Generative AI: Transforming automation in biostatistics

AI in Clinical Research and Drug Development

Ercan Şükür, Senior Scientist

25.09.2024 | Basel Biometric Society (BBS)

NOTE: ANIMATIONS AND VIDEOS FROM THE ORIGINAL POWERPOINT PRESENTATION COULD NOT BE EMBEDDED IN THIS PDF FILE.

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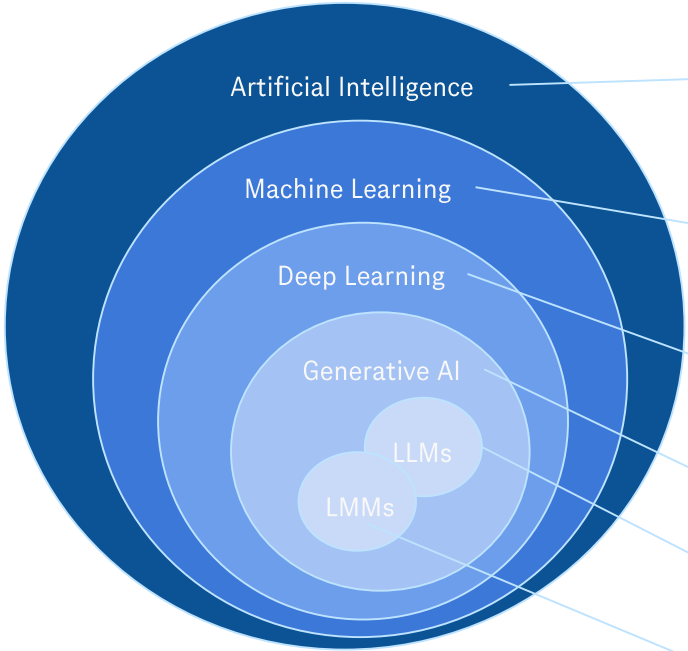
What is Generative AI and a LLM/LMM?

What is Generative AI (GenAI)?

Or: Who will soon be at the top of evolution?



1956 - The field of computer science that seeks to create intelligent machines that can replicate or exceed human intelligence.

1997 - Subset of AI that enables machines to learn from existing data and improve upon that data to make decisions or predictions. *Pattern Recognition (unstructured or structured data)*

2012 - A machine learning technique in which layers of neural networks *(unstructured data)* are used to process data.

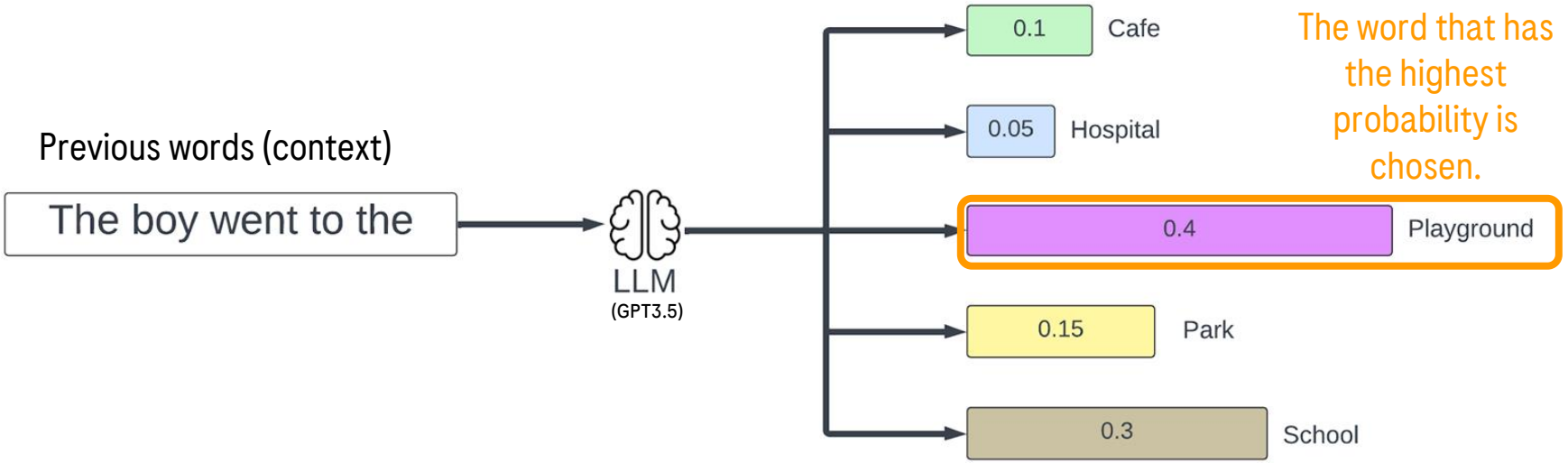
2020 - *Create new* written, visual, and auditory content given prompts or existing data.

Large Language Models *(understand natural language)*

Large Multimodal Models *(understand multiple types of data)*

What is a Large Language Model (LLM)?

