



aizon

AI in the Pharmaceutical Industry:

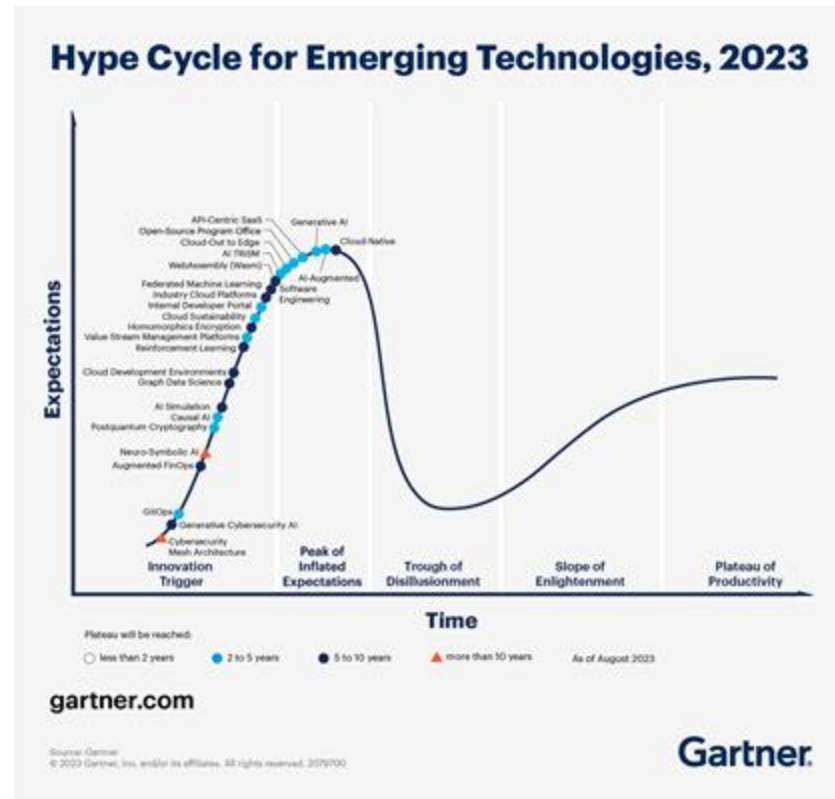
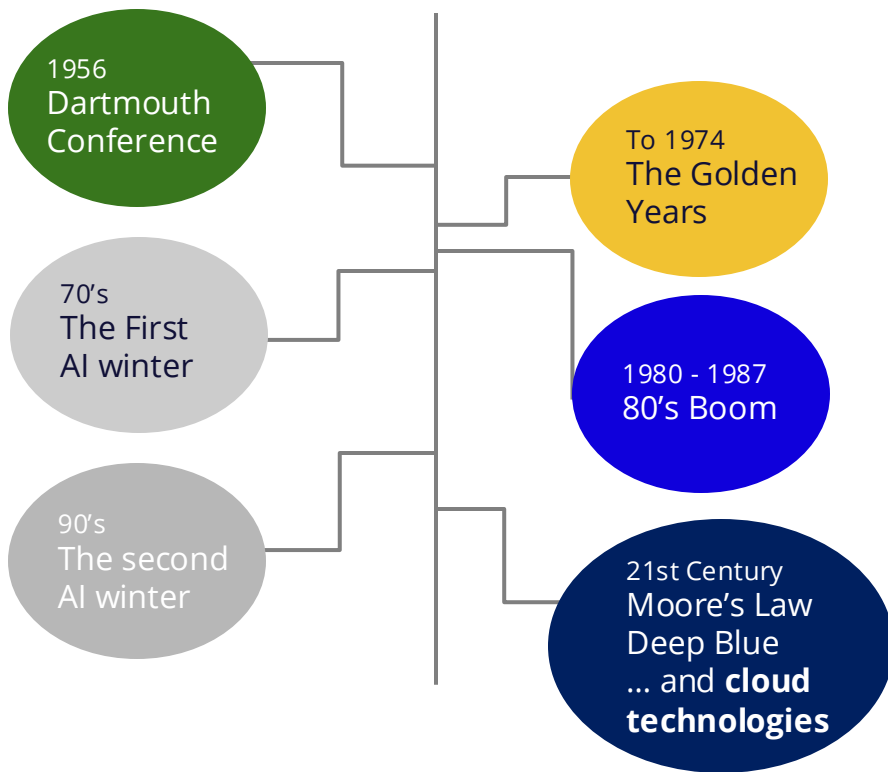
A practical guide to adopt it and implement it

Toni Manzano, CSO and co-founder of Aizon
SME for AI in United Nations

October 2024

What is AI?

A brief history of AI: It's a hype now, but It has a come a long way...



Who first imagined AI?



What is Artificial Intelligence?

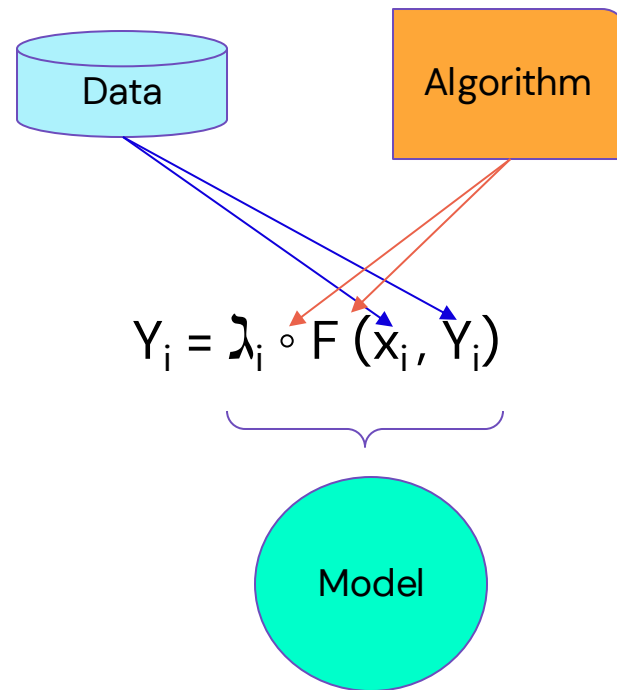
“AI can be thought of as simulating the capacity for abstract, creative, deductive thought - and particularly the ability to learn - using the digital, binary logic of computers.”

“Artificial Intelligence (AI) is no longer some bleeding technology that is hyped by its proponents and mistrusted by the mainstream. In the 21st century, AI is not necessarily amazing. Rather, it is often routine. Evidence for the routine and dependable nature of AI technology is everywhere.”

Verification and Validation and Artificial Intelligence,” Tim Menzies, Portland State University, Charles Pecheur, NASA Ames Research Center. July 2004.



What is AI, really?



The 5 Basic Concepts in AI

Training/Test Data

- Problem dataset

Algorithm

- Mathematical procedure that creates the model from training data

Model

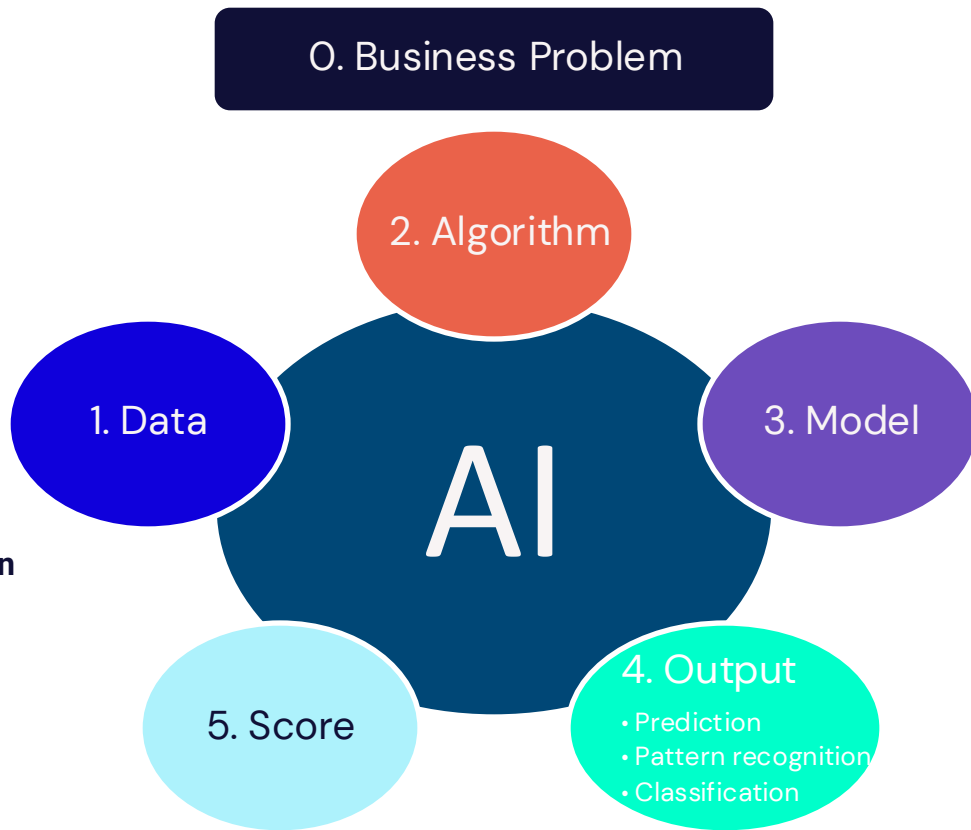
- Mathematical system that has been created from the exploration of a dataset; created after an extensive learning process referred to as training

Prediction / Classification / Recommendation / Recognition / Dimension Reduction

- Single inference over a model with an unseen sample

Evaluation

- Score evaluation of the test dataset



What Really is ML?

