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Generative AI and its Applications in Life Sciences

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Acknowledgements

The following slides about generative AI were adopted from
https://www.slideshare.net/AllThingsOpen/generative-ai-259922340
by Karthik Uppuluri at Fidelity Investments

Introduction

Artificial Intelligence, Machine Learning and Deep Learning

- The term **AI** in the broadest sense refers to simulation of human intelligence processes by computer systems
- **Machine Learning** is a subset of AI focusses on designing specific systems which can learn and make decisions/predictions based on data.
- **Deep Learning** is a subset of Machine Learning that uses a specific set of algorithms known as Neural-Networks often with many layers.

Introduction

Types of Machine Learning Models

❑ Supervised Learning

Supervised Learning is a type of Machine Learning model trained on labeled data

Email Spam Classification Model

Data: *Examples of emails either tagged as Spam or not Spam*

Training:

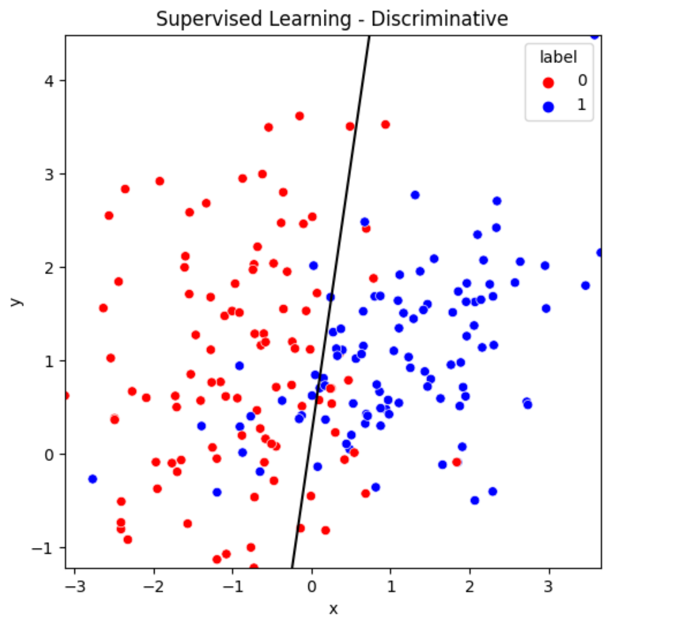
Discriminative – Learns the boundary that separates "spam" vs "not spam"

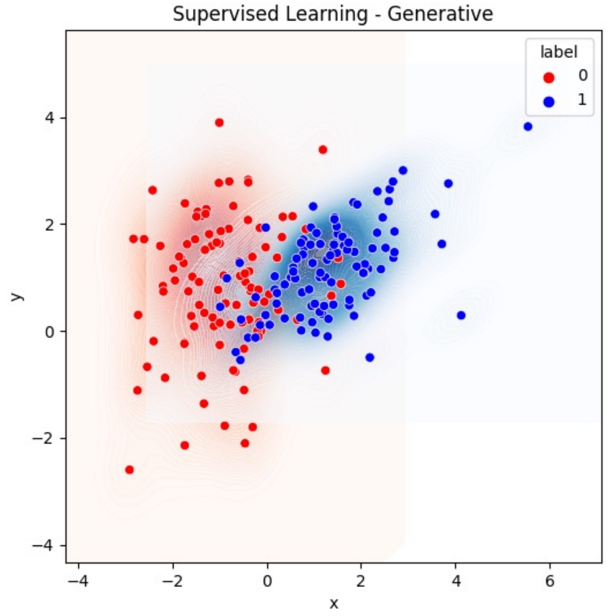
Generative – Learns the distribution of "spam" and "not spam" emails to understand how each class generates content

Inference

Discriminative – Determine on which side of the boundary a new email falls

Generative – Based on learned distributions compute the likelihood of the new email being "spam" vs "not spam"



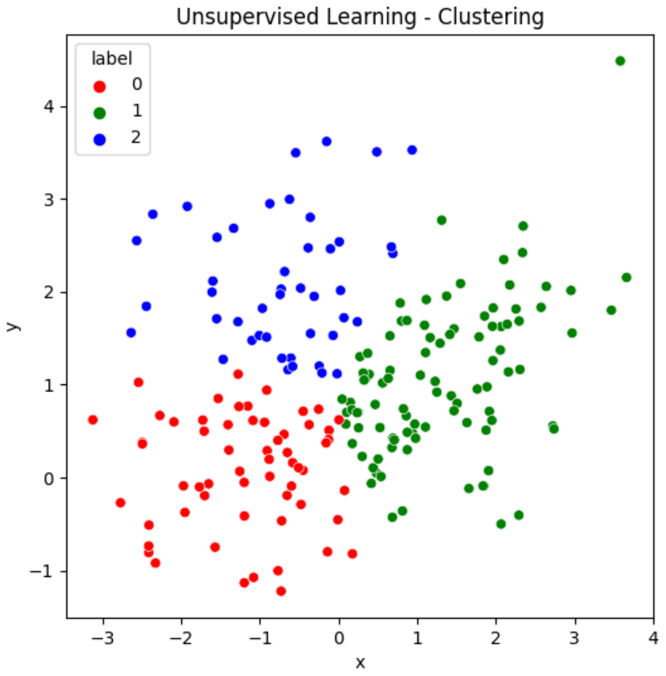


Introduction

Types of Machine Learning Models

❑ Unsupervised Learning

Unsupervised Learning is a type of Machine Learning model that identifies patterns and structures within un-labelled data



Email Topic Modeling

Data: *A large collection of emails you may want to organize by subject matter*

Training:

Learn the distribution that generates the structure within the data

Inference

- Assign new email to the cluster where they have the highest probability of belonging

Introduction

Types of Machine Learning Models

❑ Reinforcement Learning

Interaction: Agent interacts with the environment by choosing actions from its current policy

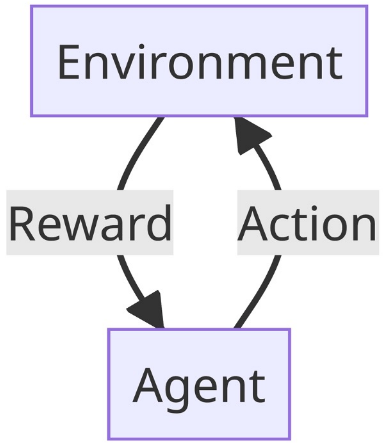
A self-driving car decides to take a left or a right based on its current strategy and current state of the road

Reward/Penalty: After each action, agent receives a reward/penalty which reflects the success of the action

If the car safely navigates traffic or obeys rules, it's a success

Policy Update: Agent updates the policy based on feedback received aiming to maximize the total reward over time.

Based on the reward/penalty received car adjusts its driving policy, actions with positive rewards will be repeated and negative rewards will be avoided



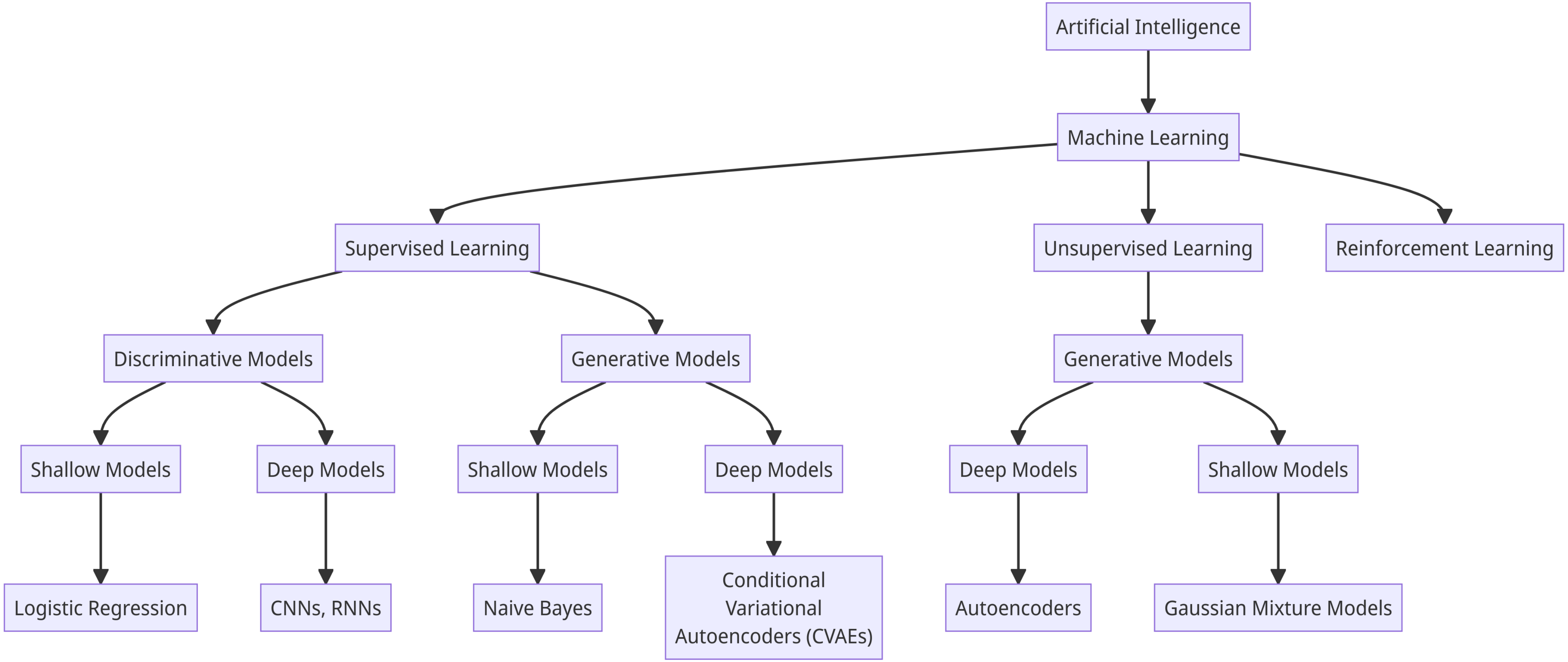
❑ Shallow and Deep Models

Models with limited layers and capable of capturing only linear and simple nonlinear relationships are called shallow models

Models with many layers and capable of capturing complex hierarchical patterns are called deep models

Introduction

Summary



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Generative AI

GPT, GAN and Diffusion Models

Applications of Generative AI

Emerging Trends, Limitations, Potential Ahead

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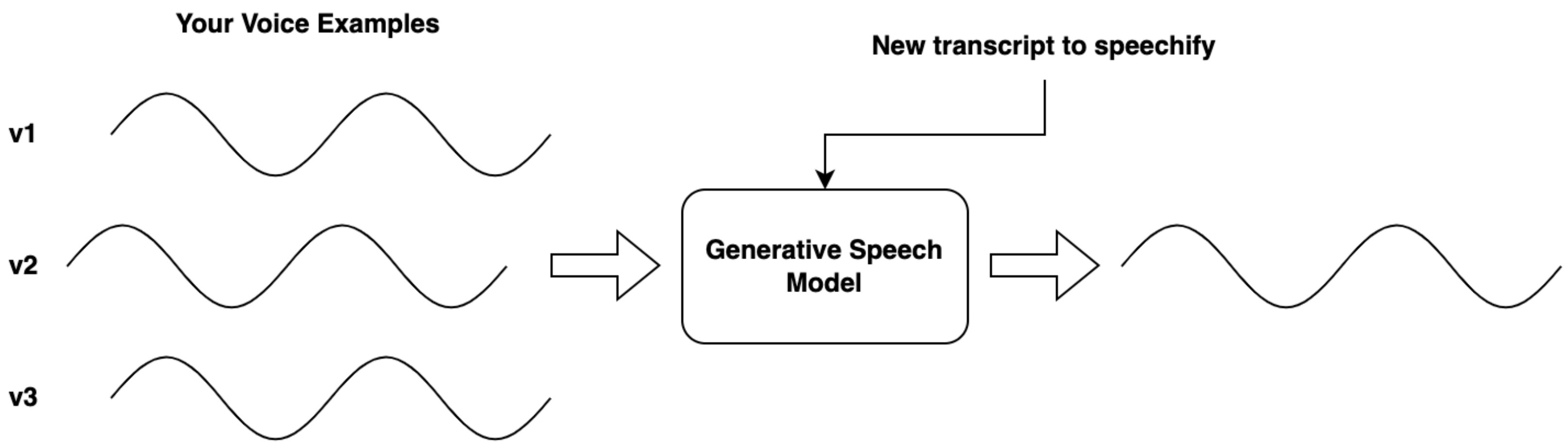
Generative AI

Definition

Generative AI refers to a set of artificial intelligence methodologies that can produce novel content that resembles the training data they were exposed to.

The content could be anything spanning from synthesizing text, generating code, realistic images, music and more



Generative AI

Generative Pre-Trained Transformer (**GPT**) - Motivation

Issues with CNNs, RNNs, LSTMs

- Convolutional Neural Networks (**CNNs**) are good at **local feature extraction** and struggle to understand long-range dependencies in data

- CNNs **do not have a mechanism to understand the order of elements** making it harder for problems involving text and time-series

- **RNNs** especially **LSTMs** can handle long range dependencies due to their ability to process data sequentially. But as the sequences get longer, they struggle from **vanishing gradient problems**

- CNNs, RNNs, LSTMs are suitable for specific data types and are **not efficient at handling multi-modal inputs**

What if you can completely avoid recurrent connections, thereby avoiding vanishing gradient issues?