Demystifying LLMs



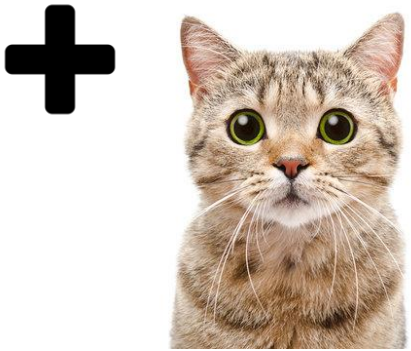
What is a Large Multimodal Model (LMM)?

Demystifying LMMs

Input (Multimodal Context*)

*text, images, video, audio, or even sensor data

“a cat playing in the park.”

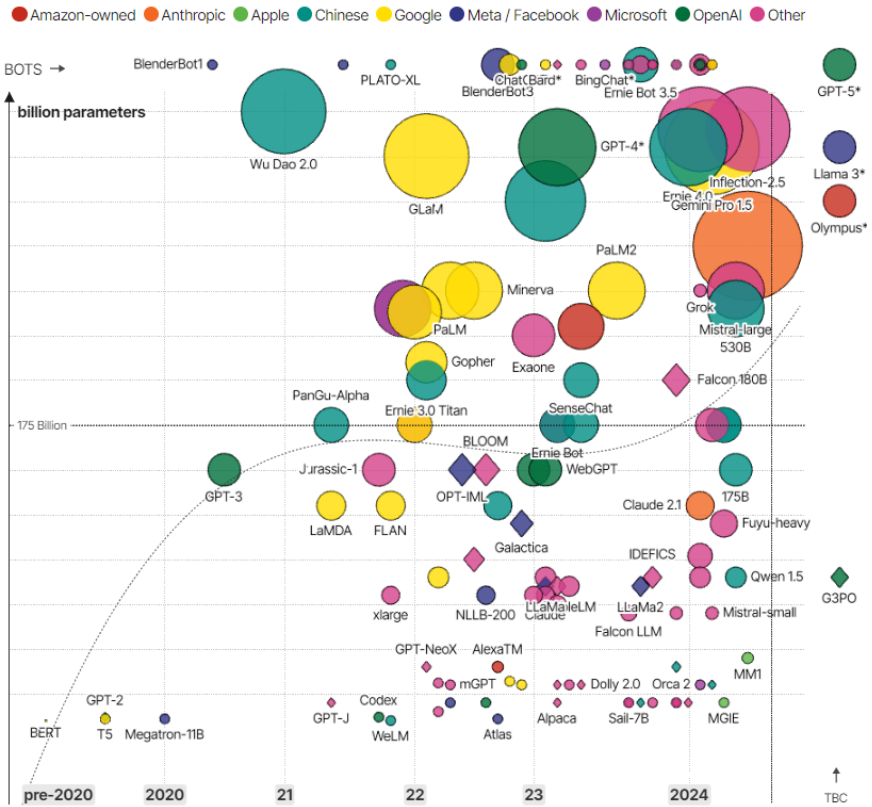


LMM

(DALL E3)

The Rise of A.I. LLMs

& their associated bots



David McCandless, Tom Evans, Paul Barton

Information is Beautiful // UPDATED 20th Mar 24

source: news reports, LifeArchitect.ai

* = parameters undisclosed // see the data

Source:https://informationisbeautiful.net/visualizations/the-rise-of-generative-ai-large-language-models-llms-like-chatgpt/

Ideas

Ideas

Personalized AI Assistant for Clinical Trial Data Analysis

Imagine you're working on a **clinical trial** to evaluate the efficacy of a new drug. You've just received a large dataset with hundreds of patient records, and your job is to analyze the **survival data** and **treatment effects** using **Cox proportional hazards models** and other statistical techniques.

Traditional Workflow

- **Data Cleaning**: You would manually clean and organize the dataset, removing outliers, handling missing values, and ensuring that all covariates are properly coded.
- **Modeling**: You'd then implement Cox models, check assumptions, and interpret results.
- **Reporting**: Finally, you'd prepare comprehensive statistical reports and visualizations for the team or regulatory bodies.

Ideas

Personalized AI Assistant for Clinical Trial Data Analysis

Automated Data Cleaning and Preprocessing:
•**Ask**: “GPT, can you clean the dataset and handle missing values using imputation techniques?”
•**Response**: The AI automatically processes the dataset, suggests the best imputation techniques (e.g., mean substitution, multiple imputation), and flags potential outliers for review.

Model Selection and Implementation:
•**Ask**: “GPT, suggest the best statistical model for this time-to-event data.”
•**Response**: GPT recommends the **Cox proportional hazards model**, explains why it’s suitable for the survival data, and generates the corresponding R or Python code.
•**Further**: You can fine-tune the model interactively by asking, “Can we adjust for these covariates: age, gender, and treatment type?”

Ideas

Personalized AI Assistant for Clinical Trial Data Analysis

Assumption Testing and Diagnostics:
•**Ask**: “GPT, check if the proportional hazards assumption holds for this model.”
•**Response**: The AI runs diagnostic tests, such as Schoenfeld residuals, and provides the output, highlighting any assumption violations with suggestions on how to address them.

Result Interpretation and Visualization:
•**Ask**: “GPT, can you generate Kaplan-Meier curves and provide a brief summary of the findings?”
•**Response**: GPT produces clear survival plots and a written summary of the results, including p-values, hazard ratios, and confidence intervals, all in a format ready for publication.