Mechanistic vs. Probabilistic

- Physics and Engineering mechanics provides the right conditions for the ideal or known scenario
- The new probability (AI models) defines the real conditions without the physical and chemical basis

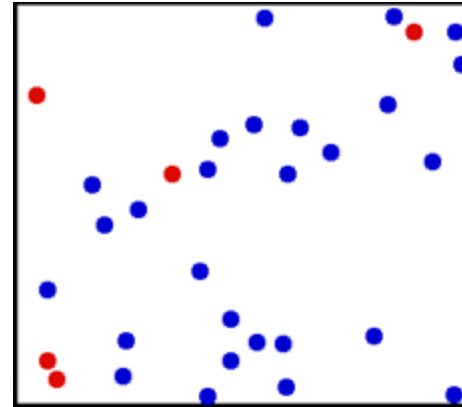
Classic mechanics



$$\frac{(p_1 - p_2)}{p_1} < F_\gamma \cdot x_T \rightarrow$$
$$Q_0 = \frac{1}{60} \cdot 4.17 \cdot C_v \cdot p_1$$
$$\cdot \left(1 - \frac{p_1 - p_2}{(3F_\gamma \cdot x_T)} \right) \cdot \sqrt{\frac{p_1 - p_2}{(T_a + 273.15)}}$$

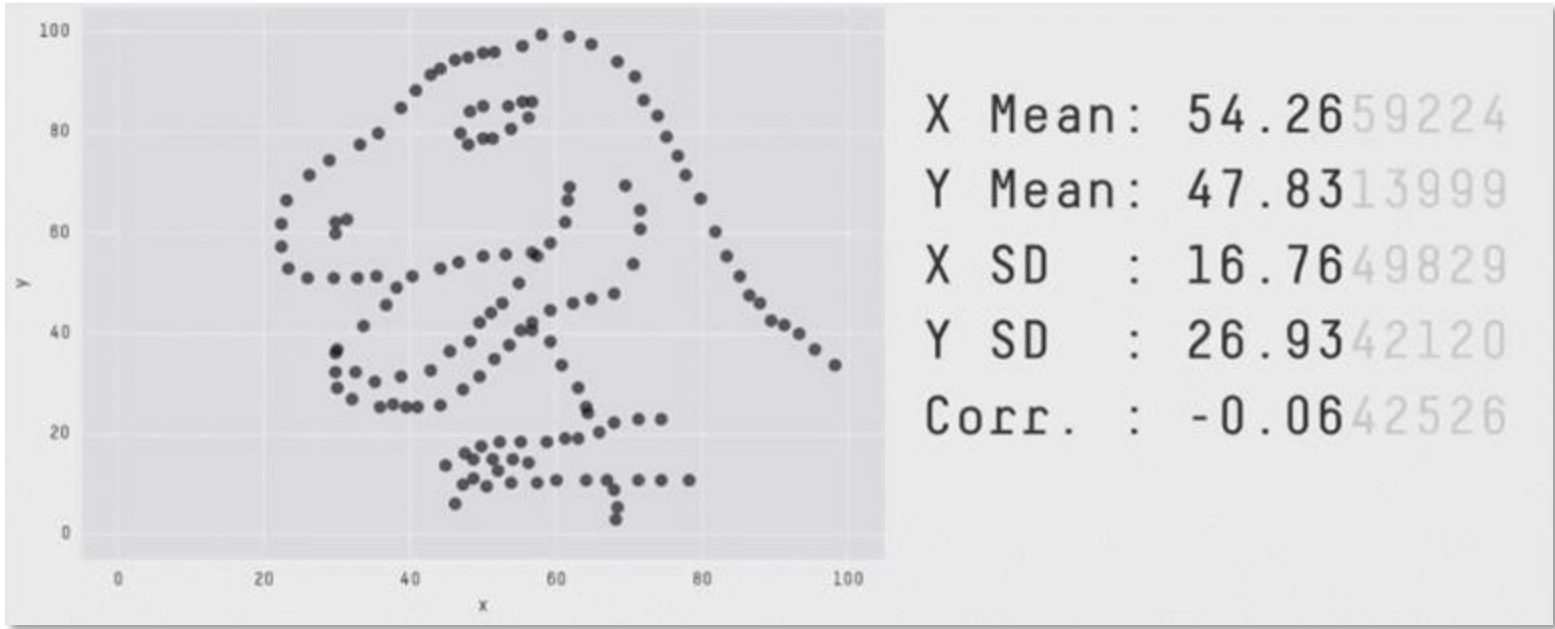
$$\frac{(p_1 - p_2)}{p_1} \geq F_\gamma \cdot x_T \rightarrow$$
$$Q_0 = \frac{1}{60} \cdot 0.667 \cdot 4.17 \cdot C_v \cdot p_1$$
$$\cdot \sqrt{\frac{F_\gamma \cdot x_T}{T_a + 273.15}}$$

Statistical mechanics



What Really is AI?

More than Just Multivariable Models...



Understanding AI: Data (the Secret Sauce)

Expected and Required Data Quality

What is FAIR DATA?



Data and supplementary materials have sufficiently rich metadata and a unique and persistent identifier.

FINDABLE



Metadata and data are understandable to humans and machines. Data is deposited in a trusted repository.

ACCESSIBLE



Metadata use a formal, accessible, shared, and broadly applicable language for knowledge representation.

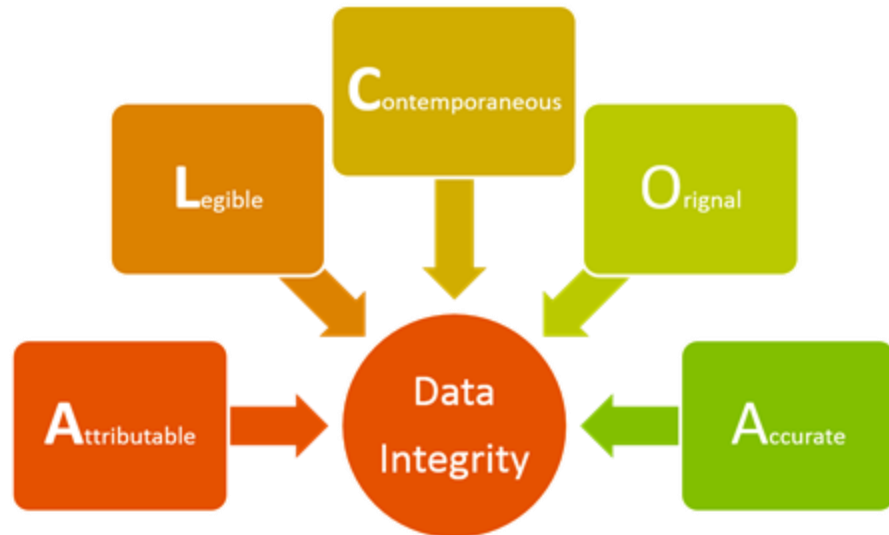
INTEROPERABLE



Data and collections have a clear usage licenses and provide accurate information on provenance.

REUSABLE

ALCOA: FDA's Data Integrity Focus



AI in Life Sciences

nature

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[nature](#) > [news](#) > [article](#)

Published: 05 April 2017

Machine learning predicts the look of stem cells

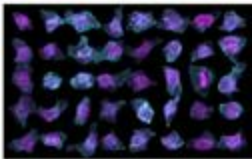
[Amy Maxmen](#)

[Nature](#) (2017) | [Cite this article](#)

610 Accesses | 4 Citations | 524 Altmetric | [Metrics](#)

Website contains thousands of 3D stem cell images and could eventually help with better understanding diseases like cancer.

No two stem cells are identical, even if they are genetic clones. This stunning diversity is revealed today in an enormous publicly available online catalogue of 3D stem cell images. The visuals were produced using deep learning analyses and cell lines altered with the gene-editing tool CRISPR. And soon the portal will allow researchers to predict variations in cell layouts that may foreshadow cancer and other diseases.



Structural differences in the DNA (purple) and cellular membrane (blue) of genetically identical stem cells. Credit: Allen Institute for Cell Science

nature

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NEWS | 22 July 2019

AI protein-folding algorithms solve structures faster than ever

Deep learning makes its mark on protein-structure prediction.

[Matthew Hudson](#)



Predicting protein structures from their sequences would aid drug design. Credit: Edward Kimbany/Science Photo Library

nature

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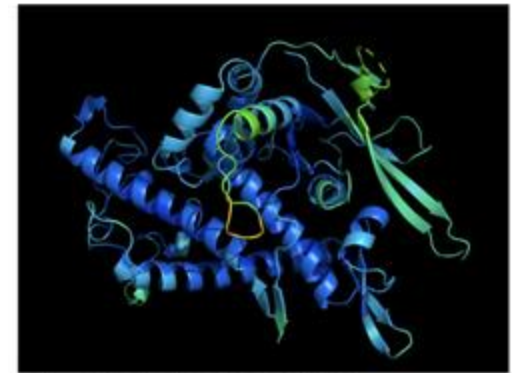
[nature](#) > [news](#) > [article](#)

NEWS | 30 November 2020

'It will change everything': DeepMind's AI makes gigantic leap in solving protein structures

Google's deep-learning program for determining the 3D shapes of proteins stands to transform biology, say scientists.