Generative AI

Generative Pre-Trained Transformer (**GPT**) - Motivation

- A new architecture called **Transformers** is proposed by scientists from Google which avoids the recurrent connections altogether by relying on an operation known as attention

- This architecture also takes care of sequential nature of inputs by using **positional embeddings**

Attention Is All You Need

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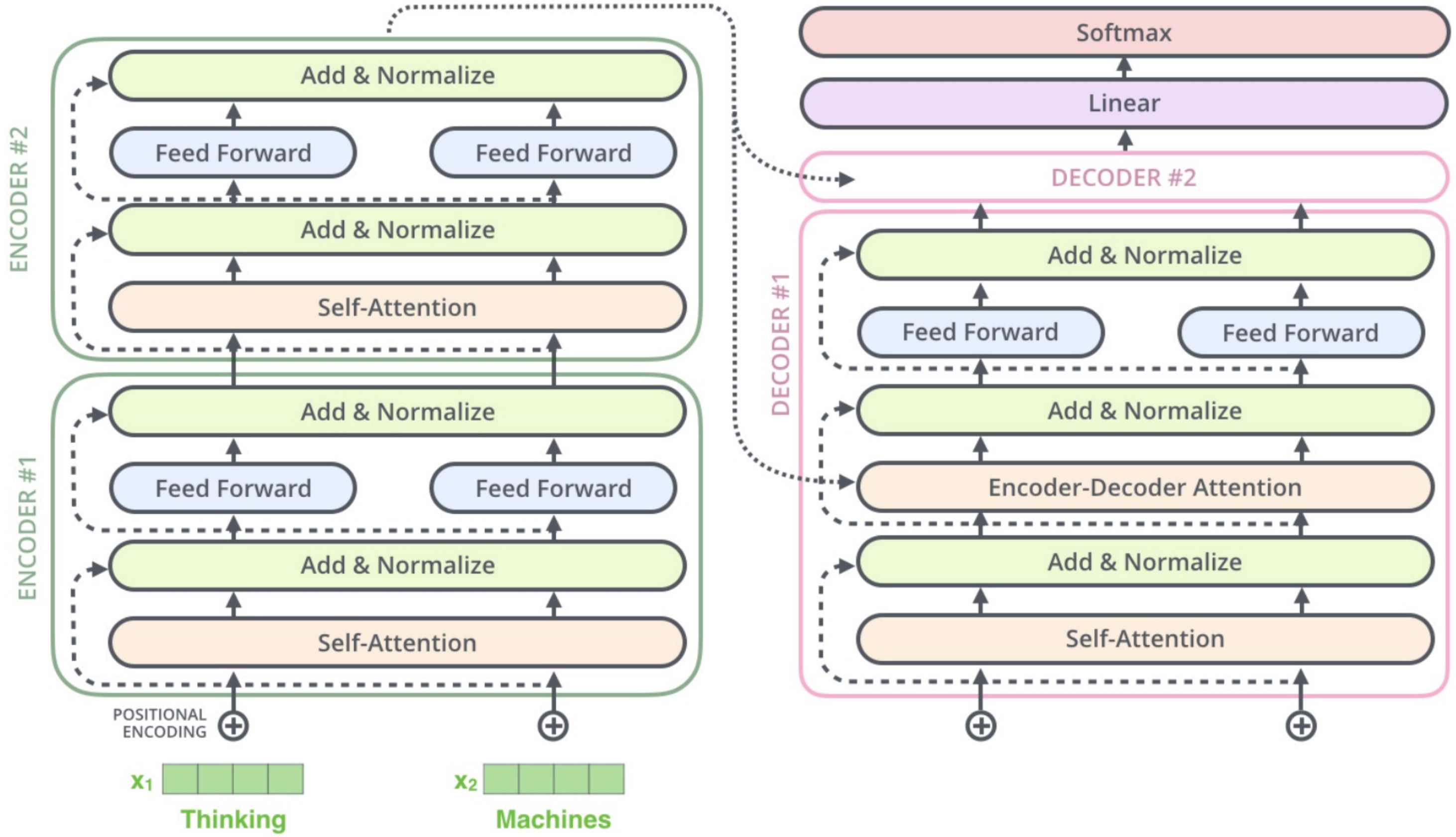
https://proceedings.neurips.cc/paper_files/paper/2017/file/3f5ee243547dee91fbd053c1c4a845aa-Paper.pdf

Generative AI

Generative Pre-Trained Transformer (**GPT**) –Transformers Architecture

Architecture

- Six Encoder layers stacked
- Six Decoder layers stacked
- Positional Embeddings
- Masked Attention (Encoder-Decoder Attention)



Advantages

- Better long-range connections
- Easier to parallelize
- Can make the networks much deeper (more layers) than RNNs

https://arxiv.org/pdf/1706.03762.pdf
http://jalammar.github.io/illustrated-transformer/
https://cs182sp21.github.io/static/slides/lec-12.pdf

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Generative AI

Generative Pre-Trained Transformer (**GPT**)

A **Generative-Pre-Trained Transformer** is a kind of transformers model developed by OpenAI for natural language processing tasks

- **Generative** refers to the model's ability to generate text
- **Pre-Trained** refers to models training process consisting of two stages
    - **Pre-Training**: Model is trained on a large corpus of text data, where the objective is to predict next word in a sentence
    - **Fine-tuning**: Once the model is pre-trained the model can be fine-tuned on a specific task with a task-specific dataset with supervised learning

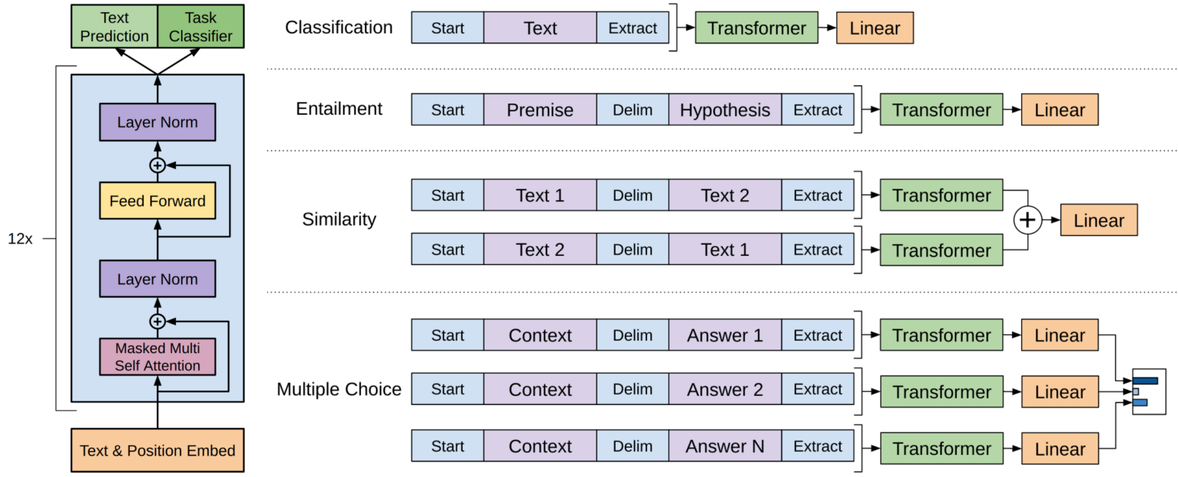


Figure 1: **(left)** Transformer architecture and training objectives used in this work. **(right)** Input transformations for fine-tuning on different tasks. We convert all structured inputs into token sequences to be processed by our pre-trained model, followed by a linear+softmax layer.

https://arxiv.org/pdf/2005.14165.pdf https://s3-us-west-2.amazonaws.com/openai-assets/research-covers/language-unsupervised/language_understanding_paper.pdf

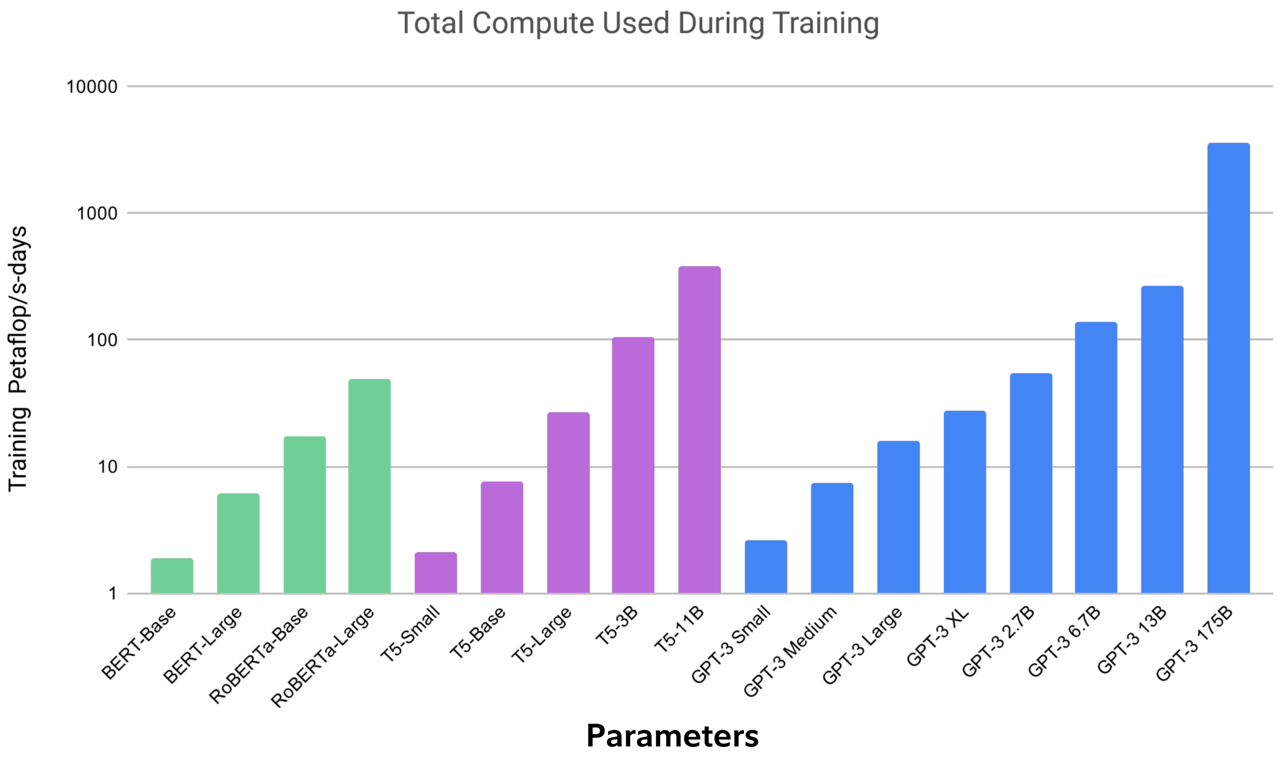
Generative AI

Generative Pre-Trained Transformer (**GPT**) – GPT 3 Training Data and Parameters

Dataset	Quantity (tokens)	Weight in training mix	Epochs elapsed when training for 300B tokens
Common Crawl (filtered)	410 billion	60%	0.44
WebText2	19 billion	22%	2.9
Books1	12 billion	8%	1.9
Books2	55 billion	8%	0.43
Wikipedia	3 billion	3%	3.4

Table 2.2: Datasets used to train GPT-3. "Weight in training mix" refers to the fraction of examples during training that are drawn from a given dataset, which we intentionally do not make proportional to the size of the dataset. As a result, when we train for 300 billion tokens, some datasets are seen up to 3.4 times during training while other datasets are seen less than once.