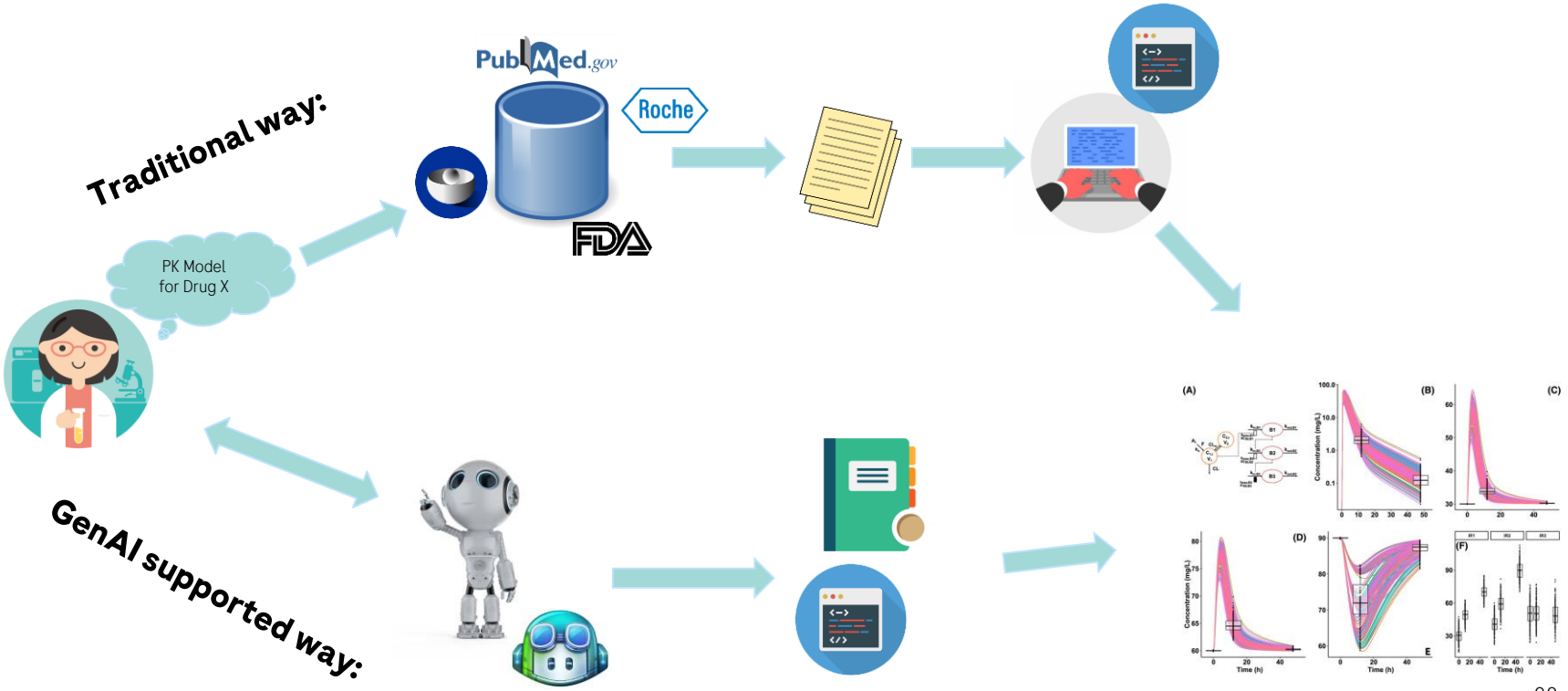
Automated Report Generation:
•**Ask**: “GPT, generate a statistical report summarizing the clinical trial results, including all assumptions, methods, and findings.”
•**Response**: The AI creates a well-structured report with narrative text, tables, and figures, saving hours of manual effort.

PMx-Bot

PMx = Pharmacometrics*
Pharmacometrics is the science of quantifying drug efficacy, safety, and pharmacokinetics through mathematical models to optimize drug development, dosing, and therapeutic decision-making

Traditional Way vs AI supported

Being more efficient to make decisions faster



Demo

Pharmacokinetic Modelling of 5-FU Production from Capecitabine—A Population Study in 40 Adult Patients with Metastatic Cancer

Published: December 2005

Volume 32, pages 817–833, (2005) Cite this article

Journal of Pharmacokinetics and Pharmacodynamics

Aims and scope →

Submit manuscript →

Saik Urien, Keyvan Rezaí & François Lokiec

Abstract

Aims: To model the biotransformation steps of 5-FU production from capecitabine and identify patient characteristics that may influence the drug disposition. Methods: Blood samples and demographic data were collected from two phase I studies in which adult patients received oral capecitabine for various malignancies. Capecitabine, 5′-deoxy-5-fluorocytidine (5′-DFCR), 5′-deoxy-5-fluorouridine (5′-DFUR) and 5-fluorouracile (5-FU) concentration-time data were analysed via a population approach using NONMEM.