[Ewen Callaway](#)



A protein's function is determined by its 3D shape. Credit: DeepMind

AI in Life Sciences

nature

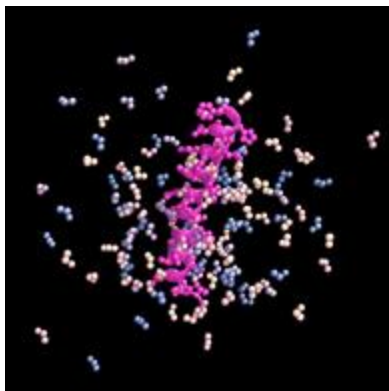
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NEWS FEATURE | 11 July 2023

AI tools are designing entirely new proteins that could transform medicine

Digital art techniques can now devise custom, working biomolecules on demand.



A Handbook of Artificial Intelligence in Drug Delivery

1st Edition - March 27, 2023

Editors: Anil Philip, Aliasgar Shahiwala, Mamoon Rashid, Md Faiyazuddin

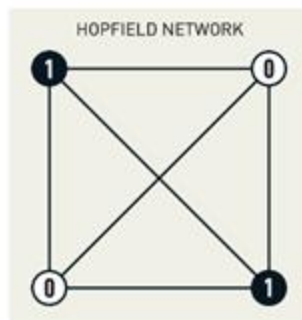
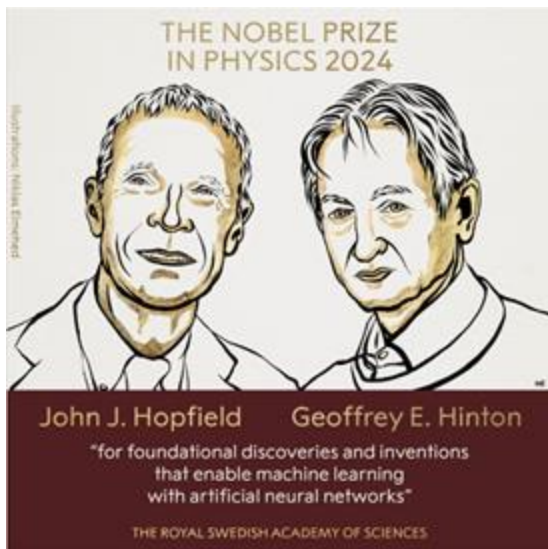
Paperback ISBN: 9780323899253 • **eBook ISBN:** 9780323903738

Description

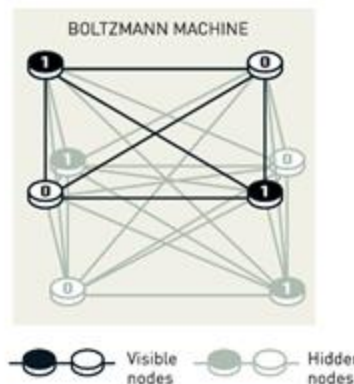
A Handbook of Artificial Intelligence in Drug Delivery explores the use of Artificial Intelligence (AI) in drug delivery strategies. The book covers pharmaceutical AI and drug discovery challenges, Artificial Intelligence tools for drug research, AI enabled intelligent drug delivery systems and next generation novel therapeutics, broad utility of AI for designing novel micro/nanosystems for drug delivery, AI driven personalized medicine and Gene therapy, 3D Organ printing and tissue engineering, Advanced nanosystems based on AI principles (nanorobots, nanomachines), opportunities and challenges using artificial intelligence in ADME/Tox in drug development, commercialization and regulatory perspectives, ethics in AI, and more.

Do you still have doubts about AI applications in Science?

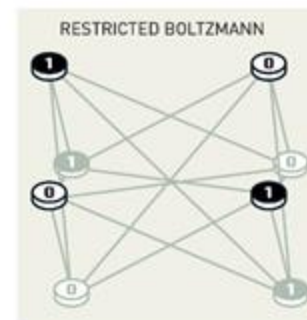
Different types of network



John Hopfield's associative memory is built so that all the nodes are connected to each other. Information is fed in and read out from all the nodes.

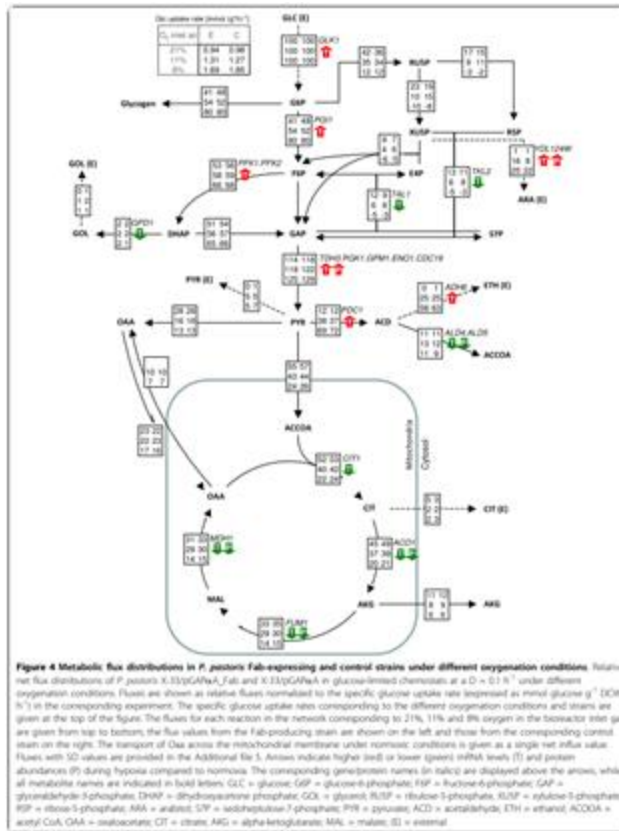


Geoffrey Hinton's Boltzmann machine is often constructed in two layers, where information is fed in and read out using a layer of *visible* nodes. They are connected to *hidden* nodes, which affect how the network functions in its entirety.



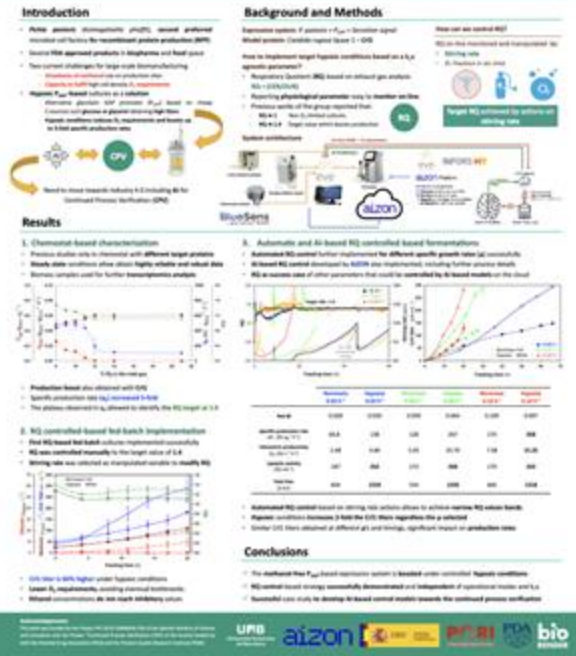
In a restricted Boltzmann machine, there are no connections between nodes in the same layer. The machines are frequently used in a chain, one after the other. After training the first restricted Boltzmann machine, the content of the hidden nodes is used to train the next machine, and so on.

AI in action: CPV of the Future



AI Models applied in RQ control to optimize recombinant protein production in *Pichia pastoris*

Xavier Garcia-Orga¹, Anna Gascón¹, Albert Salas¹, José Van Wingerden², José Luis Montañón-Seguí¹, Toni Mahiques¹ and Francisco Valero¹
¹Department of Chemical, Biological and Environmental Engineering, School of Engineering, Universitat Autònoma de Barcelona, 08193 Bellaterra (Barcelona), Spain
²NOVA, Funchal, Spain
www.garcia-olb.es



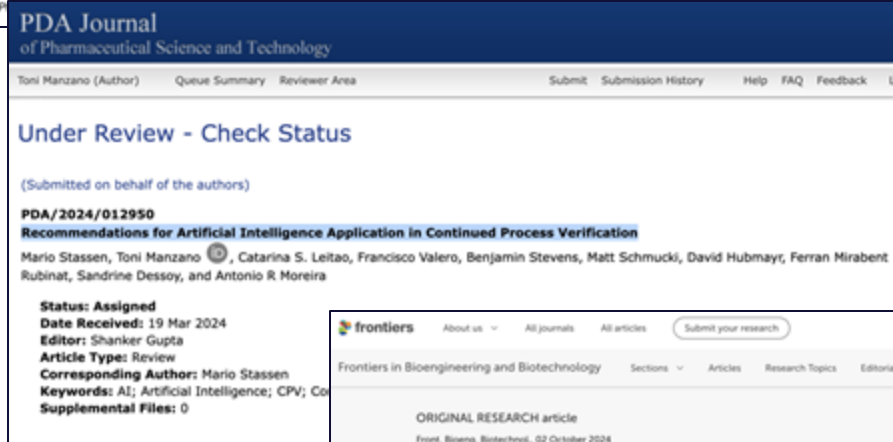
Control automation for optimal and autonomous fermentation governance

Control Strategy

- PAT & IIoT Technology
- Combination of edge & cloud
- Fully automated data pipeline
- Coverage of full AI lifecycle (train, productivise, monitor)
- Operate in near real-time

Control Parameters

- Storage of 17 raw data variables
- Critical read-out: *respiratory quotient (RQ)*
- Critical control: *agitator speed (AS)*



How a top 5 pharma realized \$20M of annual savings for a single product and site.