Dataset



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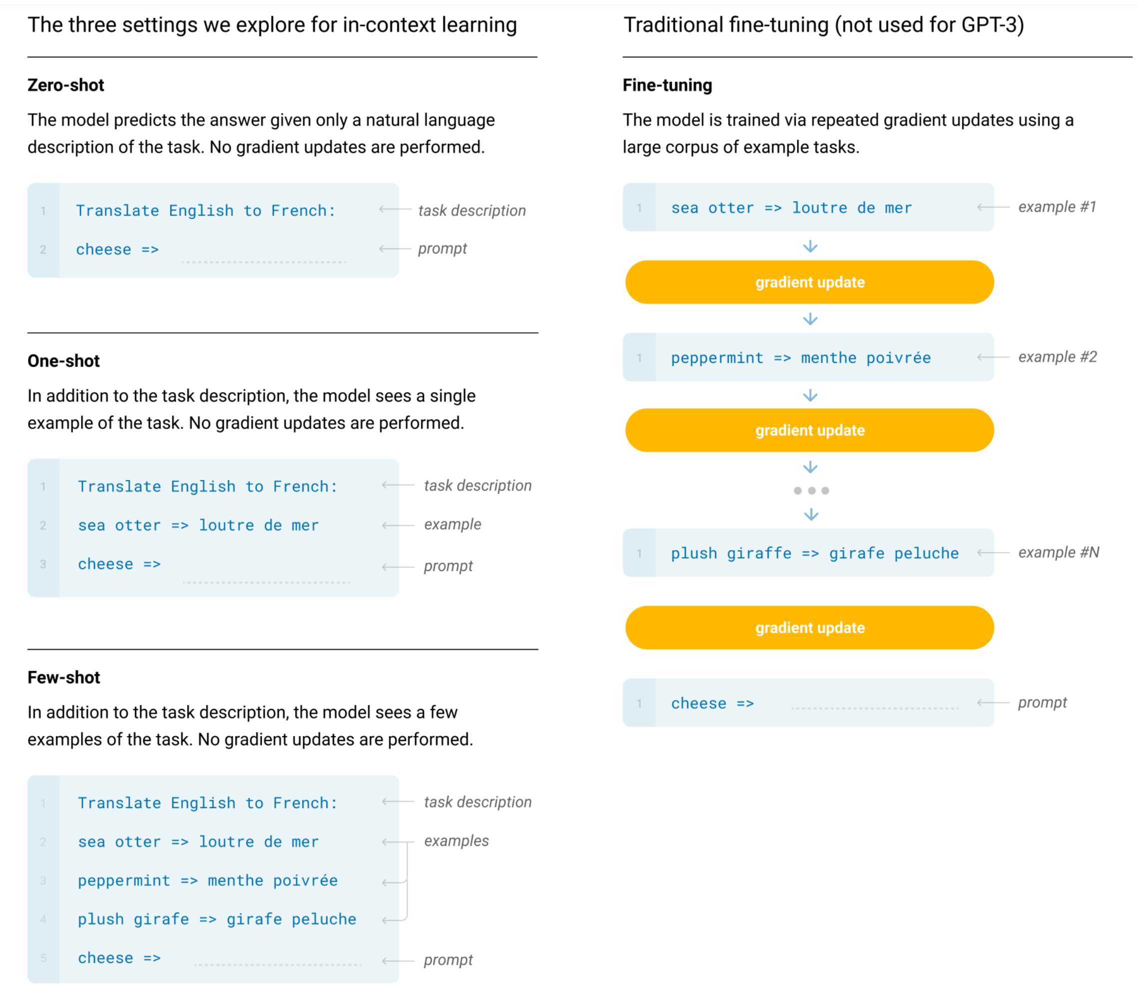
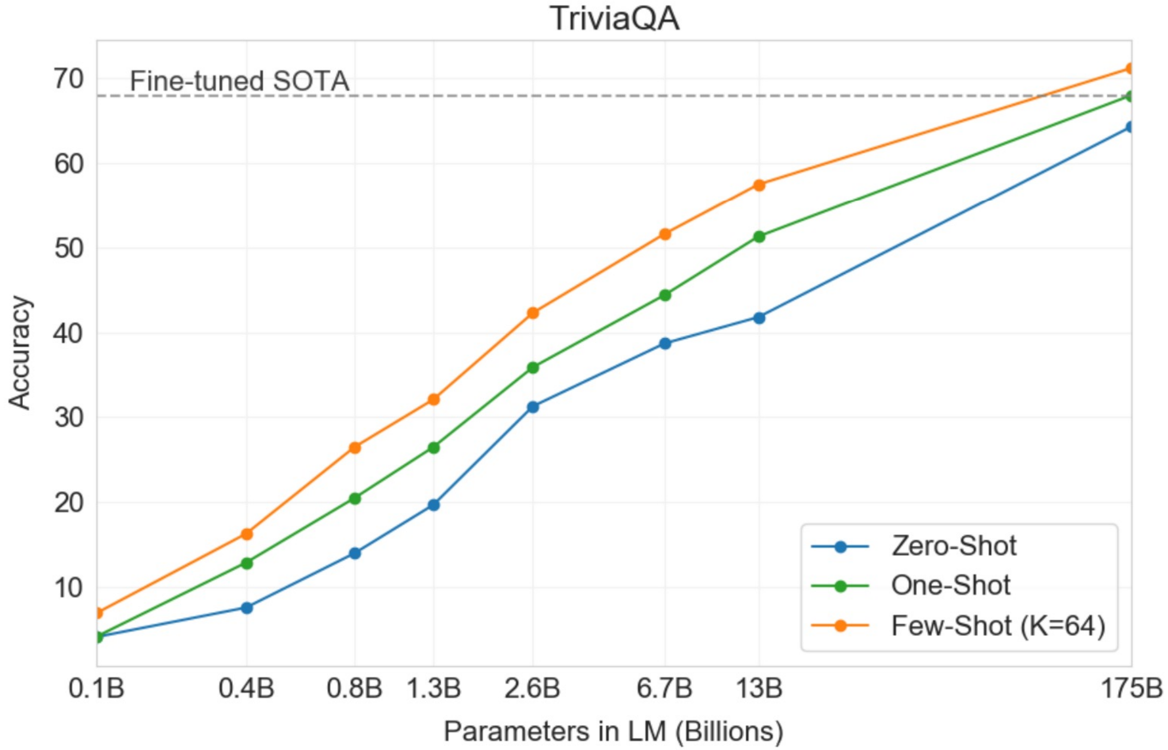
https://arxiv.org/pdf/2005.14165.pdf

Generative AI

Generative Pre-Trained Transformer (**GPT**) – GPT 3 Unreasonable Effectiveness





TriviaQA is a reading comprehension dataset containing over 650K question-answer-evidence triples. https://nlp.cs.washington.edu/triviaqa/

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https://arxiv.org/pdf/2005.14165.pdf

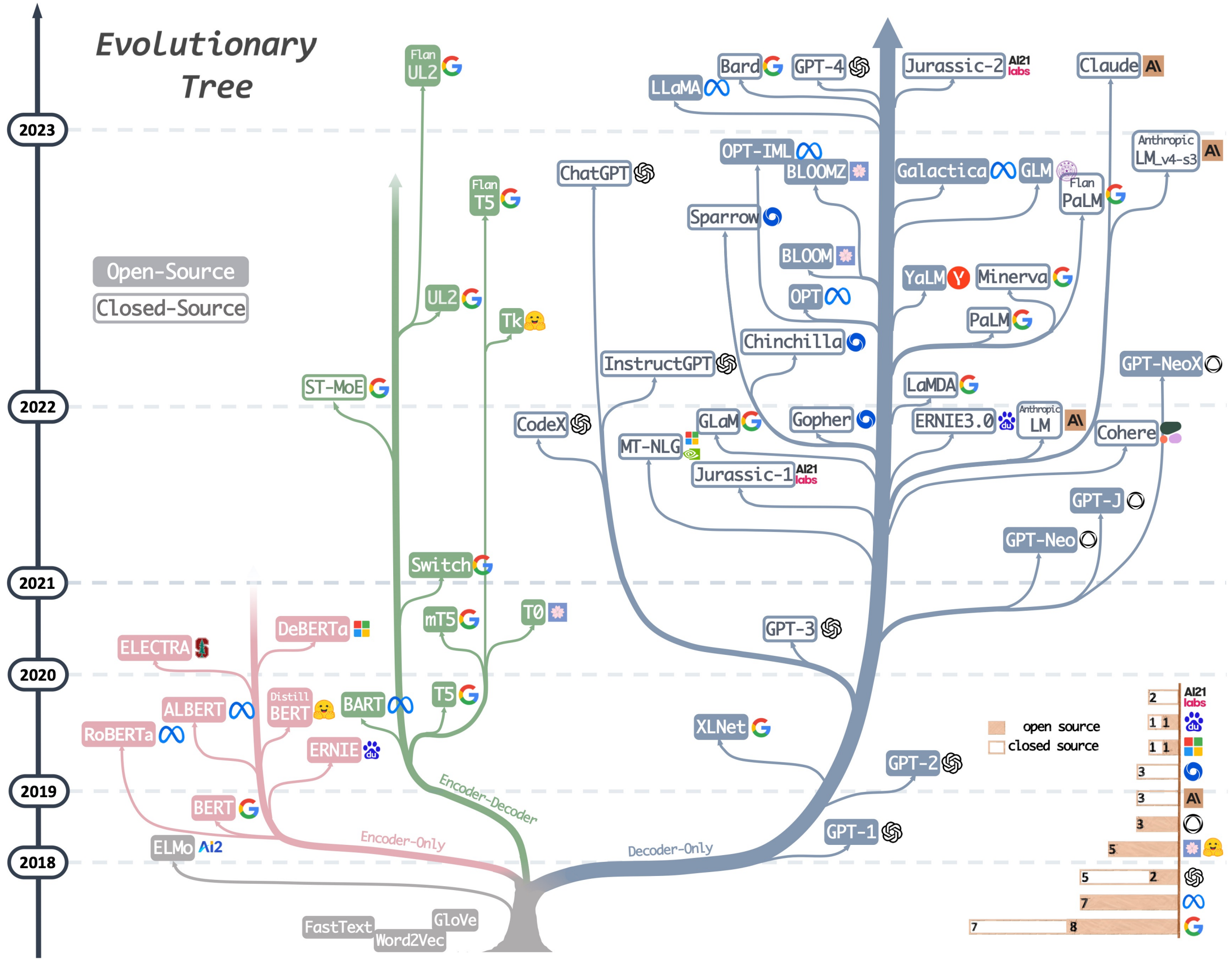
Generative AI

Generative Pre-Trained Transformer (**GPT**) – LLM Landscape

Encoder Models: These models map input sequences to a vector representation. Useful for extracting features (**BERT**)

Decoder Models: These models generate an output sequence from a fixed length input vector. Useful for generation text, images etc. (**GPT-3**)

Encoder-Decoder Models: These models are a combination of both encoder and decoder. Encoder is responsible for mapping input into vector and decoder generates output sequence from that vector. (**BART/ T5/ FLAN UL2**)



https://arxiv.org/pdf/2304.13712.pdf

https://amatriain.net/blog/transformer-models-an-introduction-and-catalog-2d1e9039f376/

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Generative AI

Generative Pre-Trained Transformer (**GPT**) – Chain-of-thought Prompting

Chain-of-Thought Prompting is a technique that enables LLMs to complex reasoning generating a chain-of-thought, a series of intermediate reasoning steps.

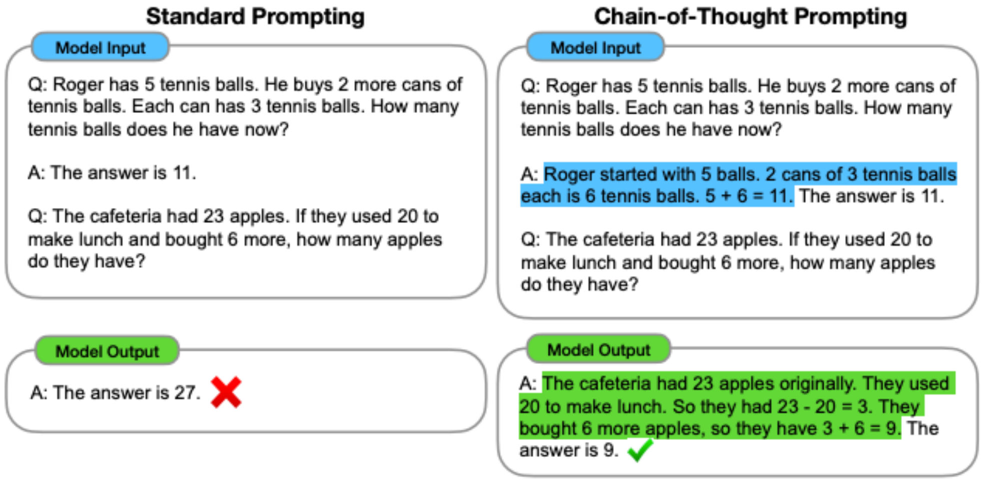


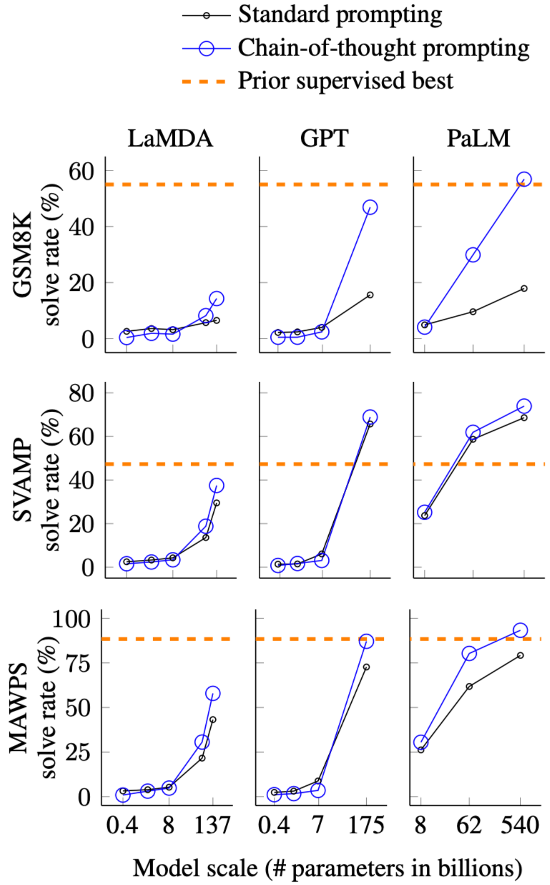
Figure 1: Chain-of-thought prompting enables large language models to tackle complex arithmetic, commonsense, and symbolic reasoning tasks. Chain-of-thought reasoning processes are highlighted.

Prompting

Table 12: Summary of math word problem benchmarks we use in this paper with examples. N: number of evaluation examples.

Dataset	N	Example problem
GSM8K	1,319	Josh decides to try flipping a house. He buys a house for $80,000 and then puts in $50,000 in repairs. This increased the value of the house by 150%. How much profit did he make?
SVAMP	1,000	Each pack of dvds costs 76 dollars. If there is a discount of 25 dollars on each pack. How much do you have to pay to buy each pack?
ASDiv	2,096	Ellen has six more balls than Marin. Marin has nine balls. How many balls does Ellen have?
AQuA	254	A car is being driven, in a straight line and at a uniform speed, towards the base of a vertical tower. The top of the tower is observed from the car and, in the process, it takes 10 minutes for the angle of elevation to change from 45° to 60°. After how much more time will this car reach the base of the tower? Answer Choices: (a) $5\sqrt{3}+1$ (b) $6\sqrt{3}+\sqrt{2}$ (c) $7\sqrt{3}-1$ (d) $8\sqrt{3}-2$ (e) None of these
MAWPS: SingleOp	562	If there are 7 bottle caps in a box and Linda puts 7 more bottle caps inside, how many bottle caps are in the box?
MAWPS: SingleEq	508	Benny bought a soft drink for 2 dollars and 5 candy bars. He spent a total of 27 dollars. How much did each candy bar cost?
MAWPS: AddSub	395	There were 6 roses in the vase. Mary cut some roses from her flower garden. There are now 16 roses in the vase. How many roses did she cut?
MAWPS: MultiArith	600	The school cafeteria ordered 42 red apples and 7 green apples for students lunches. But, if only 9 students wanted fruit, how many extra did the cafeteria end up with?