Demo

Reproducing a Paper

Pharmacokinetics and safety of candidate tocil
blind, single-dose phase I study

Kyung-Sang Yu, Byungwook Kim, Dongseong Shin, Min Kyu Park, Jun Gi Hwang, Min-Gul Kim, Hy
Edward Keystone

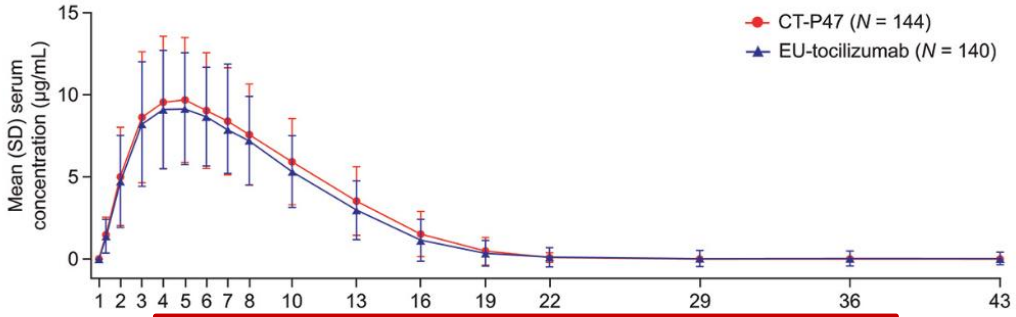
https://doi.org/10.1080/13543784.2023.2212155

Figure 2 of 2

Figure 2. Mean (SD) serum concentrations of CT-P47 and EU-tocil

Note: Values below the lower limit of quantification were set to

EU-tocilizumab = European Union-approved reference tocilizuma



Study Day	Mean (SD) serum concentration (µg/mL)	
	CT-P47 (*N* = 144)	EU-tocilizumab (*N* = 140)
1 (pre-dose)	0	0
1 (8 h post-dose)	1.47 (1.06)	1.40 (1.03)
2	5.02 (3.00)	4.72 (2.80)
3	8.61 (4.00)	8.20 (3.78)
4	9.54 (4.01)	9.08 (3.60)
5	9.66 (3.79)	9.14 (3.39)
6	9.02 (3.51)	8.65 (3.00)
7	8.39 (3.24)	7.86 (2.65)
8	7.57 (3.08)	7.20 (2.68)
10	5.92 (2.62)	5.31 (2.18)
13	3.54 (2.09)	2.97 (1.79)
16	1.52 (1.37)	1.14 (1.27)
19	0.47 (0.84)	0.36 (0.78)
22	0.09 (0.27)	0.11 (0.58)
29	0.00 (0.01)	0.04 (0.48)
36	0	0.04 (0.46)
43	0	0.03 (0.39)

https://doi.org/10.1080/13543784.2023.2212155

Demo

Reproducing a Paper

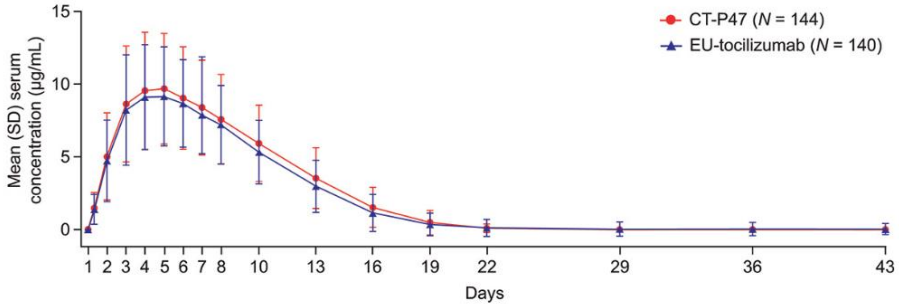


Table 2 of 4

Table 2. Summary of PK variables (PK set; Part 2).

	CT-P47 (*N* = 144)	EU-tocilizumab (*N* = 140)
AUC_{0-inf} (day*µg/mL)		
n	138[a]	136[a,b]
Mean (SD)	94.34 (40.95)	85.98 (36.23)

https://doi.org/10.1080/13543784.2023.2212155

PMx-Bot

By Ercan Suekuer

Your guide for pharmacometrics modeling and data interpretation.

How do I model a two-compartment PK model?

What are common issues with nonlinear mixed-...