SITUATION

Increased competition and rising COGS were crunching profitability for one of Customer's top selling products.

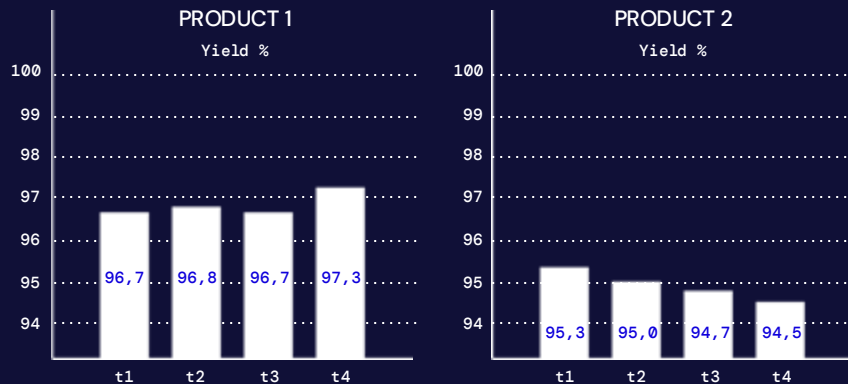
CONTEXT

Production identified centrifugation step as a key factor to recover margins, but improving 97% yield proved daunting.

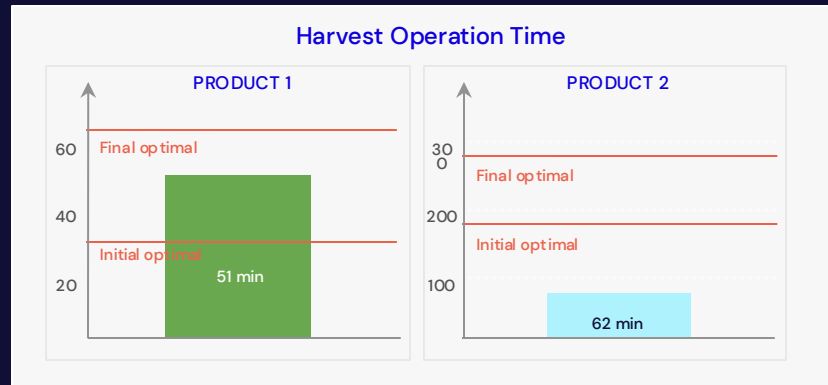
ACTION

Used Unify's multidimensional analysis to identify root causes across candidate stages (initial hold up volume, harvest operation, clarification); leveraged Predict to optimize centrifugation operational times, resulting in 1.5%+ increase in yield. Ensured cross-factory consistency by implementing a real-time monitoring dashboard.

HARVEST OPERATION TIME, ANALYSIS PROCESS



REAL-TIME DASHBOARD MONITORING CROSS-PRODUCT TIMES



How a top biotech achieved Full Right First Time as a product standard

SITUATION

Recirculations at the ultrafiltration process were burdening operational efficiency for a leading Product.

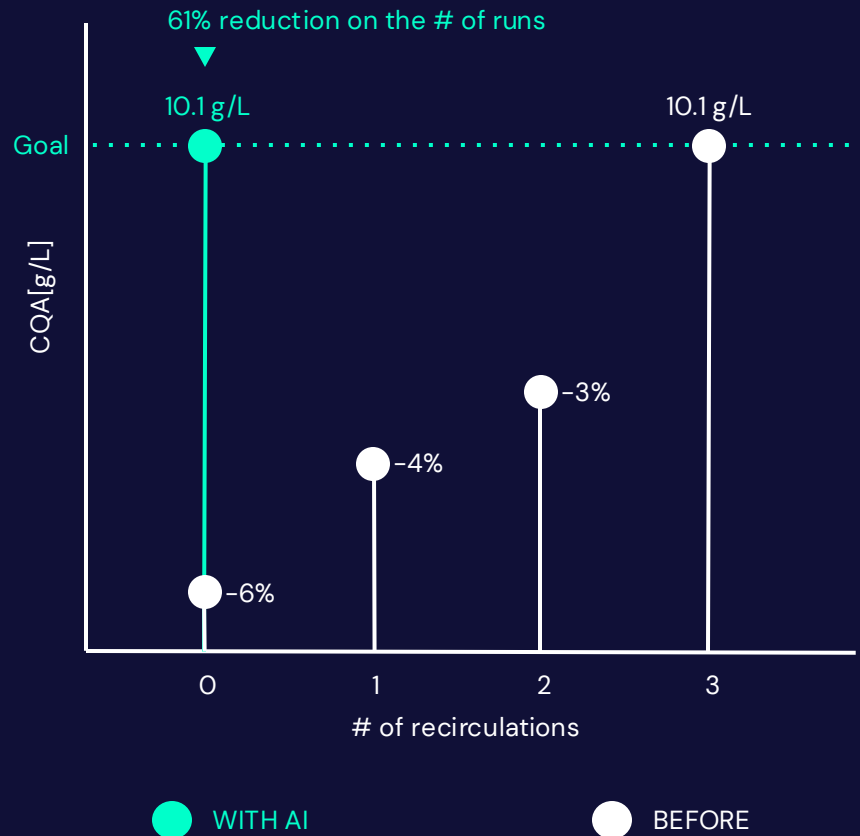
CONTEXT

Almost half of all batches were Right First Time; analyzing the process was a challenge because data was well spread across disparate sources like ERP, MES and LIMS.

ACTION

After integrating purification line multivariate real-time batch monitoring was a reality. Then, used AI to define the optimal CPPs that were affecting target CQA. Once changes were implemented, achieved Right First Time for all batches, reducing the number of runs by 61%.

RECIRCULATION ELIMINATION



How a leading CDMO increased throughput & reduced cost - “right first time” (90%)

SITUATION

CDMO could not accurately predict how much substance to manually add in the reactor as it is highly dependent on previous batches. If the CQA was not achieved the product had to go through multiple cycles and delayed production deadlines.

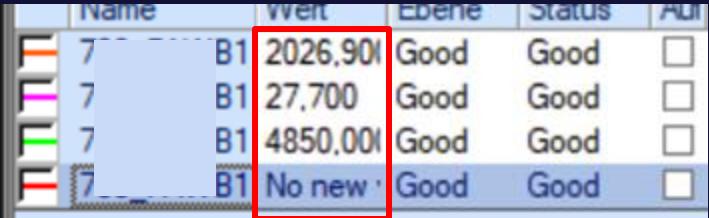
CONTEXT

CDMO has one “expert” technician that can “guess” the amount of material to use. They could only achieve “right first time” ~70% of the time. They tried AI modeling but failed to implement given lack of expertise and technological limitations.

ACTION

Leveraged AI to integrate operator input data and real-time process values from the SCADA system to deploy an AI model that delivers the exact volume (in Liters) to use in the process. The model enabled the most stable campaign in history and led to ~90% of batches being right first time.

Operator Screen (AI Model results directly to operator)