Datasets and Example Problems



Performance

https://arxiv.org/pdf/2201.11903.pdf

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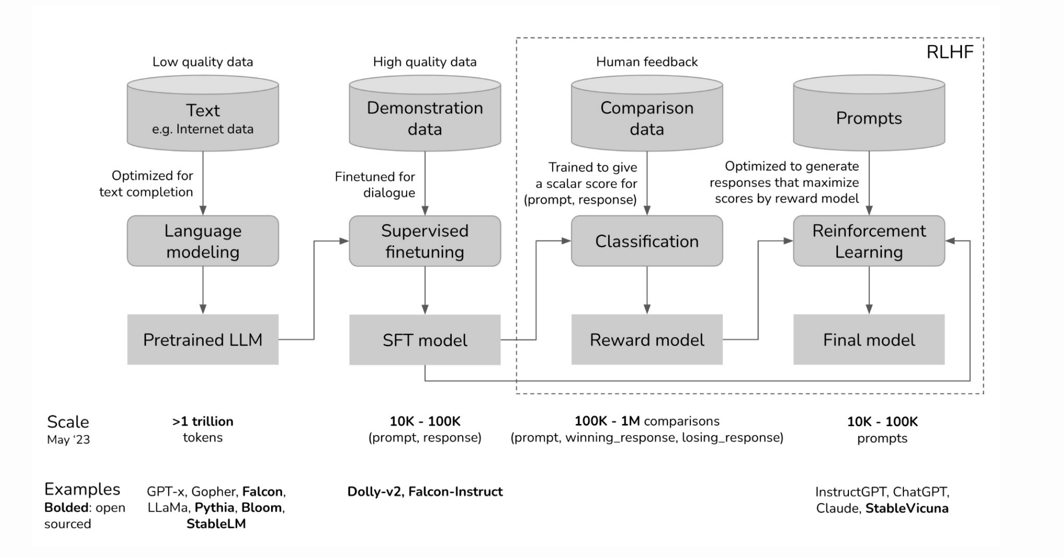
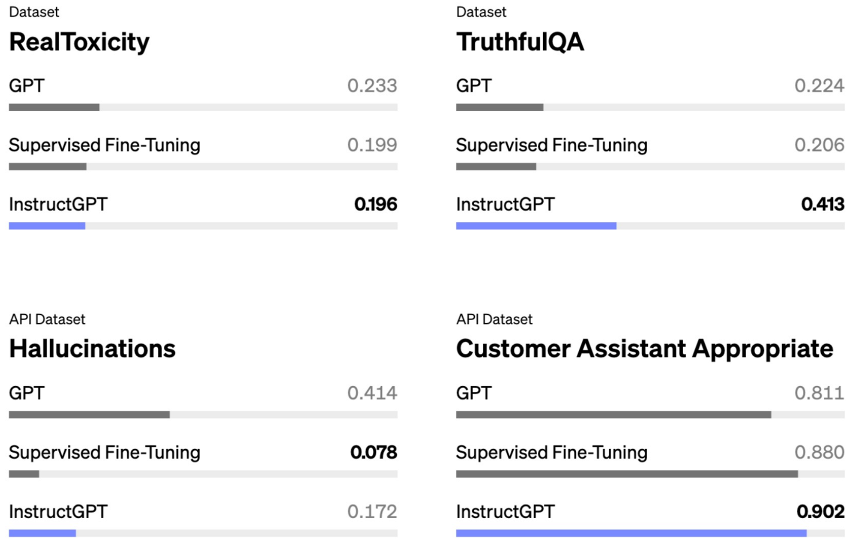
Generative AI

Generative Pre-Trained Transformer (**GPT**) – Alignment - RLHF

- **Reinforcement Learning through Human Feedback** is technique that allows models to learn directly from human feedback (like prompting) without the need for labeled data

- Due to the nature of training data being scrapped from internet (contains a lot of mis-information, conspiracy theories etc..) the models must be **further polished/aligned using RLHF** to make it user appropriate





Evaluating InstructGPT for toxicity, truthfulness, and appropriateness. Lower scores are better for toxicity and hallucinations, and higher scores are better for TruthfulQA and appropriateness. Hallucinations and appropriateness are measured on our API prompt distribution. Results are combined across model sizes.

https://arxiv.org/pdf/2212.08073.pdf
https://huyenchip.com/2023/05/02/rlhf.html

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Generative AI

Generative Adversarial Networks (**GANs**)

Imagine you have a bunch of **cat images**, and you want a machine learning model to create similar images. This is exactly what a GAN does.

Generator: Takes in random numbers as input and generates the images of interest (**the forger**)

Discriminator: Takes both the images from the generator and the real images from the data and spots the difference between them (**the detective**)

Both the generator and the discriminator are trained together. And, over the duration of training, the generator gets better at creating images which look real, and the discriminator gets better at spotting fakes.

Adversarial Objective: These two networks are pitted against each other where the **generator creates more realistic synthetic images to fool the discriminator** while the **discriminator networks tries to get better at detecting fake images**. This back-and-forth strategy forces both the networks to improve until the generator can create highly realistic synthetic images, that indistinguishable from real images

https://arxiv.org/pdf/1406.2661.pdf

Generative AI

Diffusion Models

Diffusion models are another class of Generative models which work by adding noise to the images in the training data by a process called **forward diffusion process** and then reversing the process to recover the original image using **reverse diffusion**. These models can be trained on **large unlabeled datasets in an unsupervised manner**.

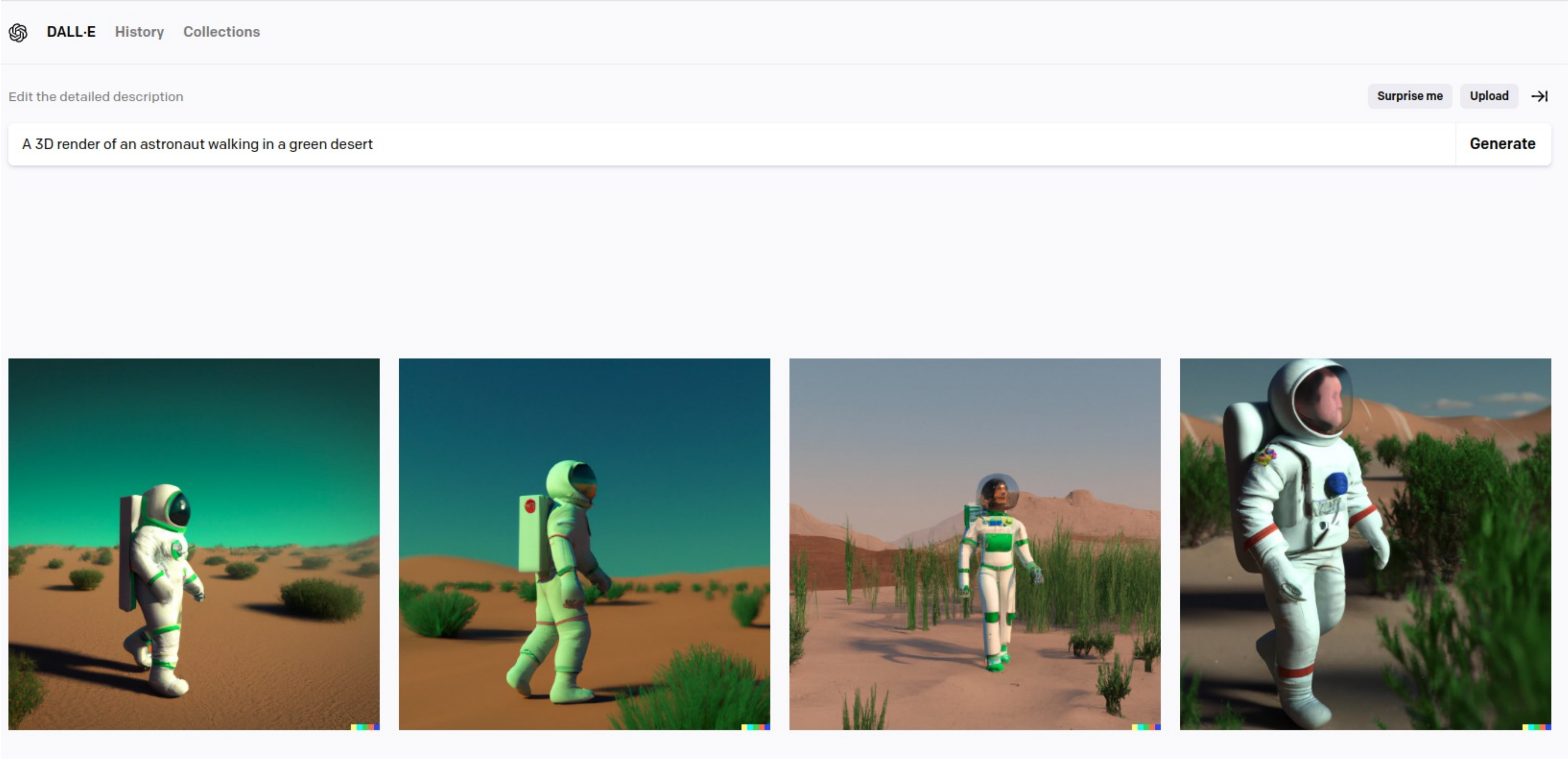
Stable Diffusion: Stable Diffusion is **a text-to-image model**. A stable diffusion model has four important elements

- **Diffusion Probabilistic Model**
- **U-Net Architecture**
- **Latent Text Encoding**
- **Classifier-Free Guidance**

https://stablediffusionweb.com/

Applications

Dall-E Example 1



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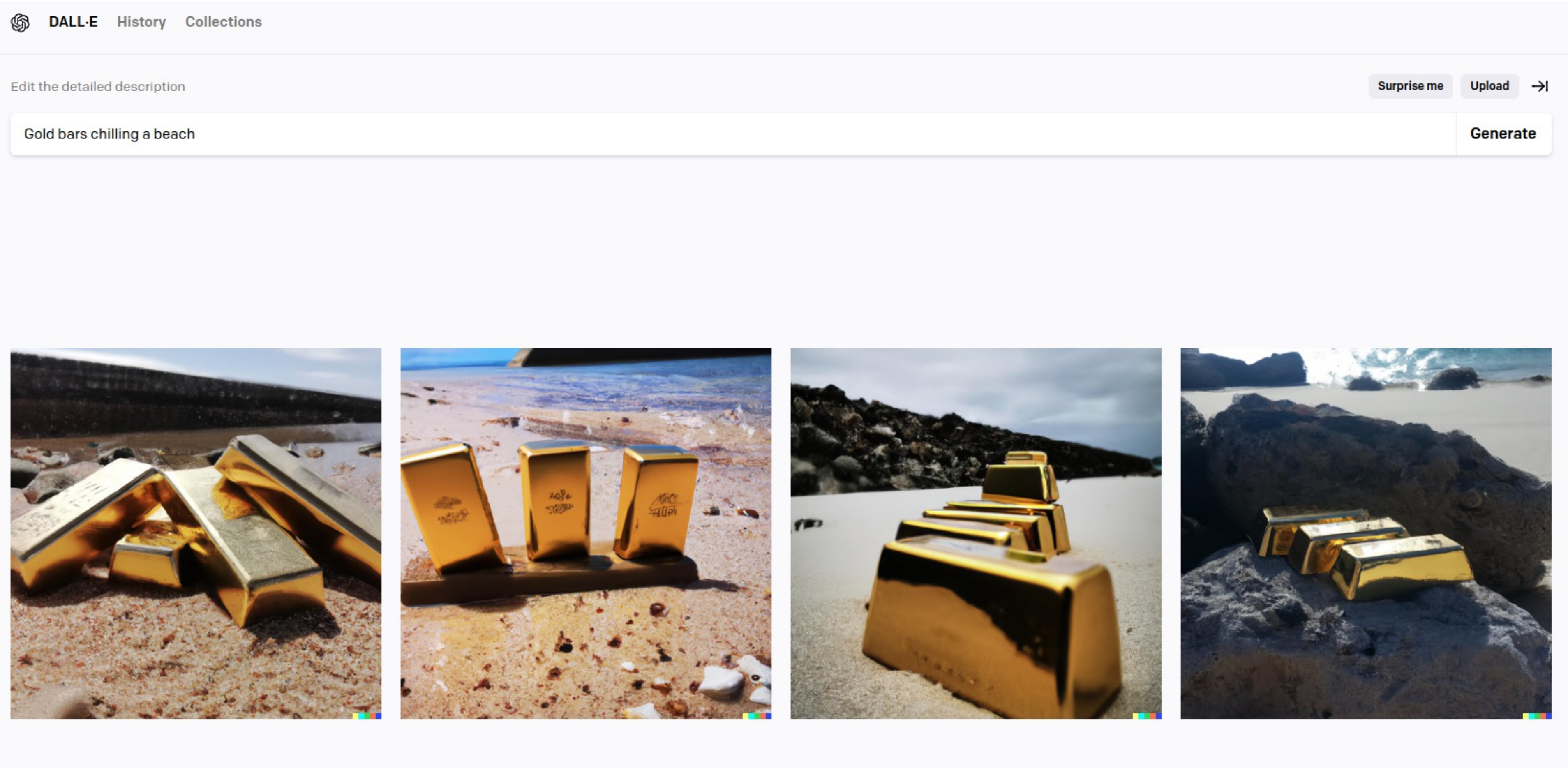
Applications