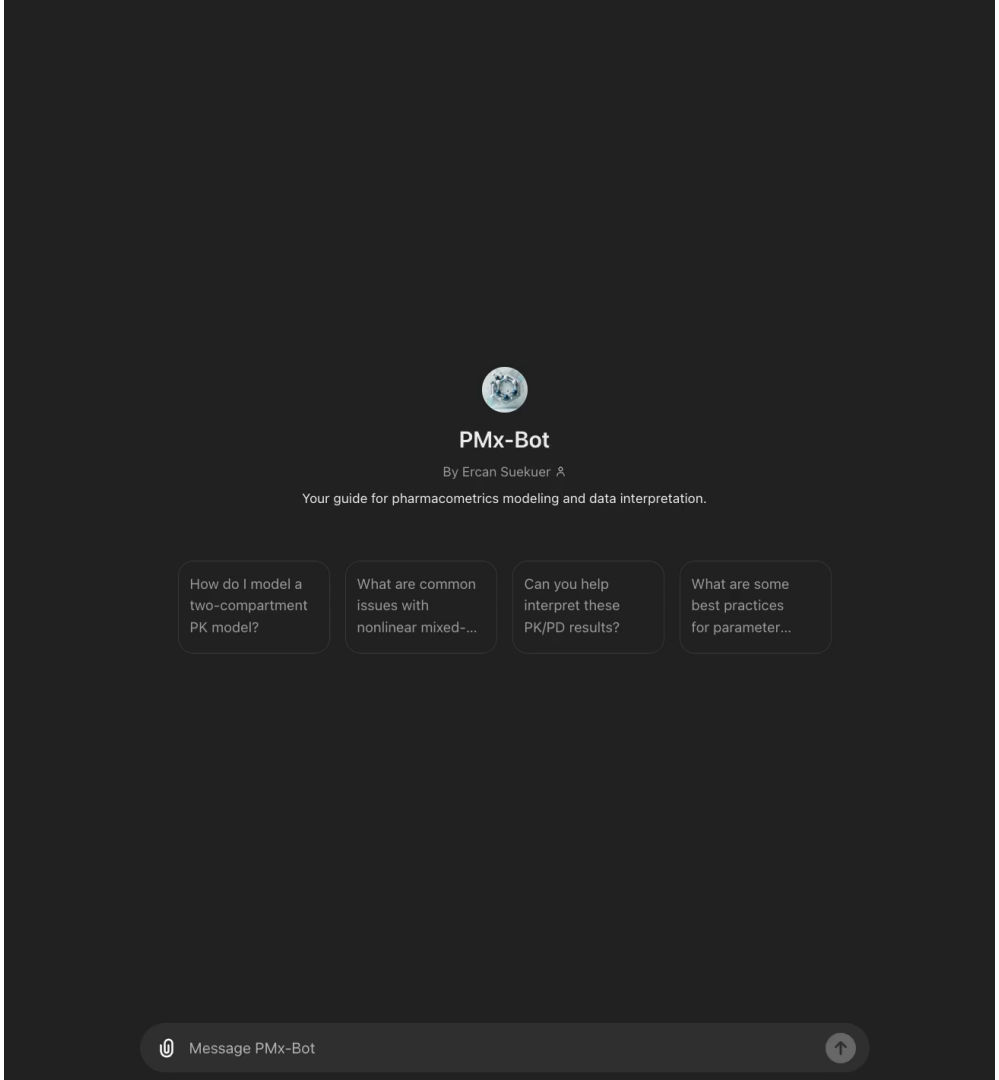
Can you help interpret these PK/PD results?

What are some best practices for parameter...