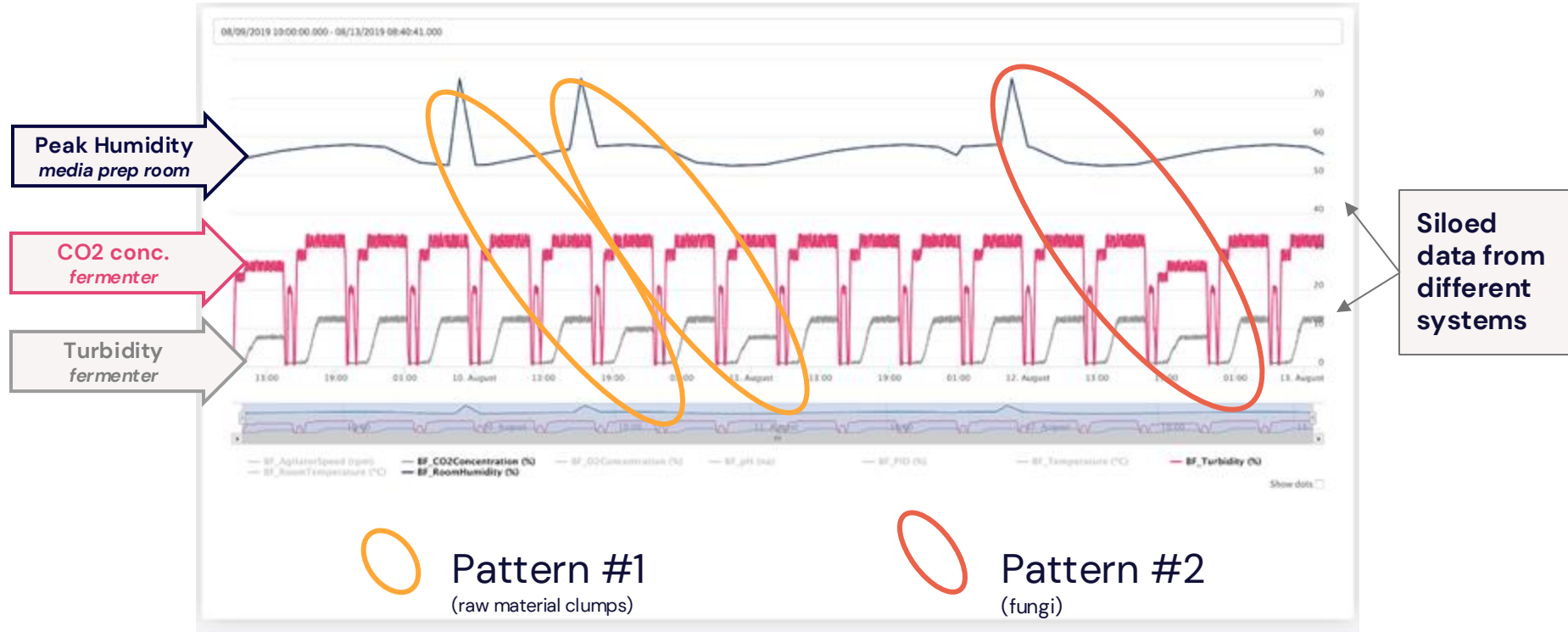
Name	B1	Wert	Ebene	Status	Ad
7	B1	2026,90	Good	Good	☐
7	B1	27,700	Good	Good	☐
7	B1	4850,00	Good	Good	☐
7	B1	No new	Good	Good	☐

Setpoint from the prediction sent to operators screen

Process Stability Monitored in Real-Time

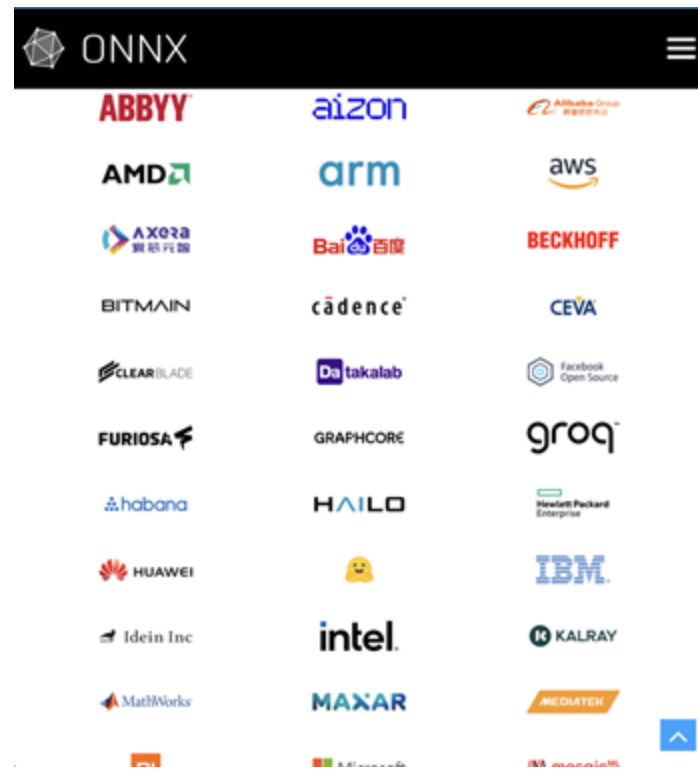
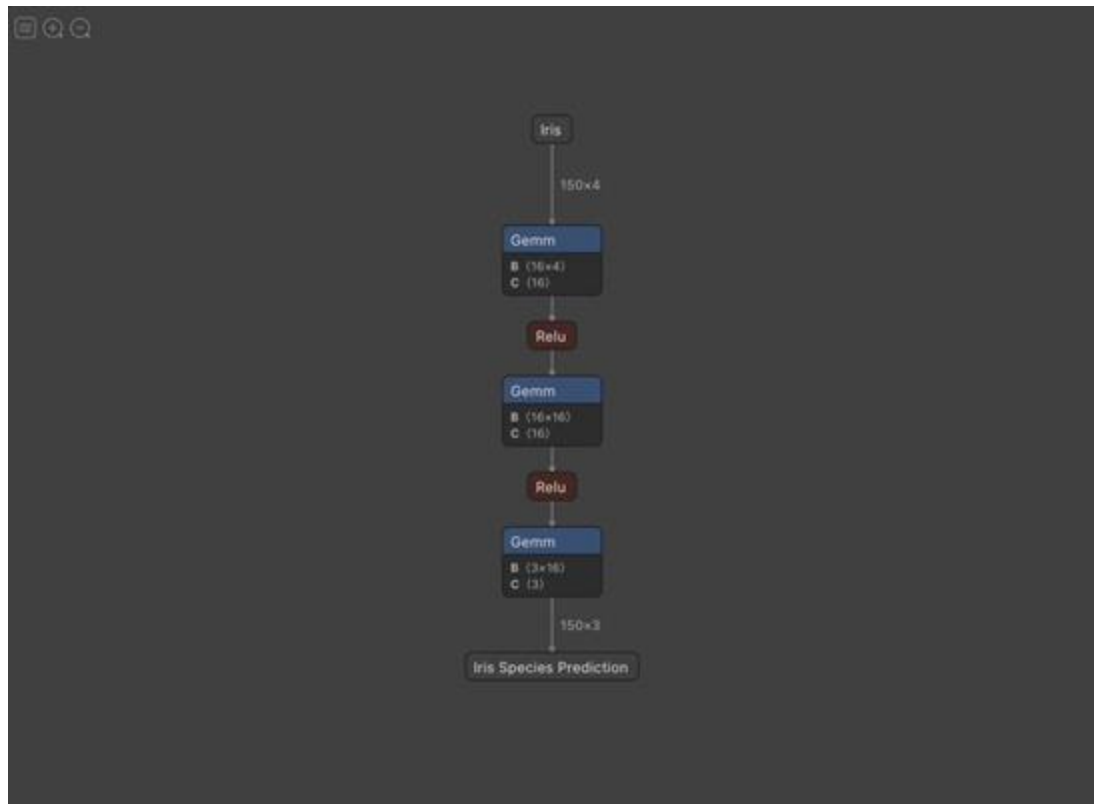


Unifying siloed data + AI integration: Deviation Detection: Clear Patterns in the CPPs



AI to detect how humidity in the media prep room impacts the fermentation process

How AI looks like in action?



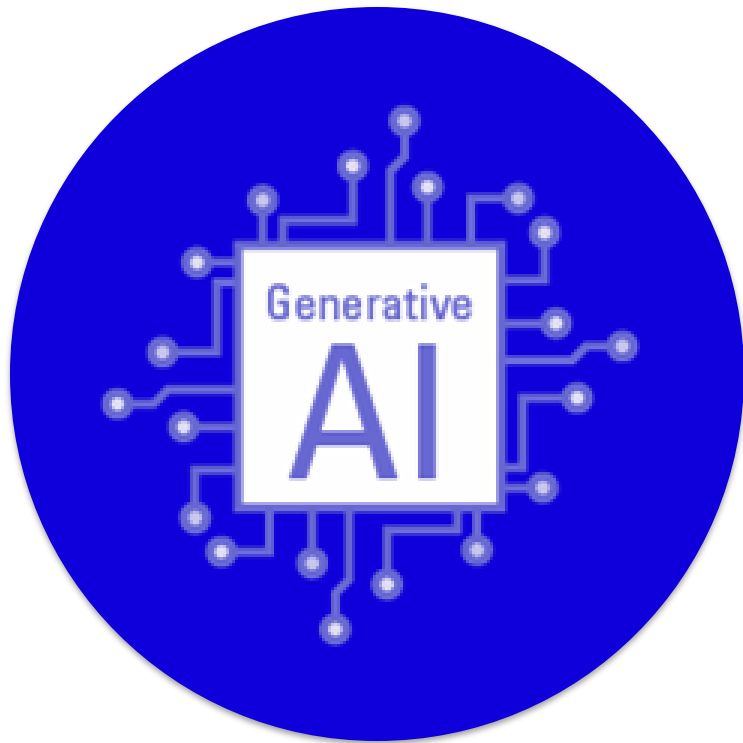
Generative AI



aizon

Still on paper-
based
generating
knowledge?

What is Generative AI?



Generative AI, like ChatGPT, uses machine learning to create new content. While generative AI tools can help explore new ideas, write text, and get feedback, there are important limitations to these tools to keep in mind.