Dall-E Example 2



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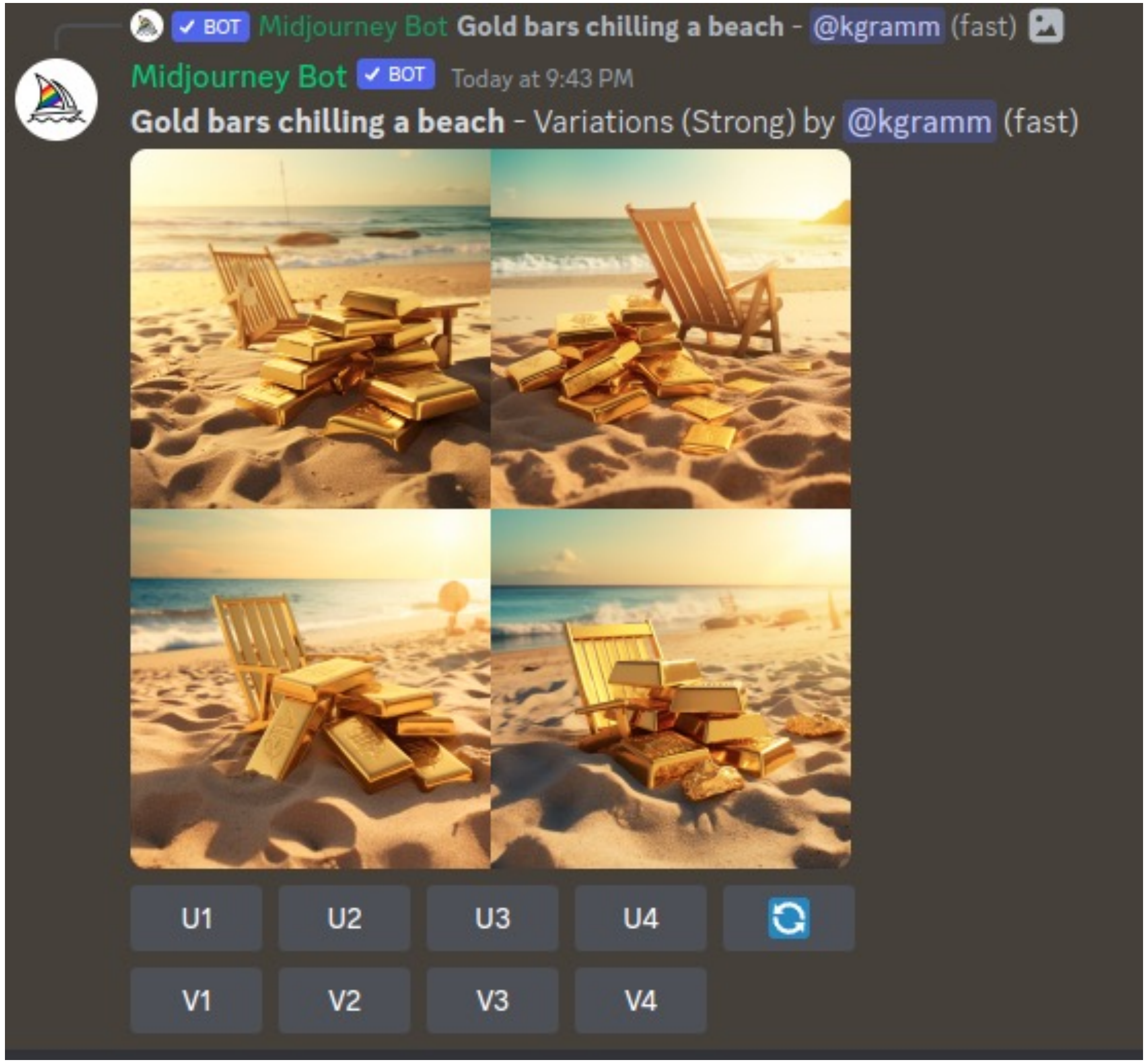
Applications

Midjourney



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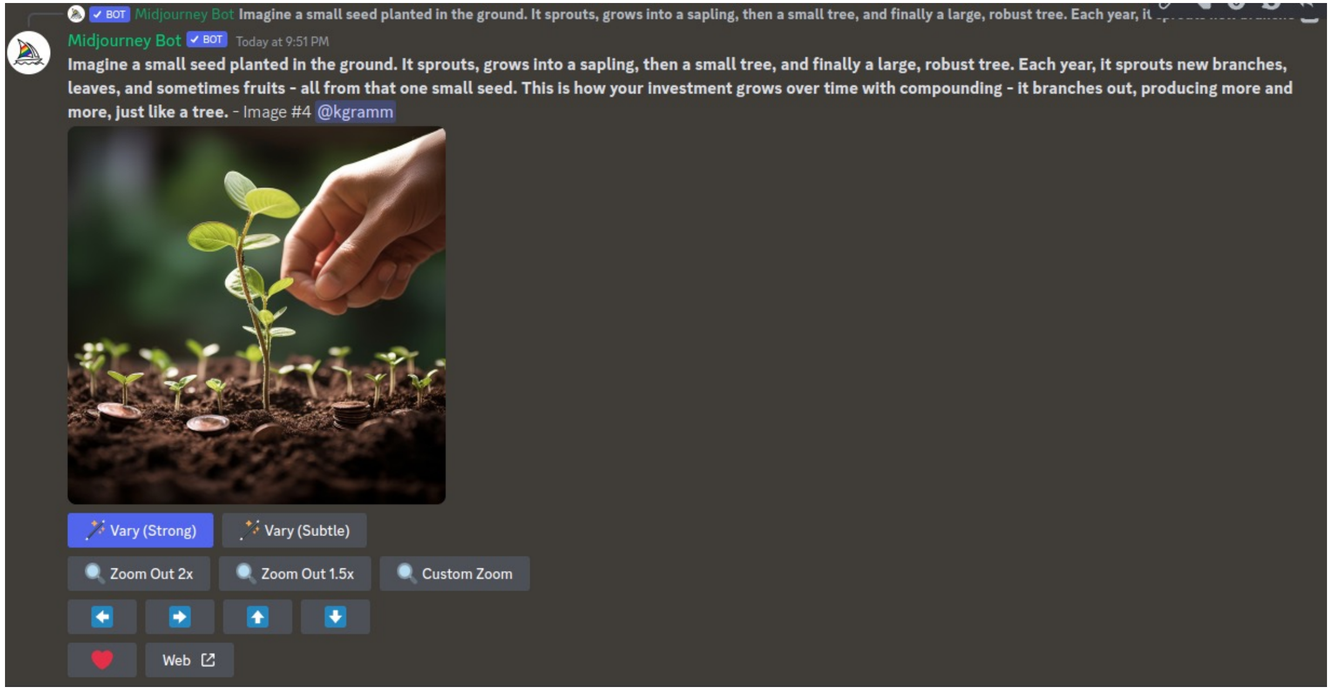
Applications

Midjourney

Prompt: *Imagine a small seed planted in the ground. It sprouts, grows into a sapling, then a small tree, and finally a large robust tree. Each year, it sprouts new branches, leaves and sometimes fruits – all from that small seed. This is how your investment grows with compounding – It branches out producing more and more just like a tree*



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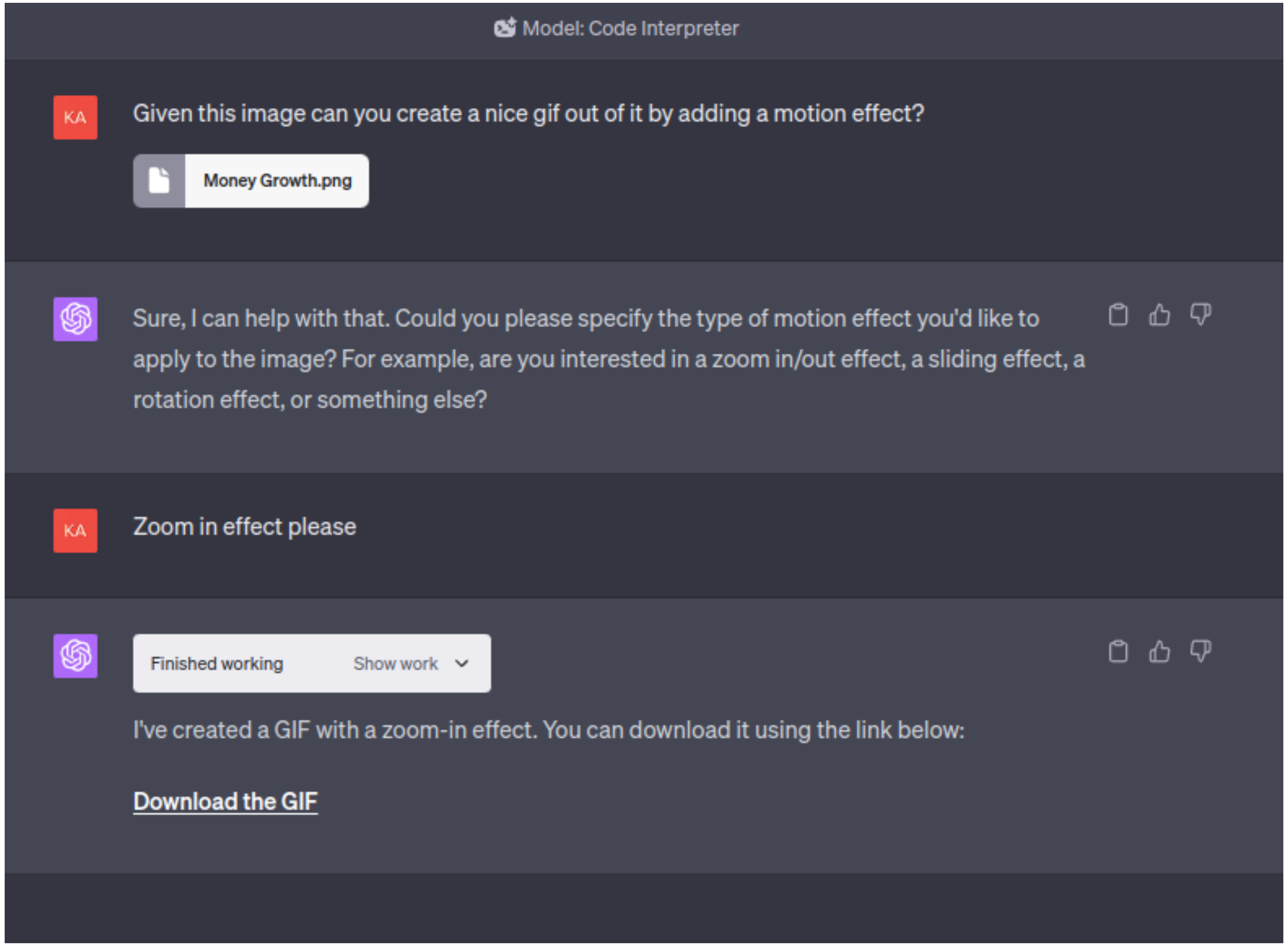
Applications

ChatGPT



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Potential of Generative AI

1. **Low Resource Languages** – Ability to understand, generate any language, especially low resource ones, could help study languages and historical documents in general

2. **Inclusion and Accessibility** – Avatars proficient in sign languages, high precision caption generation etc., could increase accessibility for all people

3. **Personalized Content Generation** – Video games, music, movies can be created that cater to users and individual interests at scale

4. **AI Tutors** – Imagine a world where you can conjure up a tutor to teach you any skill you would like to learn at your own pace