Message PMx-Bot

Demo

My little Data Scientist Assistant



https://opensource.nibr.com/xgx/Single_Ascending_Dose_PK.html

Impact on Programming

AI Coding

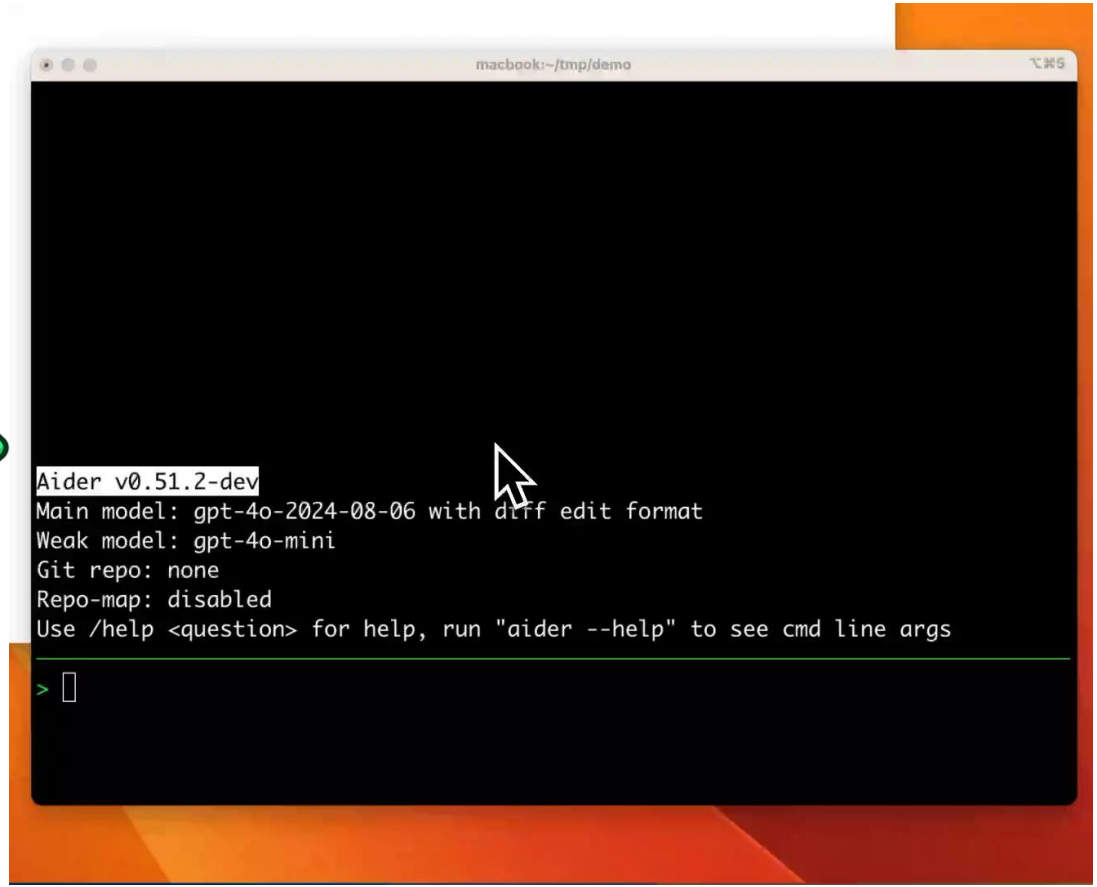
One of many tools

Top 3 AI coding bots:

CURSOR

aider

GitHub Copilot

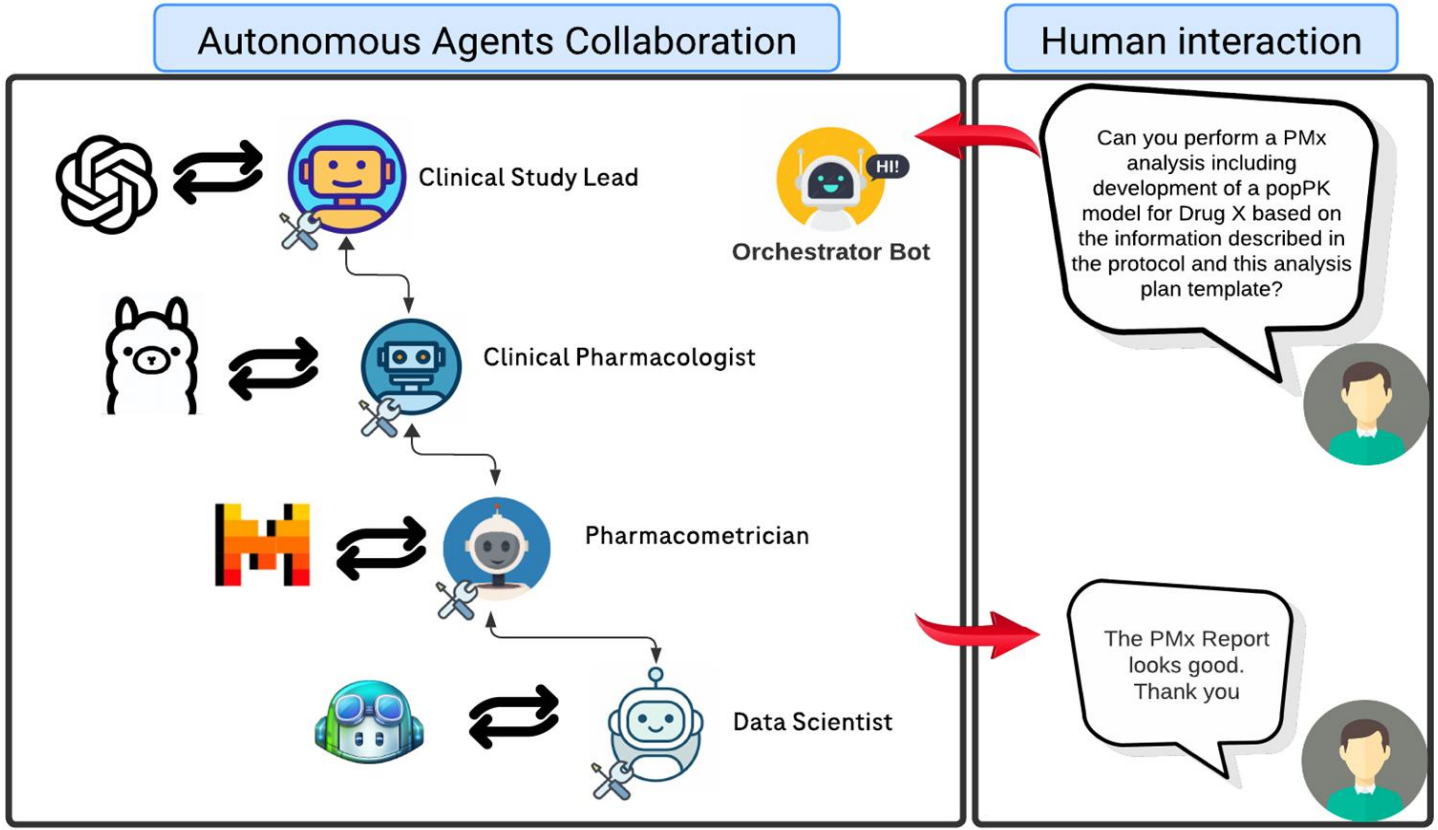


Future Horizon

~~Future~~ Horizon

Autonomous Agents

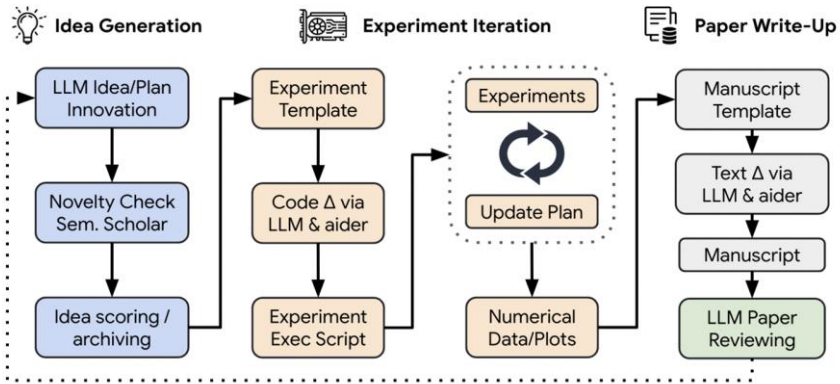
AI Bots by their own



Agent based approaches are making waves in the scientific community

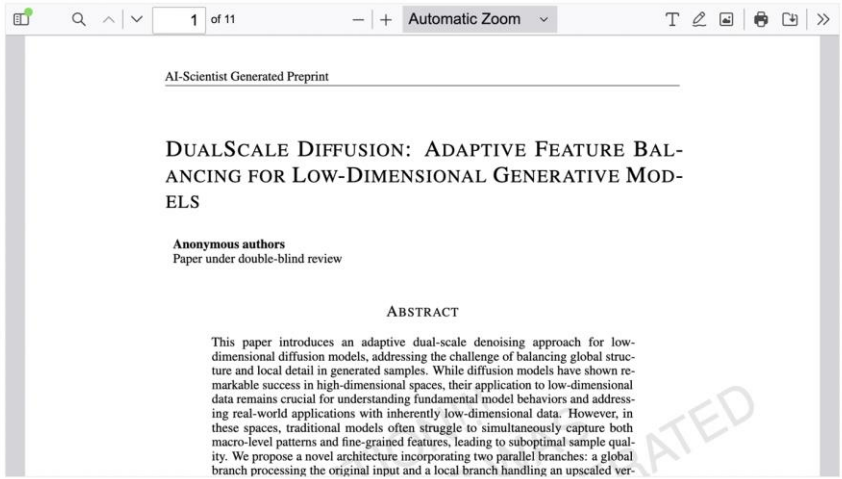
The AI Scientist: Towards Fully Automated Open-Ended Scientific Discovery

August 13, 2024



***Conceptual illustration of The AI Scientist**. The AI Scientist first brainstorms a set of ideas and then evaluates their novelty. Next, it edits a codebase powered by recent advances in automated code generation to implement the novel algorithms. The Scientist then runs experiments to gather results consisting of both numerical data and visual summaries. It crafts a scientific report, explaining and contextualizing the results. Finally, the AI Scientist generates an automated peer review based on top-tier machine learning conference standards. This review helps refine the current project and informs future generations of open-ended ideation.*