Generative AI $\subset$ ML $\subset$ AI

cohere



Gpt4All



GPT-3

BLOOM

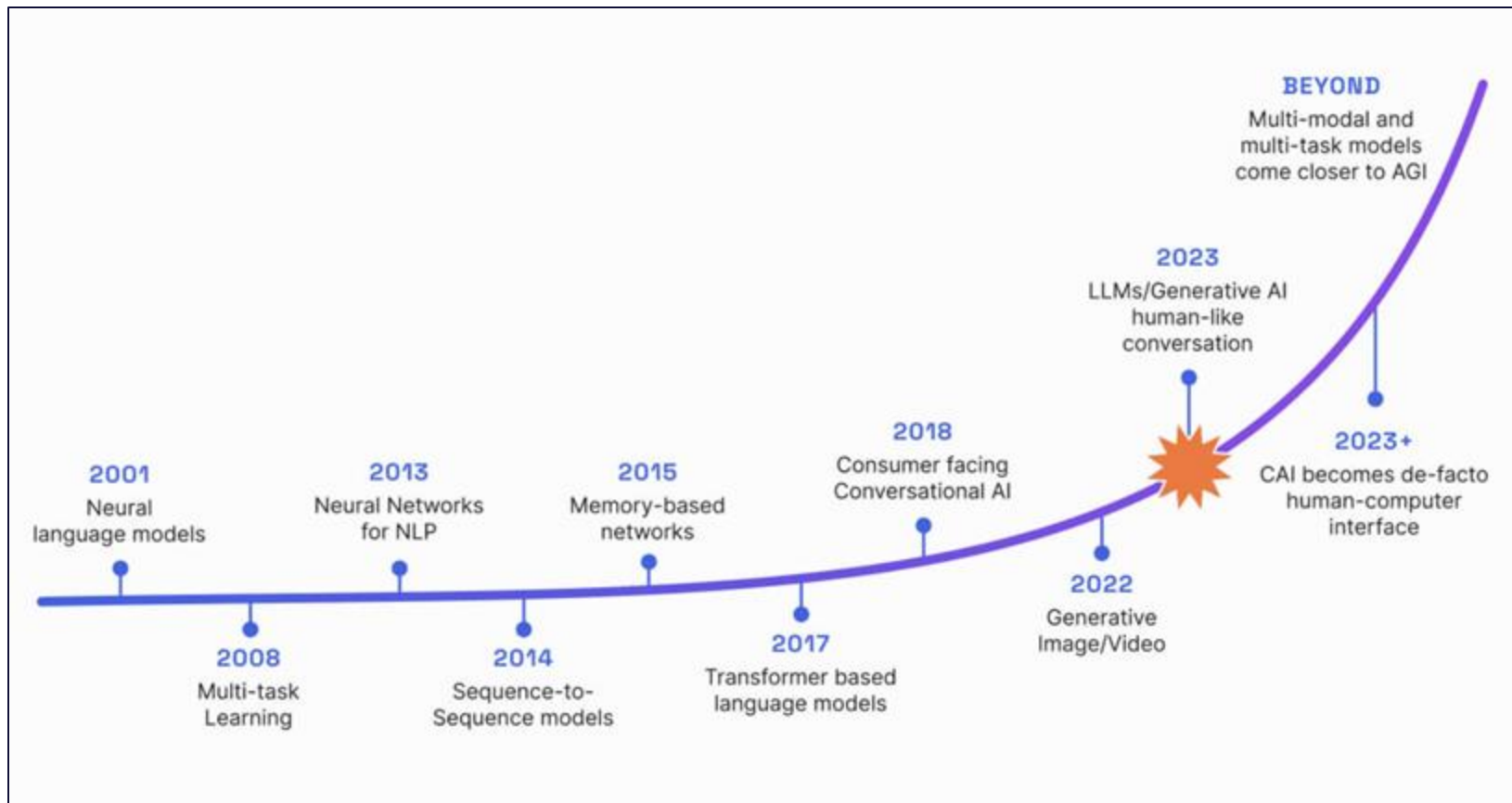


Bard

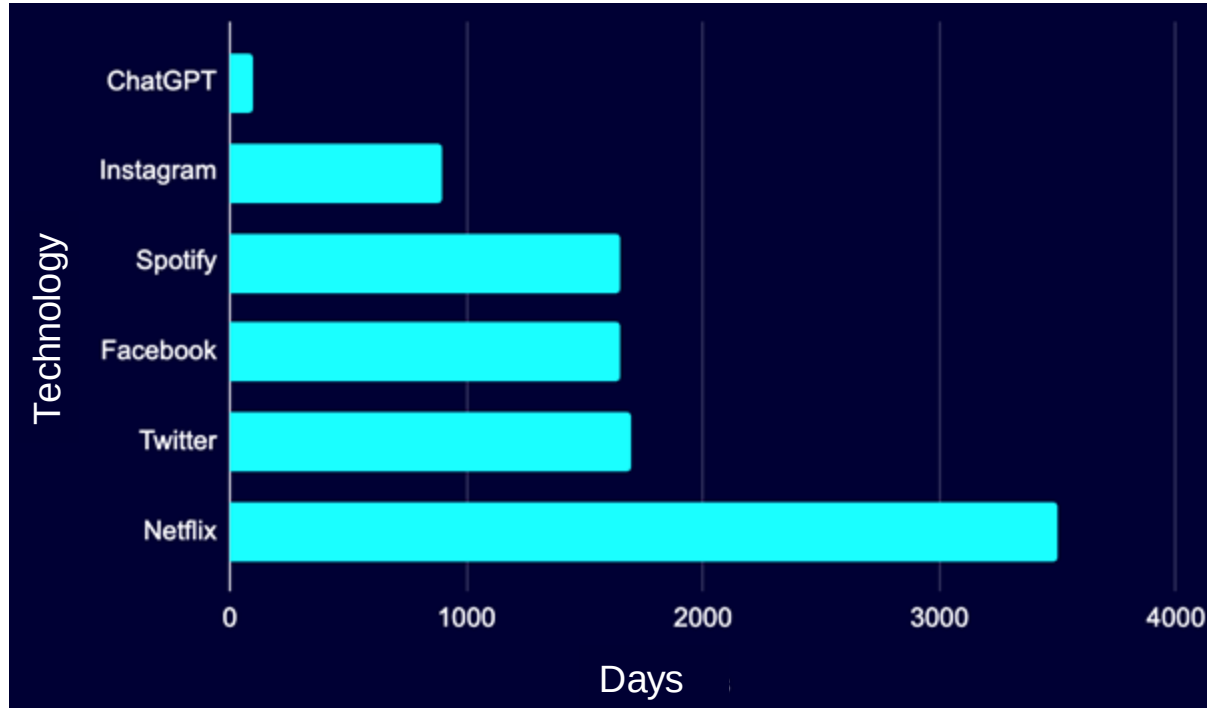


Google Flan-T5

AI's exponential growth: The Foundation Model inflection point



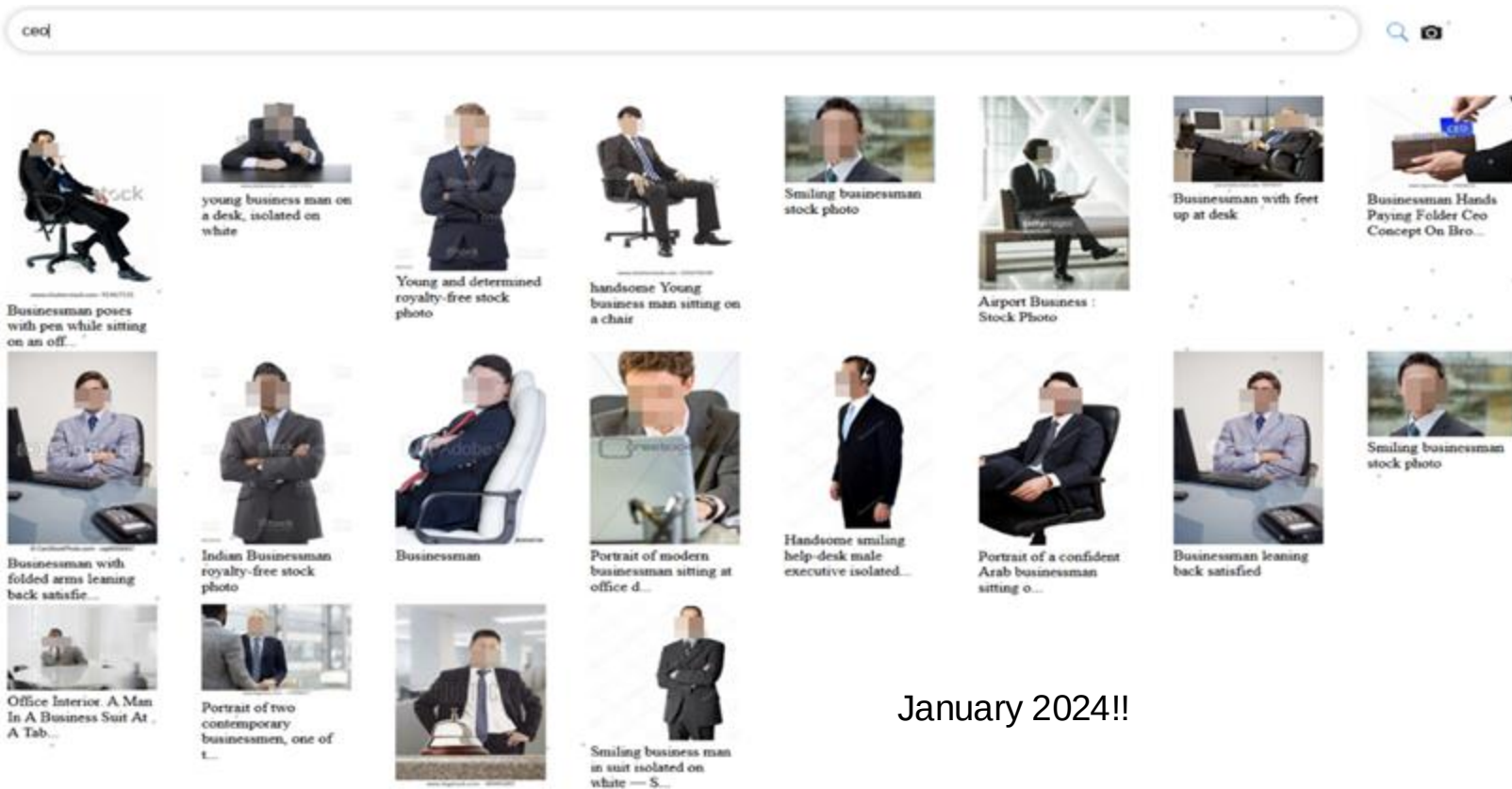
Generative AI expansion (measured in 100M users)