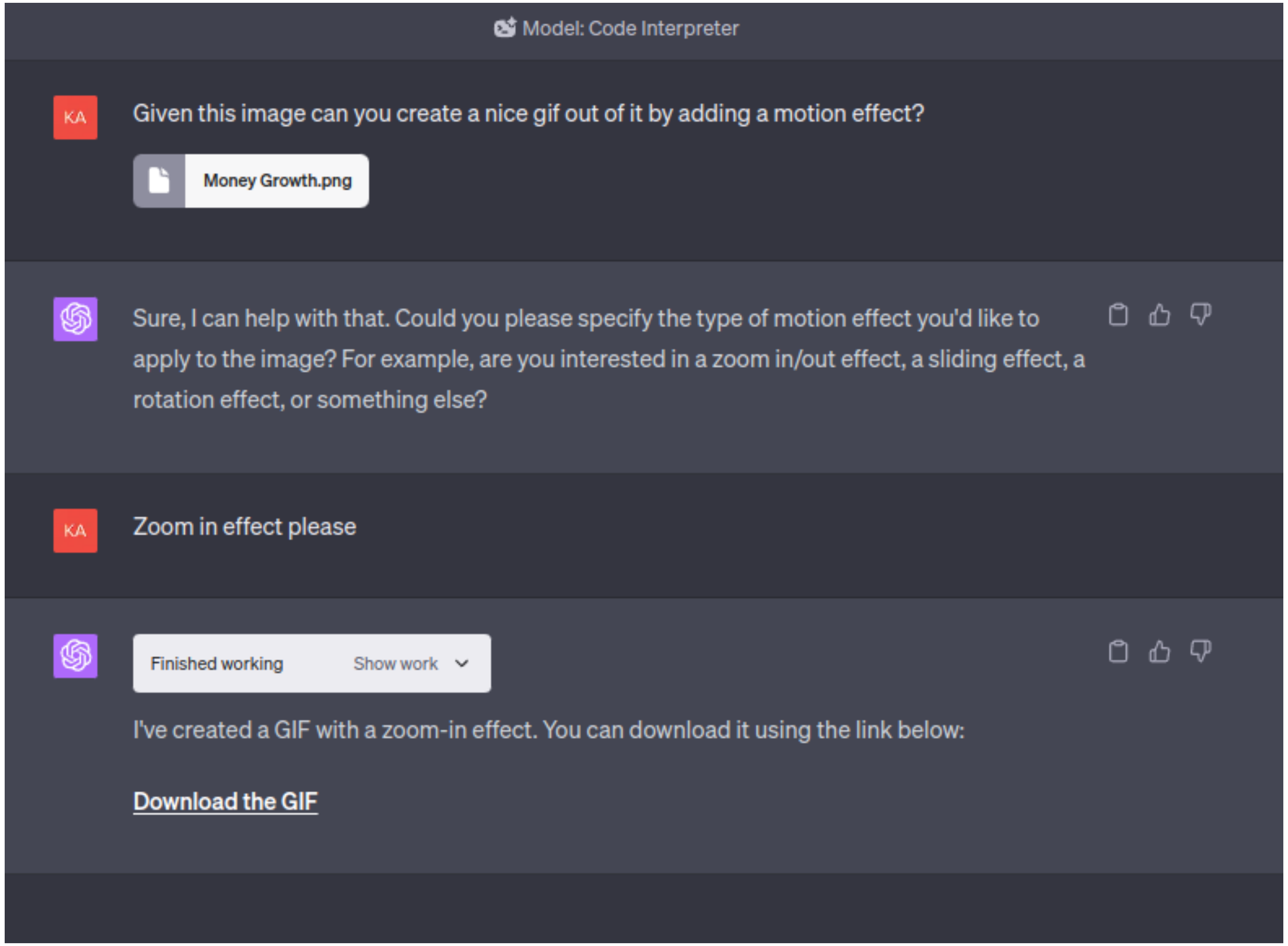
5. **Intelligent Assistants** – Laborious and repetitive tasks can be delegated to Intelligent Assistants allowing humans to focus on critical thinking and decision making

6. **Accelerating Scientific Discovery**- General advances in AI can help accelerate scientific discovery by generating deep insights from massive datasets and design new algorithms. This can help solve most challenging problems we face today.

https://www.forbes.com/sites/bernardmarr/2023/05/31/the-future-of-generative-ai-beyond-chatgpt/?sh=161c85da3da9

Applications

ChatGPT



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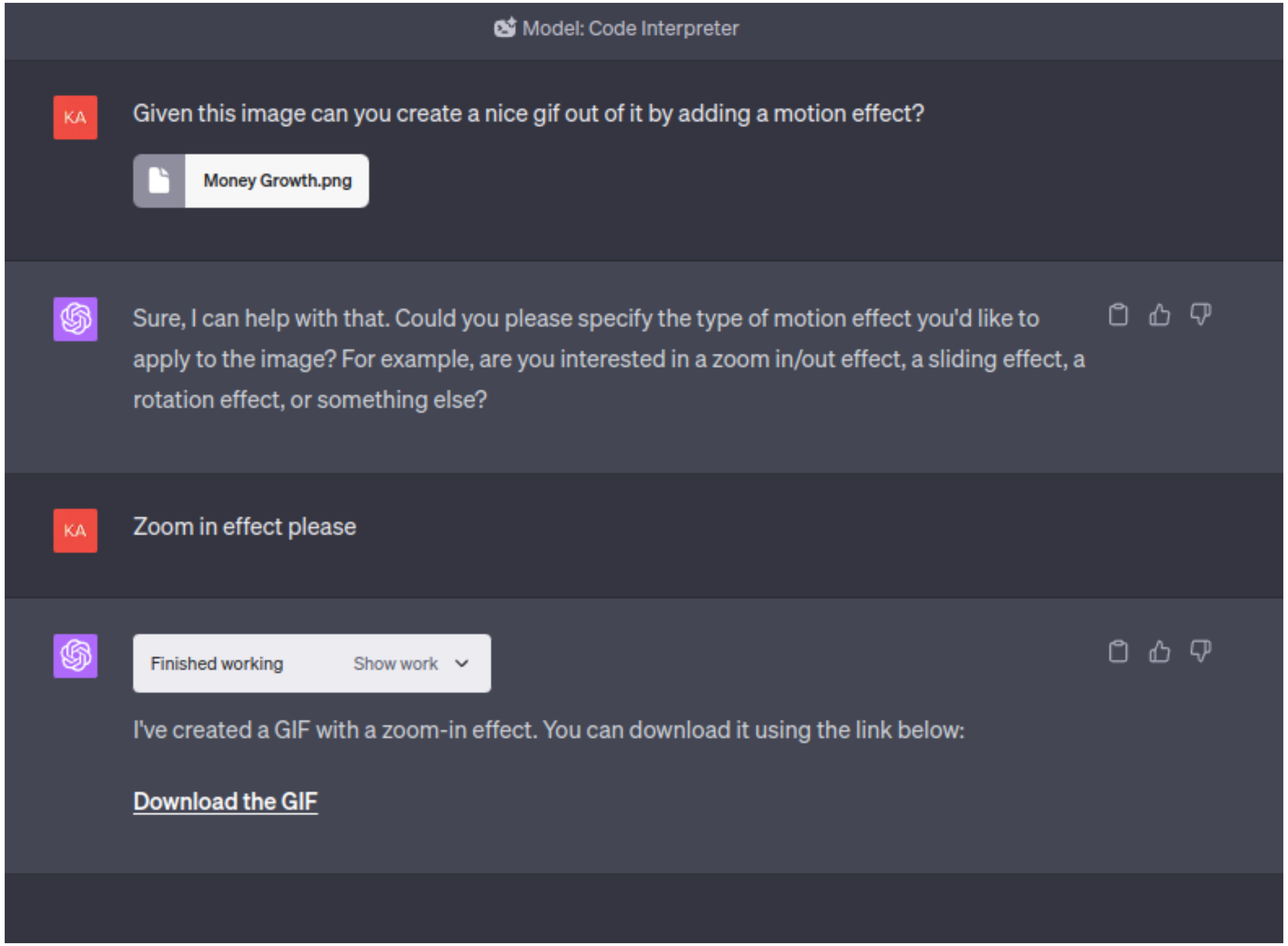
Applications

ChatGPT



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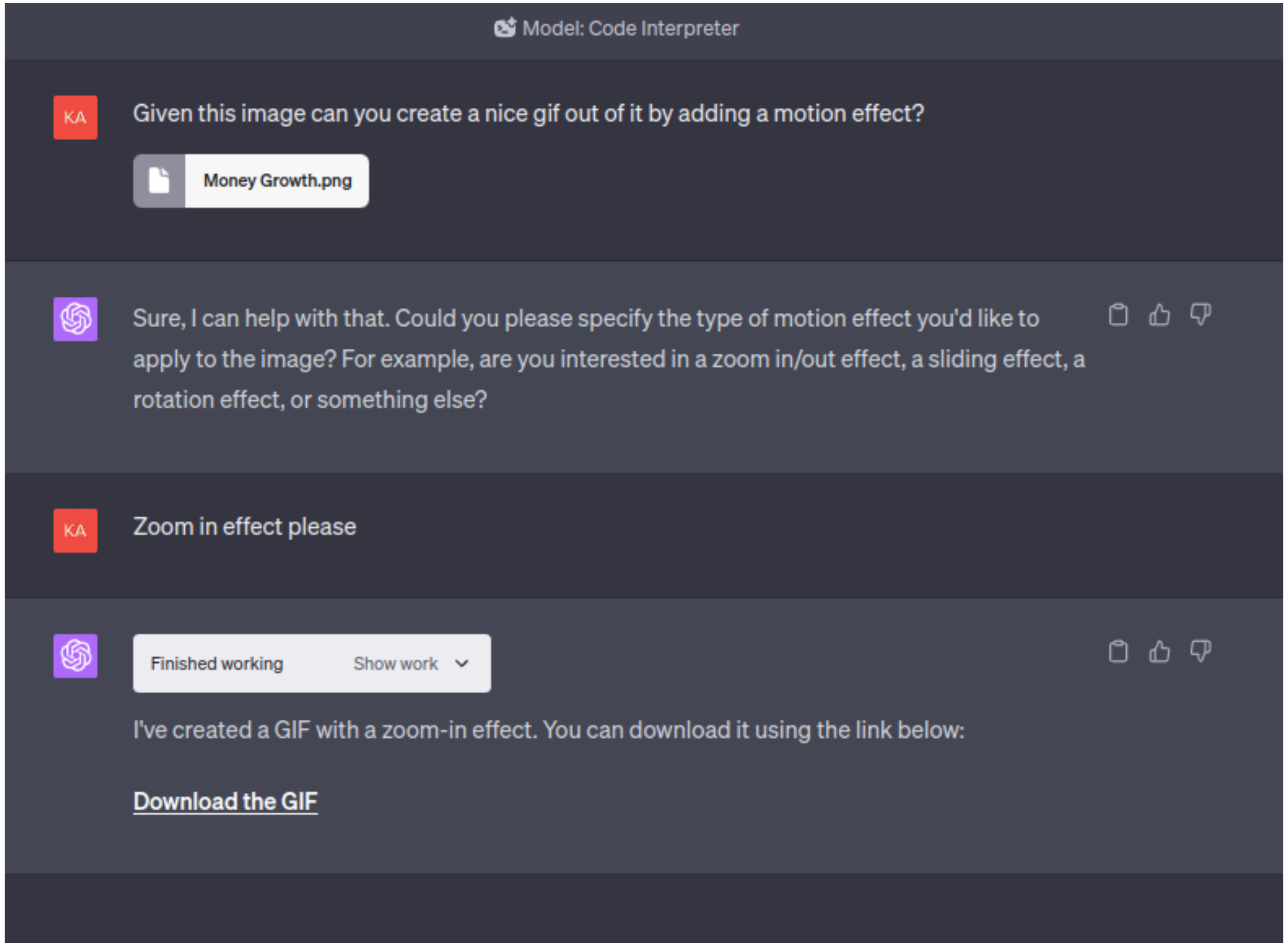
ChatGPT



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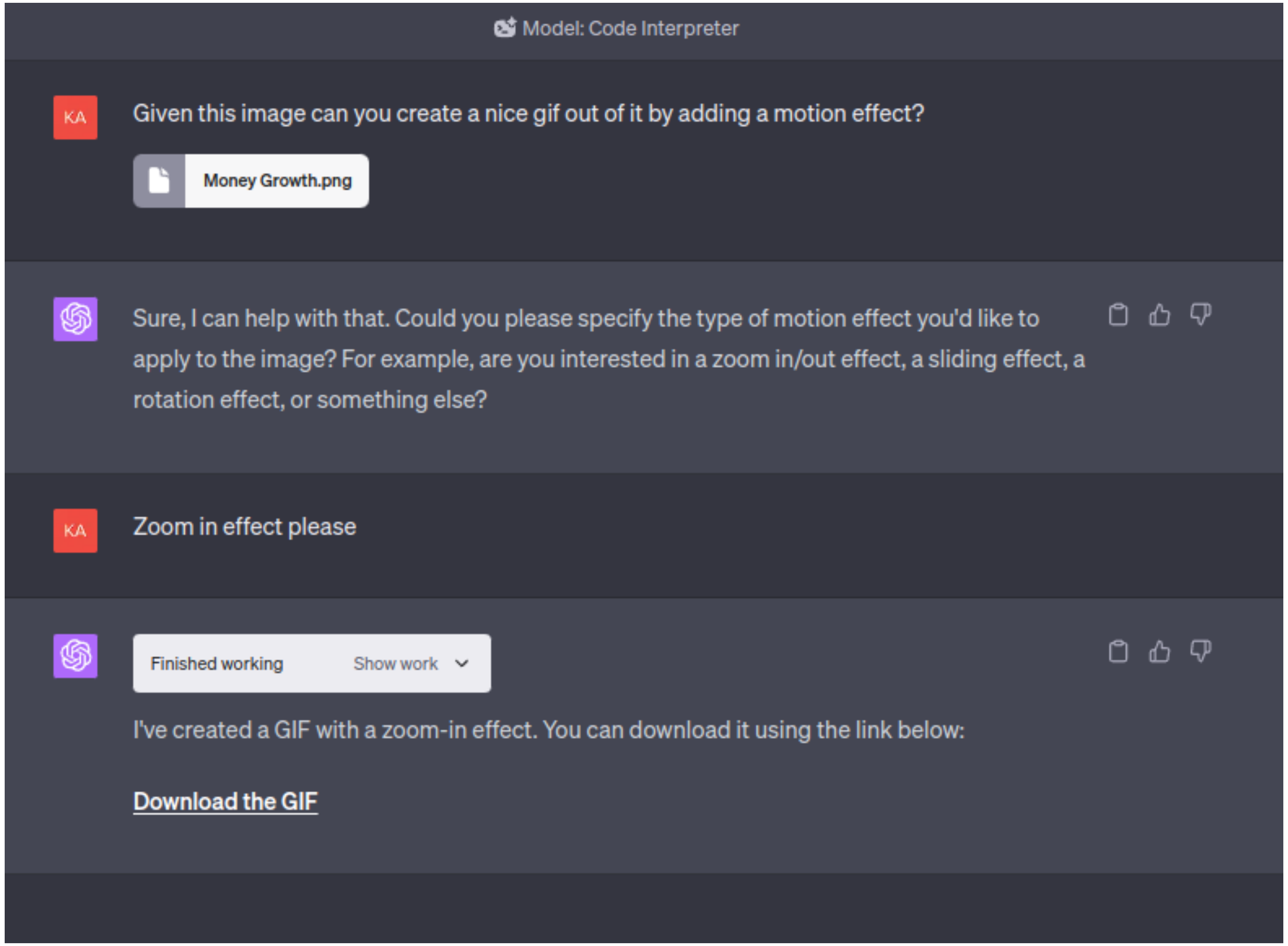
ChatGPT



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Things to Keep in Mind

1. **Lack of Consistency (Hallucination)**: LLMs tend to produce wildly different answers, when the same question is asked multiple times

2. **Bias**: As the models are trained on data scrapped from internet, they might have inherited the biases present in the training data

3. **Interpretability**: It is difficult to understand why a particular response or content is generated, making it very challenging for use cases where explainability is inherently required.

