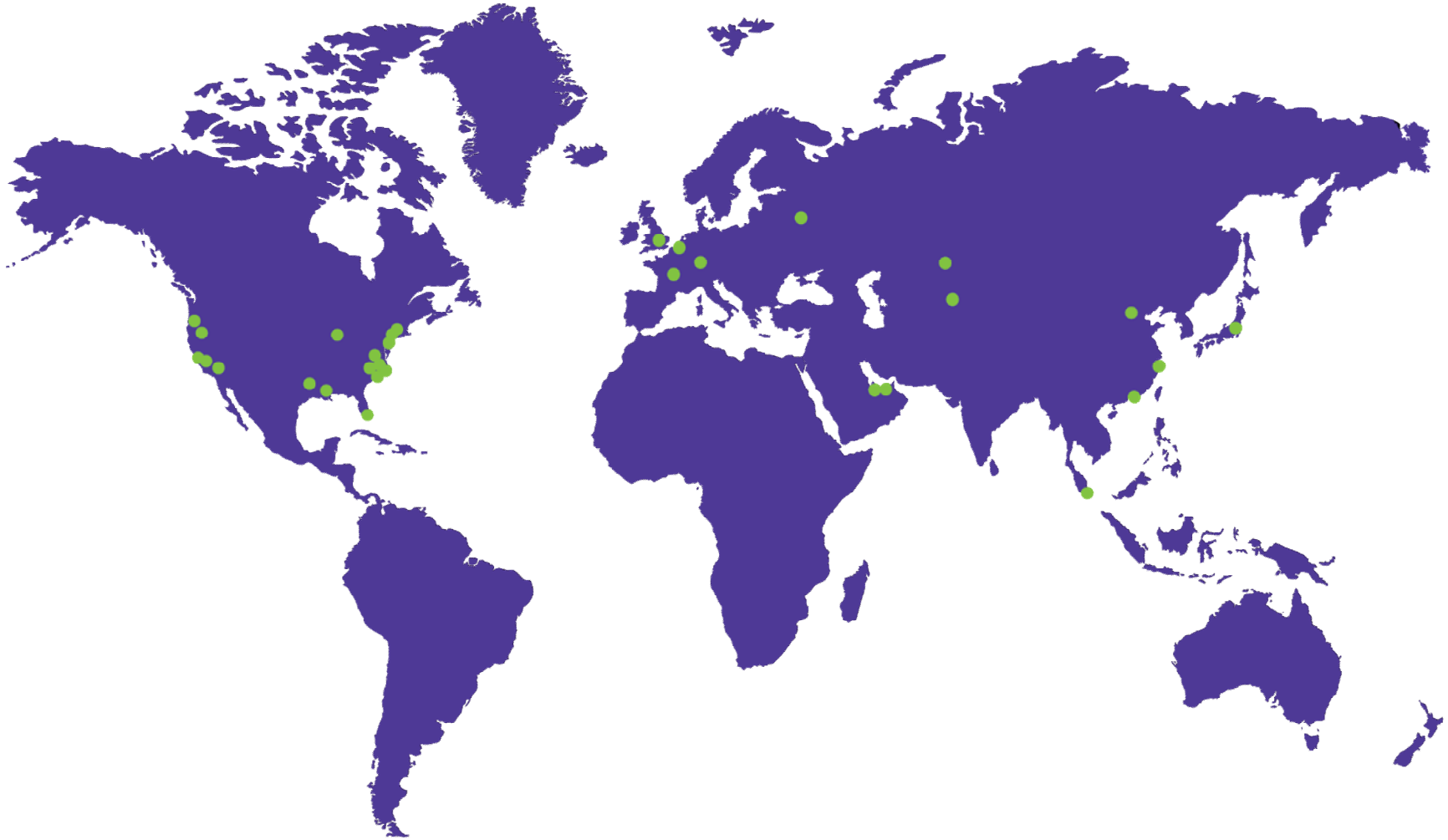
Serving as the leader of Morgan Lewis's semiconductor practice and as a member of the firm's fintech and technology practices, Andrew J. Gray IV concentrates his practice on intellectual property (IP) litigation and prosecution and on strategic IP counseling. Andrew advises both established companies and startups on Blockchain, cryptocurrency, computer, and Internet law issues, financing and transactional matters that involve technology firms, and the sale and licensing of technology. He represents clients in patent, trademark, copyright, and trade secret cases before state and federal trial and appellate courts throughout the United States, before the US Patent and Trademark Office's Patent Trial and Appeal Board, and before the US International Trade Commission.

Our Global Reach

Africa
Asia Pacific
Europe
Latin America
Middle East
North America

Our Locations

Abu Dhabi
Almaty
Beijing*
Boston
Brussels
Century City
Chicago
Dallas
Dubai
Frankfurt
Hartford
Hong Kong*
Houston
London
Los Angeles
Miami
Moscow
New York
Nur-Sultan
Orange County
Paris
Philadelphia
Pittsburgh
Princeton
San Francisco
Shanghai*
Silicon Valley
Singapore*
Tokyo
Washington, DC
Wilmington



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