LLMs are not fit for Enterprises out of the box

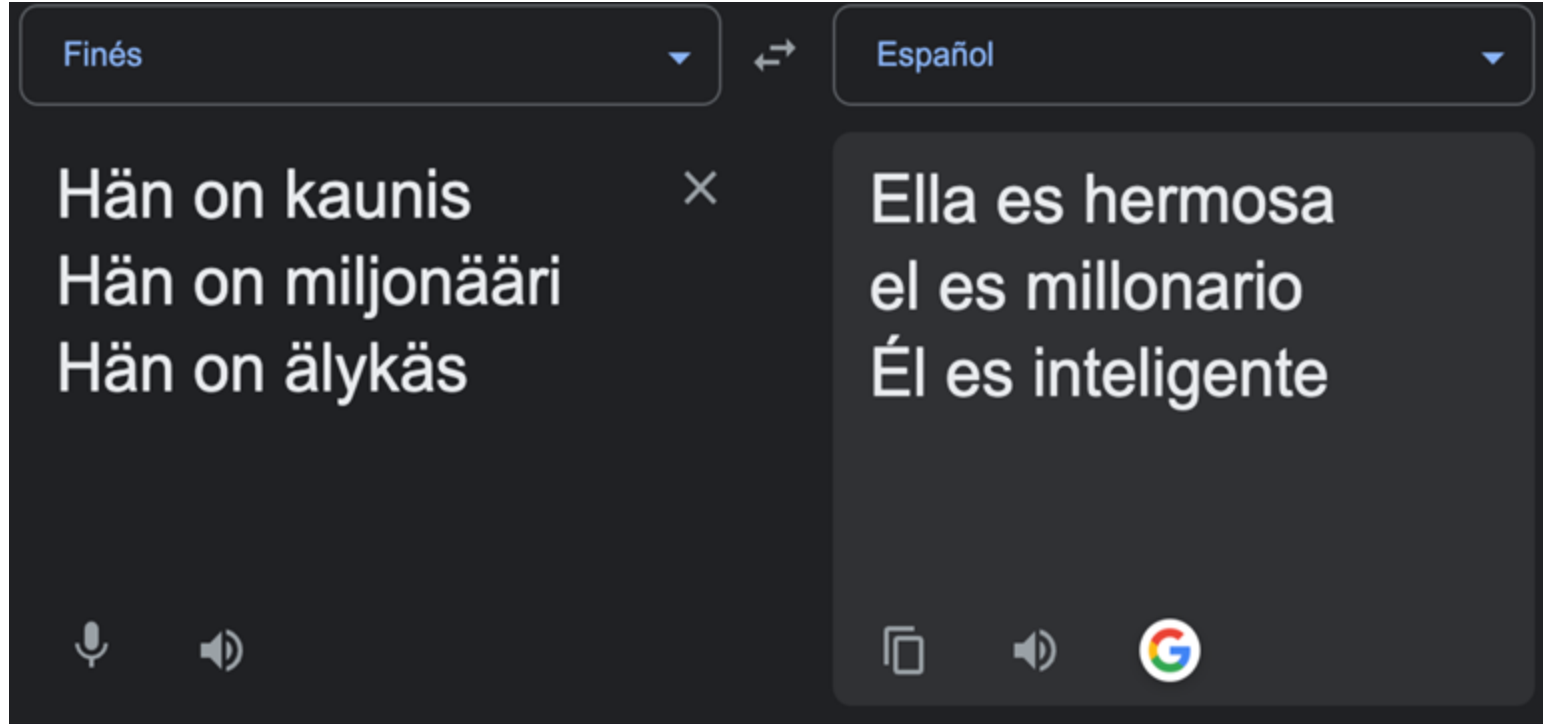


LLMs are not fit for Enterprises out of the box: bias is just an example

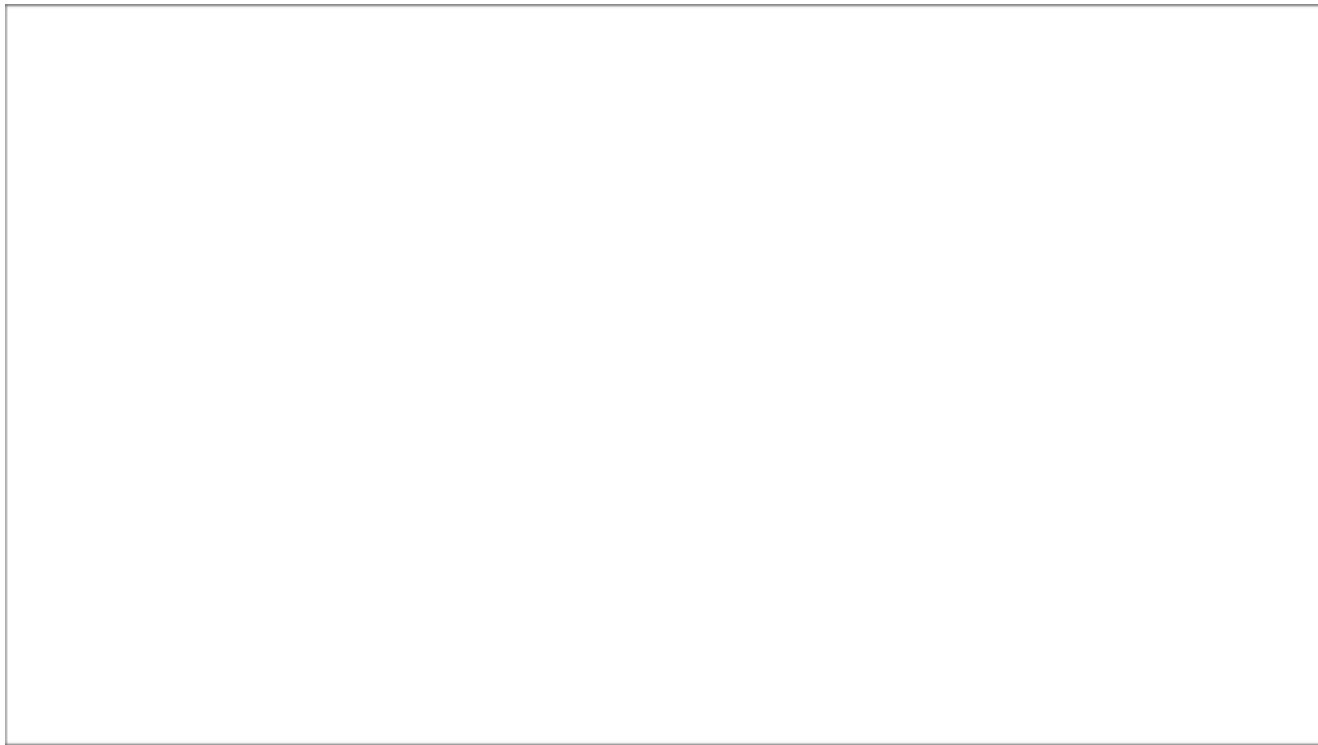


January 2024!!

LLMs are not fit for Enterprises out of the box: bias is just an example



Please, be aware and pay attention to evolution of GEN-AI!



Something is Changing the World Perspective Regarding AI



ChatGPT banned in Italy over privacy concerns

"ChatGPT is scary good. We are not far from dangerously strong AI."

Elon Musk, A Founder of Open AI (Chat GPT) in 2015, and investor and advisor to this day.

UK spy agency says AI chatbots like ChatGPT pose a security threat

Sawdah Bhaimiya and Beatrice Nolan Mar 15, 2023, 8:53 AM



 Read in app



Google Dismantling Health Division

AUGUST 24, 2021

Google Health is dead. (But this isn't the end of 'Google health'.)