4. **Real-time Knowledge**: As the models are trained on a fixed dataset at a particular point in time, they lack information/changes that occurred after that point.

5. **Memory**: Even though these models are getting good with context lengths that can be supported, having an efficient memory remembering the important details of conversations over a long period of time is still a challenging task.

6. **Engineering Challenges**: Operating these semi-non-deterministic models especially in a multi-model setting (including voice, text, images etc..) at scale remains a significant challenge

Generative AI

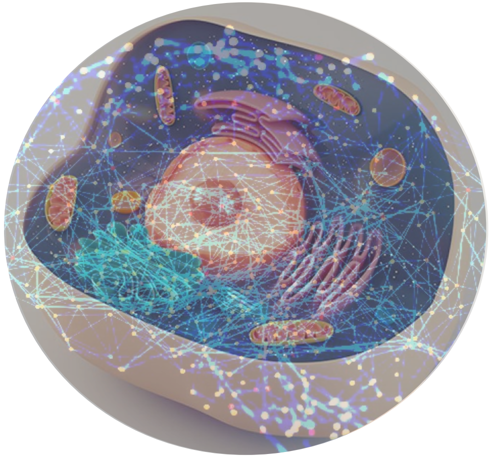
Emerging Trends

- Major breakthroughs in deep learning architectures like Transformers and Generative Adversarial Networks
- Availability of massive datasets and GPU/TPU compute
- New advances in techniques like RLHF/Prompting made it much easy to align these models
- Low barrier of entry due to intuitive and user-friendly interfaces and strong open-source ecosystem
- GenAI holds potential to create photo-realistic images, human-like speech and text and generate working code from natural language descriptions which was not possible until recently

AICell Lab (https://aicell.io)

Building AI Systems for Data-driven Cell and Molecular Biology

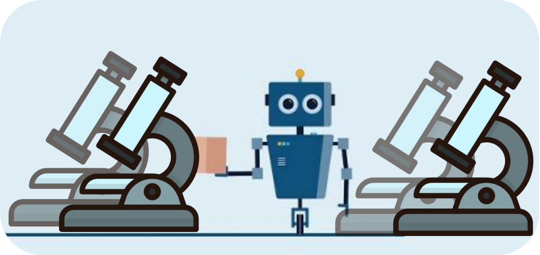
Data-driven Human Cell Simulator



AI: Data- & Compute-hungry!

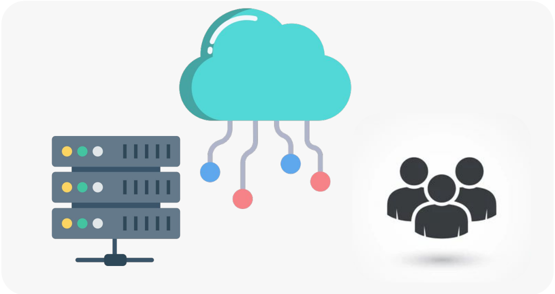
Data Generation

Microscopy Imaging Farm



AI Models Execution

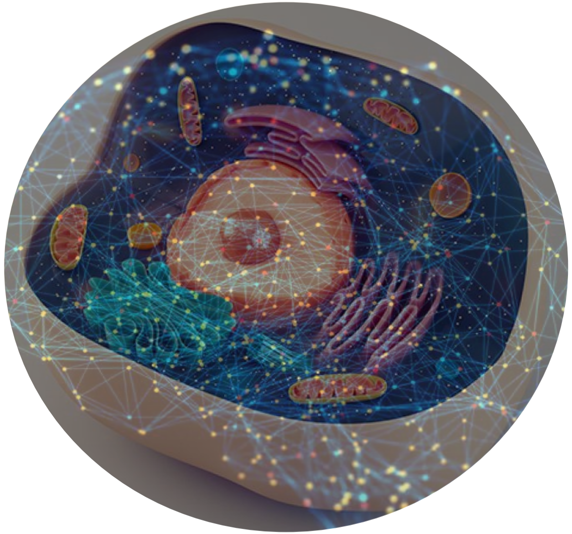
AI Cloud Infrastructure



Building a Human Cell Simulator

Motivation:

To enable *in silico* cell experimentation and drug screening



Challenges:

- Highly complex ~20,000 genes
- Unknown processes / pathways
- Highly dynamic
- …

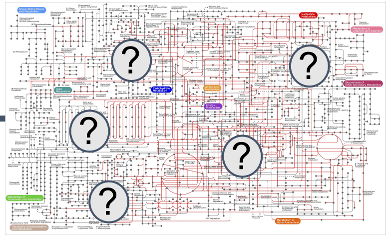
All-atom MD simulation? Almost impossible!

State-of-the-art: E. coli with ~4,400 genes

(Macklin et al., Science 2020)

Conventional Predictive Cell Modeling

How to validate?



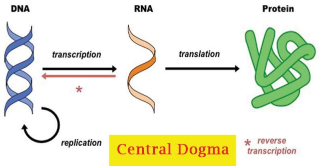
Statistics
(e.g. cell count)

Experimental conditions

Phenotype
Cell line

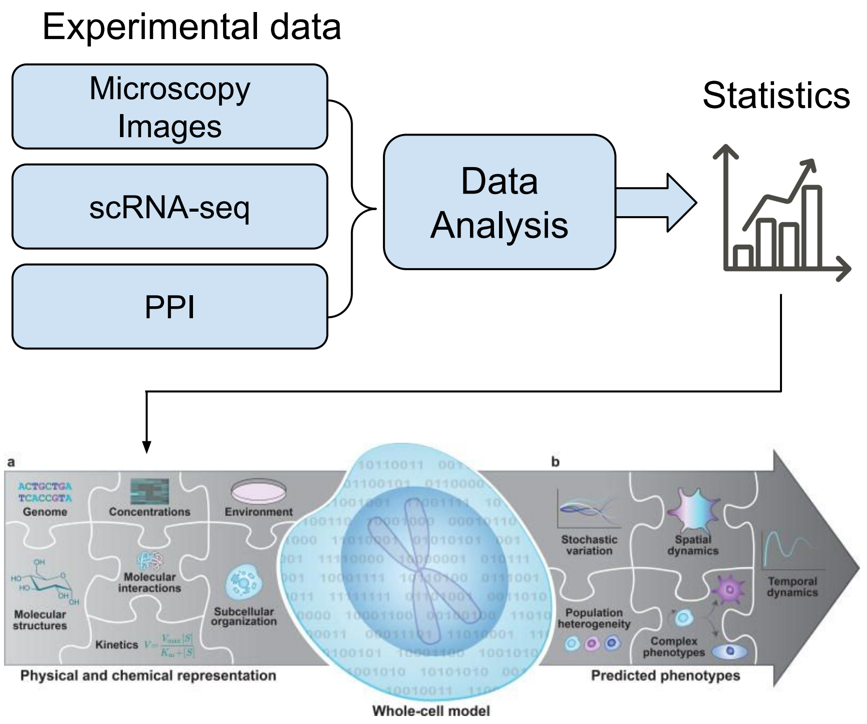
Instruments
(e.g. Microscope)

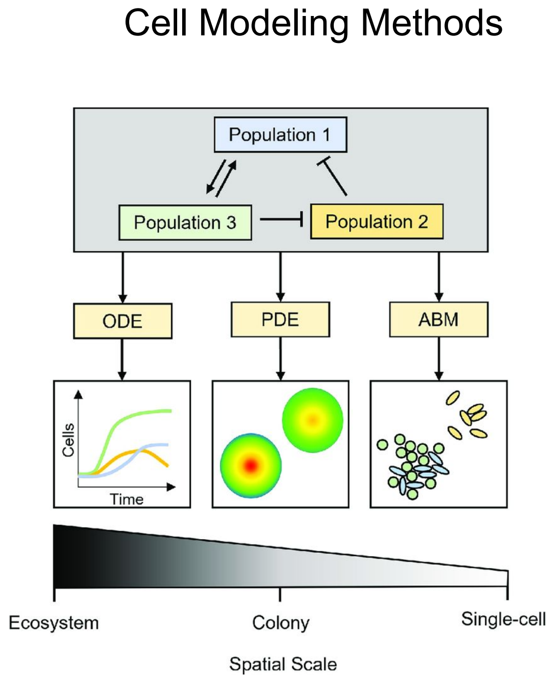
Data
(e.g. images)



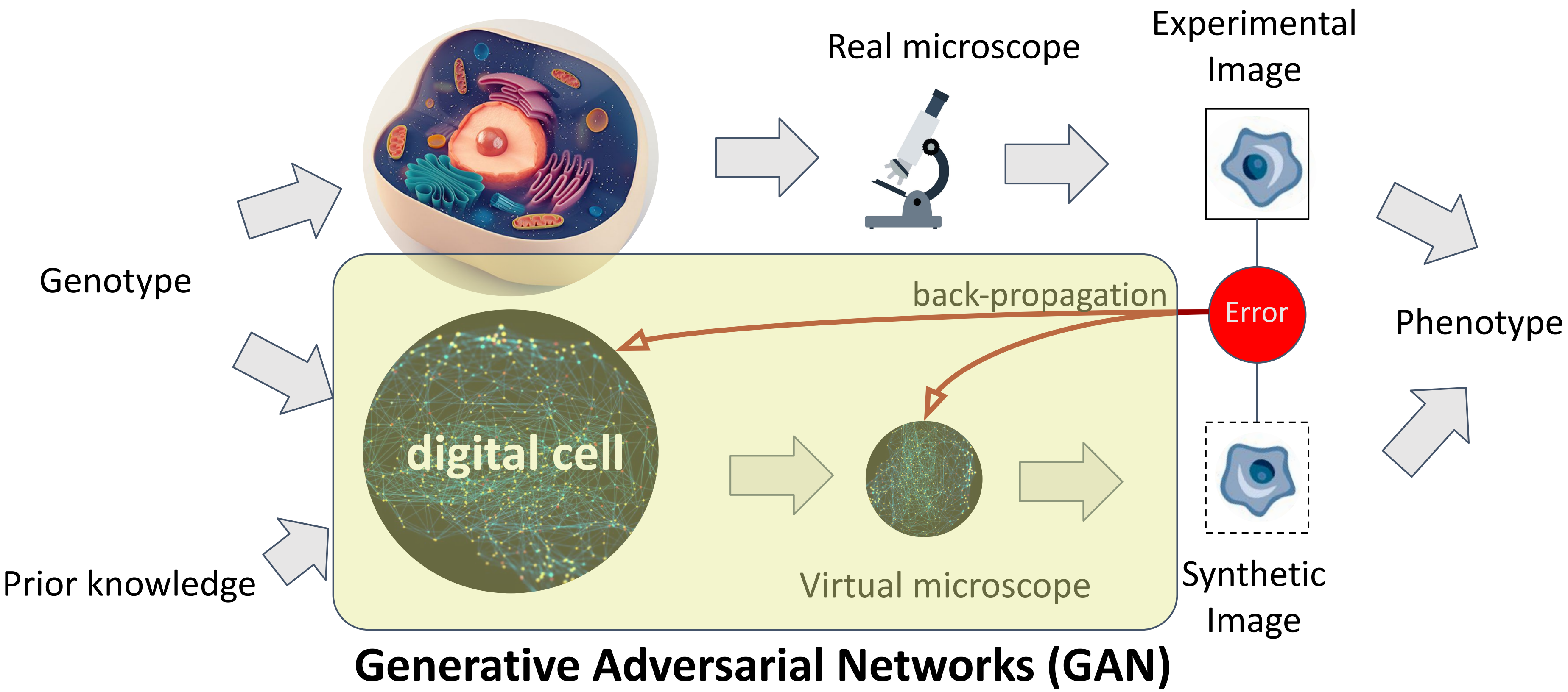
A similar pattern apply to most life science research!