Diffusion Modeling



AI-Scientist Generated Preprint

DUALSCALE DIFFUSION: ADAPTIVE FEATURE BALANCING FOR LOW-DIMENSIONAL GENERATIVE MODELS

Anonymous authors
Paper under double-blind review

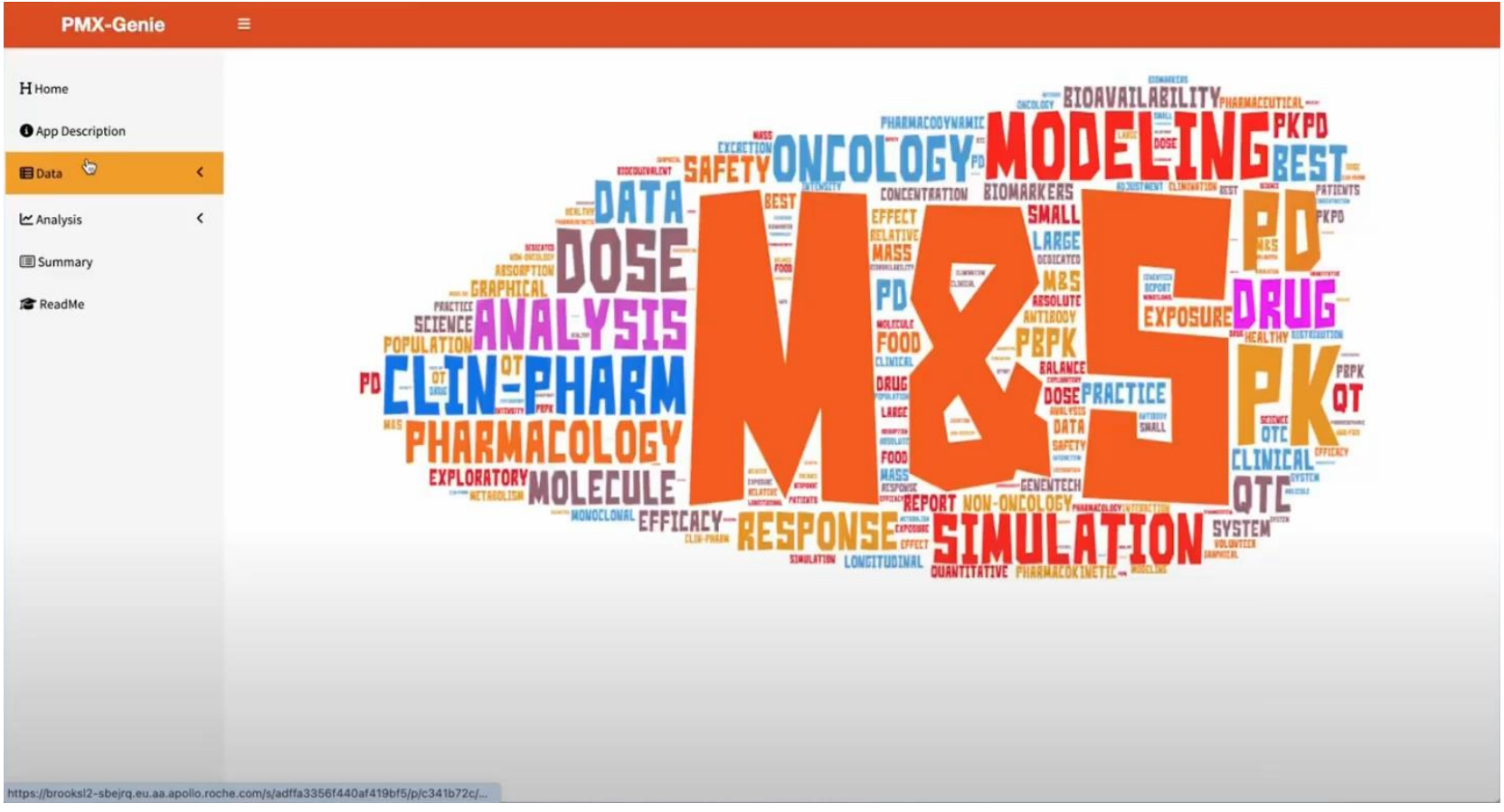
ABSTRACT

This paper introduces an adaptive dual-scale denoising approach for low-dimensional diffusion models, addressing the challenge of balancing global structure and local detail in generated samples. While diffusion models have shown remarkable success in high-dimensional spaces, their application to low-dimensional data remains crucial for understanding fundamental model behaviors and addressing real-world applications with inherently low-dimensional data. However, in these spaces, traditional models often struggle to simultaneously capture both macro-level patterns and fine-grained features, leading to suboptimal sample quality. We propose a novel architecture incorporating two parallel branches: a global branch processing the original input and a local branch handling an upscaled ver-

DualScale Diffusion: Adaptive Feature Balancing for Low-Dimensional Generative Models

sakana.ai/ai-scientist/

First building blocks



Artificial general intelligence (AGI)

Artificial general intelligence (AGI) on the horizon?

Artificial General Intelligence (AGI) is a theoretical form of AI capable of performing any intellectual task that a human can, unlike current AI, which is specialized for specific tasks.
For a biostatistician, think of current AI as a tool that helps with specific tasks like data analysis, model fitting, or hypothesis testing. AGI, in contrast, would be like having a highly skilled colleague who can not only understand biostatistics but also adapt seamlessly to any other domain—whether it's genomics, epidemiology, or even completely new fields—**without needing retraining.** AGI doesn't exist yet...

Artificial general intelligence (AGI) on the horizon?

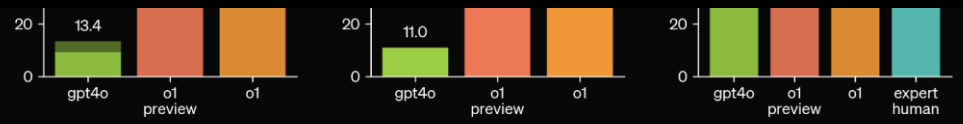
Artificial General Intelligence (AGI) is a theoretical form of AI capable of performing any intellectual task that a human c
For a biostatistician ke data analysis, model fitting, or hyp ly skilled colleague who can not only un er domain—whether it's genomics, epide **etraining.** AGI doesn't exist yet...

Intro view

Derya Unutmaz, MD
@DeryaTR_

I just had o1 write a major cancer treatment project based on a very specific immunological approach. It created the full framework of the project in under a minute, with highly creative aims, approaches, and even considerations for potential pitfalls and alternative strategies (this is usually missing in 4o). This would have taken me days, if not longer, to prepare, and I still would have missed several of o1's points. In fact, there was at least one idea unique enough that I might not have thought of it, even with 30 years of deep expertise in this field! People have no idea what's happening!

9:50 PM · Sep 14, 2024 · **58.6K** Views



o1 greatly improves over GPT-4o on challenging reasoning benchmarks. Solid bars show pass@1 accuracy and the shaded region shows the performance of majority vote (consensus) with 64 samples.

Artificial general intelligence (AGI) on the horizon?

OpenAI's five levels towards AGI

OpenAI Imagines Our AI Future

Stages of Artificial Intelligence	
Level 1	Chatbots, AI with conversational language
Level 2	Reasoners, human-level problem solving
Level 3	Agents, systems that can take actions
Level 4	Innovators, AI that can aid in invention
Level 5	Organizations, AI that can do the work of an organization

Conclusion & Call to Action

Conclusion & Call to Action

We need a mindset change - asap

Rejection

Positive

Panic

Doing now what patients need next