Daily Briefing

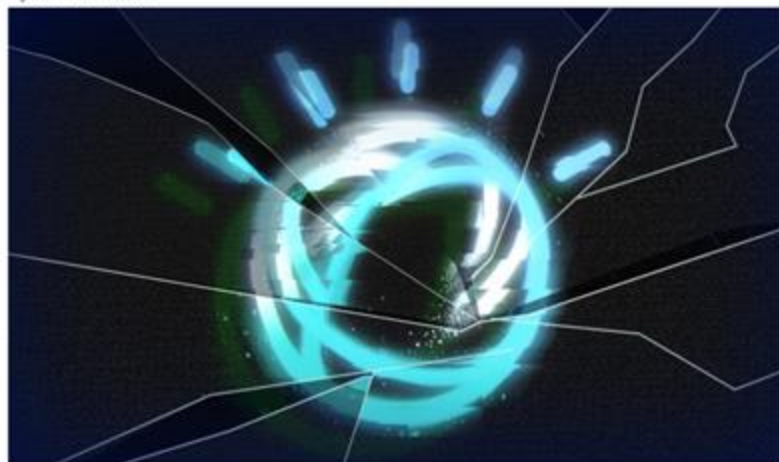
ON THIS PAGE

Our take: What does Google Health's dismantling mean moving forward?

Despite outlining ambitious goals when it launched, Google has closed Google Health, its stand-alone health division, according to an internal memo obtained by *Business Insider* and confirmed by Google—but the company says it still plans to continue its numerous health initiatives.

STAT+: Once billed as a revolution in medicine, IBM's Watson Health is sold off in parts

By CASEY ROSS



HYACINTH EMPINADO/STAT; EROS DERVISHI FOR STAT

IBM will sell core assets of Watson Health to a private equity firm, marking the collapse of its ambitious artificial intelligence effort.

Credibility of Computational Models Program: Research on Computational Models and Simulation Associated with Medical Devices

*Contains Nonbinding Recommendations
Draft – Not for Implementation*

Regulatory Science Gaps and Challenges

Major regulatory science gaps and challenges that drive the Credibility of Computational Models Program are:

- **Unknown or low credibility of existing models:** Many established or proposed models have never been rigorously evaluated and therefore have unknown credibility or suffer from known deficiencies which limit model credibility.
- **Insufficient data:** Quality experimental or clinical data for model development and validation, especially human physiological data under *in vivo* conditions and data on physiological variability, is scarce.
- **Insufficient analytic methods:** These methods include test problems in code verification, appropriate validation metrics, as well methods to evaluate acceptability of individual members of a virtual cohort.
- **Lack of established CM&S best practices:** These include good simulation practices and full end-to-end examples of the entire credibility assessment process across the wide range of applications process.
- **Lack of credibility assessment tools:** These tools include those associated with performing code verification, calculation verification, identifiability analysis, and so forth, as well as lack of decision-making frameworks for overall credibility assessment.

Assessing the Credibility of Computational Modeling and Simulation in Medical Device Submissions

Draft Guidance for Industry and Food and Drug Administration Staff

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff or Office responsible for this guidance as listed on the title page.

AI Regulations

PAT concept - ICH Q8

A control strategy can include, but is not limited to, the following:

- Control of input material attributes (e.g., drug substance, excipients, primary packaging materials) based on an understanding of their impact on processability or product quality;
- Product specification(s);
- Controls for unit operations that have an impact on downstream processing or product quality (e.g., the impact of drying on degradation, particle size distribution of the granulate on dissolution);
- In-process or real-time release testing in lieu of end-product testing (e.g. measurement and control of CQAs during processing);
- A monitoring program (e.g., full product testing at regular intervals) for verifying multivariate prediction models.

A control strategy can include different elements. For example, one element of the control strategy could rely on end-product testing, whereas another could depend on real-time release testing. The rationale for using these alternative approaches should be described in the submission.



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

22 June 2017
EMA/CHMP/ICH/167068/2004
Committee for Human Medicinal Products

ICH guideline Q8 (R2) on pharmaceutical development Step 5

Transmission to CHMP	December 2004
Transmission to interested parties	December 2004
Deadline for comments	June 2005
Final adoption by CHMP	November 2005
Date for coming into effect	May 2006
Editorial corrections	August 2009

Link to: [ICH Q8/Q9/Q10 Training material](#)

Link to: [ICH Q8/Q9/Q10 Points to consider](#)



What About the Regulations....



Good Machine Learning Practice for Medical Device Development:
Guiding Principles
 October 2021



POLICY AND LEGISLATION | Publication 21 April 2021

Coordinated Plan on Artificial Intelligence 2021 Review

The 2021 Coordinated Plan on Artificial Intelligence (AI) is the next step in creating EU global leadership in trustworthy AI. It builds on the strong collaboration between the Commission and Member States established during the 2018 Coordinated Plan.



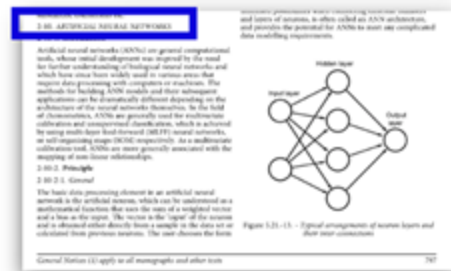
Brussels, 25.4.2018
 COM(2018) 237 final

COMMUNICATION FROM THE COMMISSION

Artificial Intelligence for Europe



Credibility of Computational Models Program: Research on Computational Models and Simulation Associated with Medical Devices



What About the Regulations....



AI in Europe

Brussels, 19.2.2020
COM(2020) 65 final

WHITE PAPER

On Artificial Intelligence - A European approach to excellence and trust



Medicines ▾ Human regulatory ▾ Veterinary regulatory ▾ Committees ▾ News & events ▾ Partners & networks ▾ About us ▾

[Home](#) > [News](#) > Reflection paper on the use of artificial intelligence in the lifecycle of medicines

Reflection paper on the use of artificial intelligence in the lifecycle of medicines

19 July 2023

[News](#) [Human](#) [Veterinary](#) [Data on medicines](#)

EMA has published a [draft reflection paper](#) outlining the current thinking on the use of artificial intelligence (AI) to support the safe and effective development, regulation and use of human and veterinary medicines. This paper, which is now open for public consultation, reflects on principles relevant to the application of AI and machine learning (ML) at any step of a medicines' lifecycle, from drug discovery to the post-authorisation setting.



- 1 13 July 2023
- 2 EMA/CHMP/CVMP/83833/2023
- 3 Committee for Medicinal Products for Human Use (CHMP)
- 4 Committee for Medicinal Products for Veterinary Use (CVMP)

5 Reflection paper on the use of Artificial Intelligence (AI) in 6 the medicinal product lifecycle

7 Draft

Draft agreed by Committee for Medicinal Products for Human Use (CHMP) Methodology Working Party	July 2023
Draft adopted by CVMP for release for consultation	13 July 2023
Draft adopted by CHMP for release for consultation	10 July 2023
Start of public consultation	19 July 2023
End of consultation (deadline for comments)	31 December 2023

8 Comments should be provided using this [EUSurvey form](#). For any technical issues, please contact
9 the [EUSurvey Support](#).

Keywords	Artificial intelligence, AI, machine learning, ML, regulatory, medicine, human medicinal product, veterinary medicinal product
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AI & Annex 11



19 September 2022
EMA/INS/GMP/781435/2022
GMP/GDP Inspectors Working Group (GMP/GDP IWG)

PS/INF 94/2022

Concept Paper on the revision of Annex 11 of the guidelines on Good Manufacturing Practice for medicinal products – Computerised Systems

Agreed by EMA GMP/GDP IWG and PIC/S	31 October 2022
Start of public consultation	16 November 2022
End of consultation (deadline for comments)	16 January 2023

The proposed guideline will replace:

- Eudralex Volume 4: Annex 11 Computerised Systems
- for PIC/S participating authorities: PE 009-15: Annex 11 – Computerised Systems

Comments should be provided using this [template](#). The completed comments form should be sent to ADM-GMDP@ema.europa.eu

Keywords GMP, medicinal product, annex 11



HMA/EMA multi-stakeholder workshop on artificial intelligence (AI) - enabling the safe and responsible use of AI

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Event

Corporate

[Add to calendar](#)

Page contents

[Event summary](#)

[Registration](#)

[Live broadcast](#)

Date

Tuesday, 5 November 2024

Location

Online

European Medicines Agency, Amsterdam, the Netherlands

Live broadcast

AI/ML Validation

Artifcact	Data	Algorithm	Model	Model Validity	Validation
URS/SRS	Data sources	Purpose Intended use	Input feed Output consumption	Expected range of confidence	PQ
FS	DoE Coverage Training/testing Contextualization	Generic/Ad-hoc Maths & Statistics Justification Inputs/outputs	Results Format Model Meta data Life cycle Audit	Accuracy Performance Efficiency Confusion Matrix	OQ
DS	Methods and scripts Clean-up and preprocessing	Fine tuning Hyperparameters	Storage Execution	Fine tuning Triangulated validity	IQ
Risk Assessment	Bias Clean-up criteria Processing Automation	Conditioning Variability Complexity Continuous Learning	Computing and storage capabilities Monitoring Overfitting/underfitting	Data divergence Data drift	Continuous monitoring

The Right Drug Supported by AI

- Identifying relevant factors
- Recognizing patterns
- Recommending actions
- Detecting anomalies
- Predicting deviations
- Establishing improvements
- Executing repetitive analysis
- Simulating processes

**Working closely with humans,
full commitment with patients!**

THREE COMMANDMENTS
Safety, Efficiency, Quality

ONE REQUIREMENT
Keep the Human
Healthy

A CURRENT NEED
Speed, accuracy
and fast deployment



aizon

Thank You for Your Time

toni.manzano@aizon.ai

ai