Conventional Predictive Cell Modeling



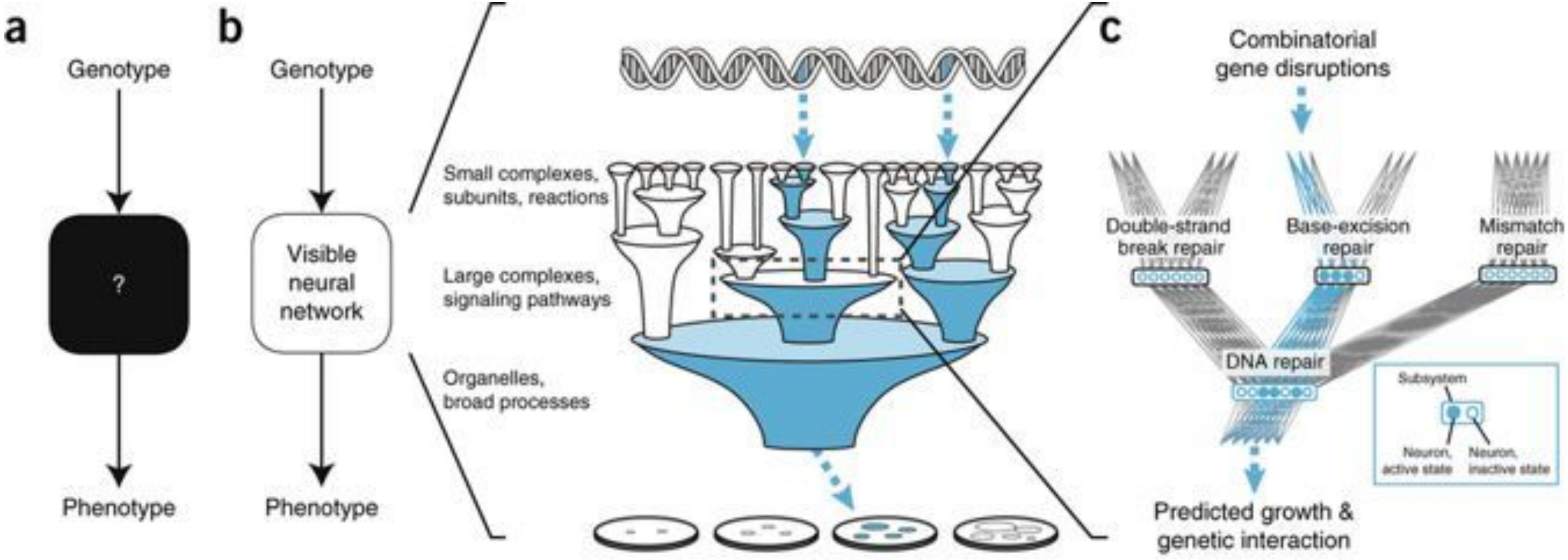


Our approach: AI-powered whole-cell modeling



Related work 1: whole-cell modeling

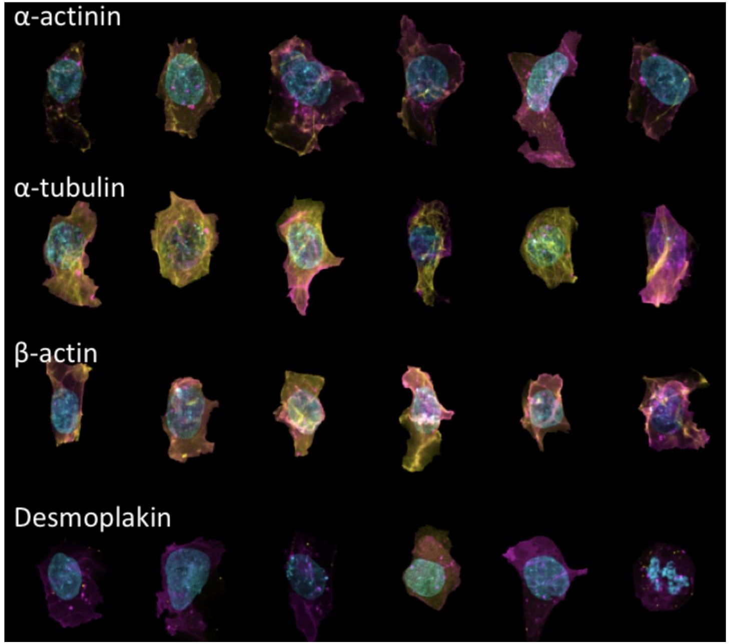
- Using deep learning to model the hierarchical structure and function of a cell

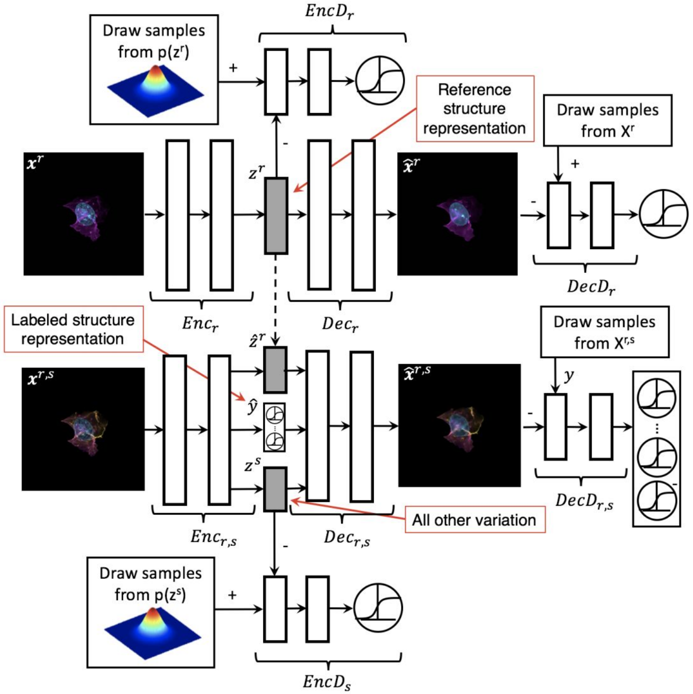


Ma et al, Nat Meth 2018

Related work 2: integrated cell image generation

- Generative Modeling with Conditional Autoencoders

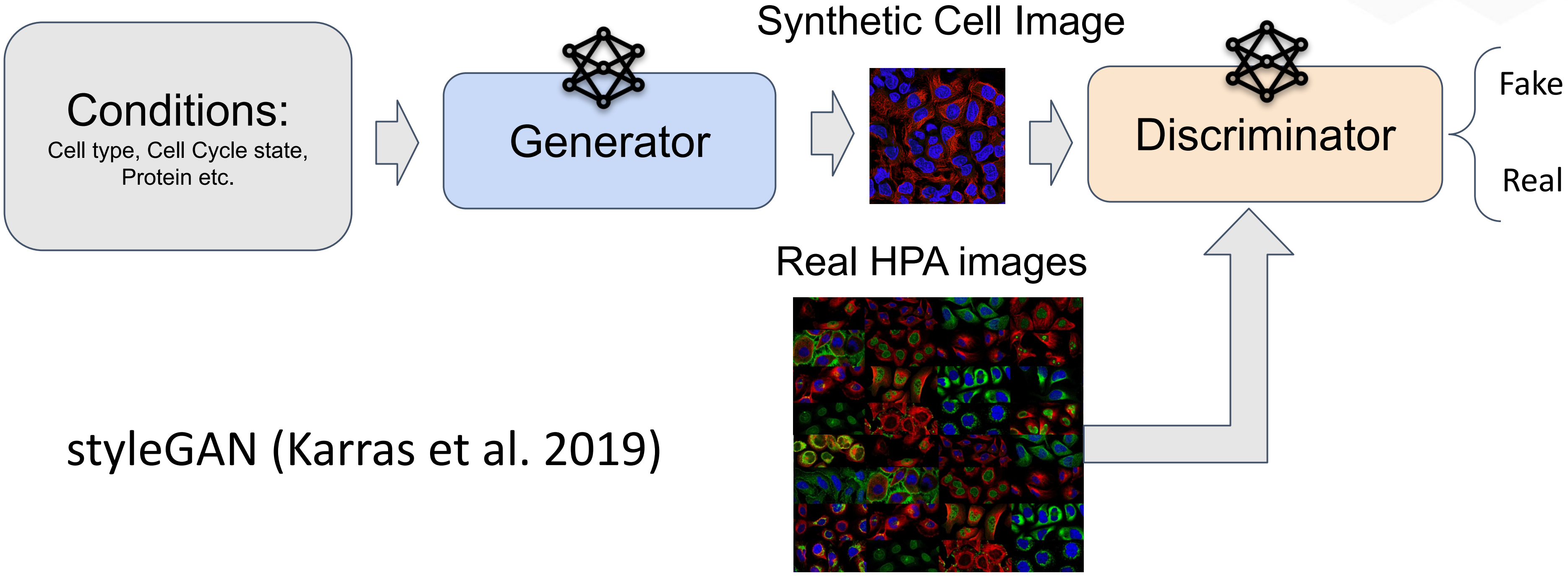




Johnson et al 2017, https://arxiv.org/abs/1705.00092

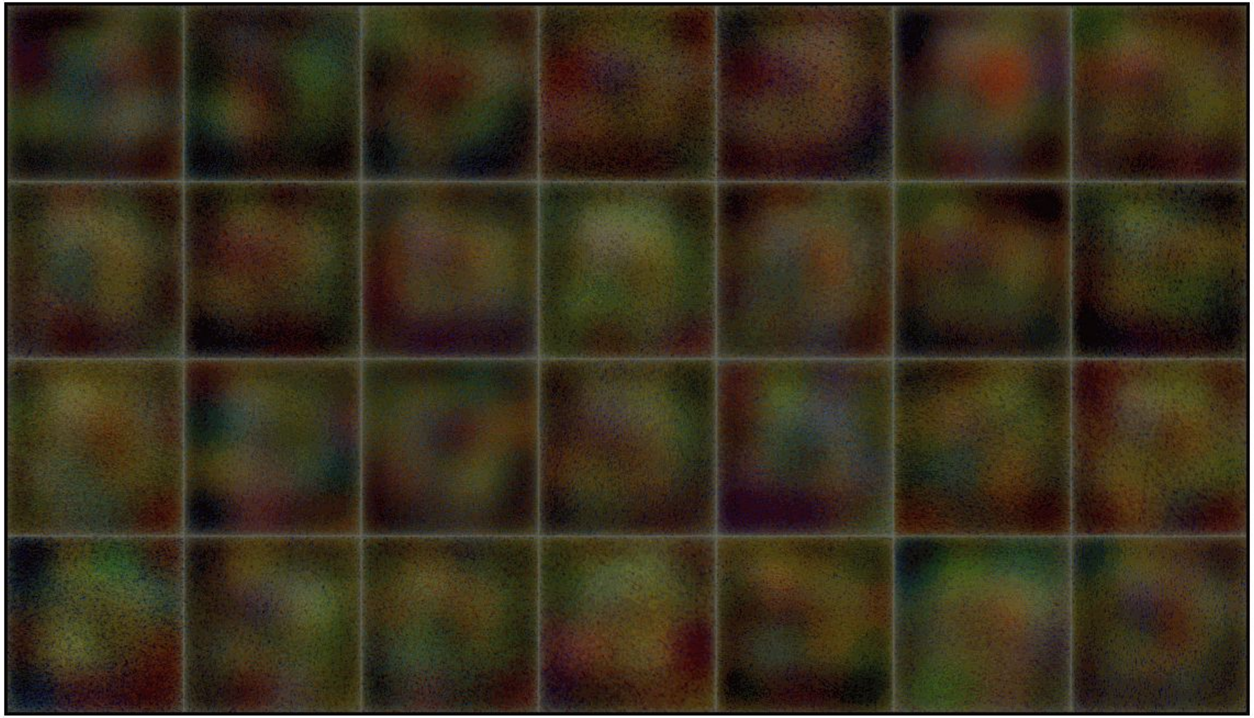
Generative Modeling with conditional-GAN

GAN: Generative Adversarial Networks, by Goodfellow, 2014



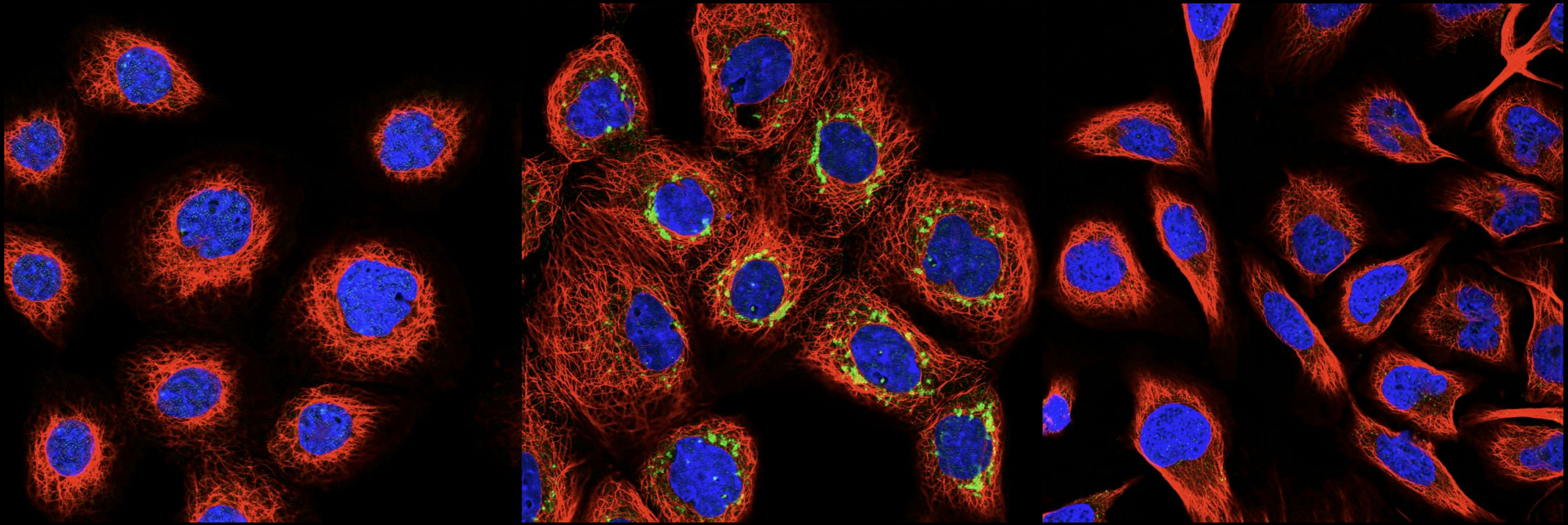
styleGAN (Karras et al. 2019)

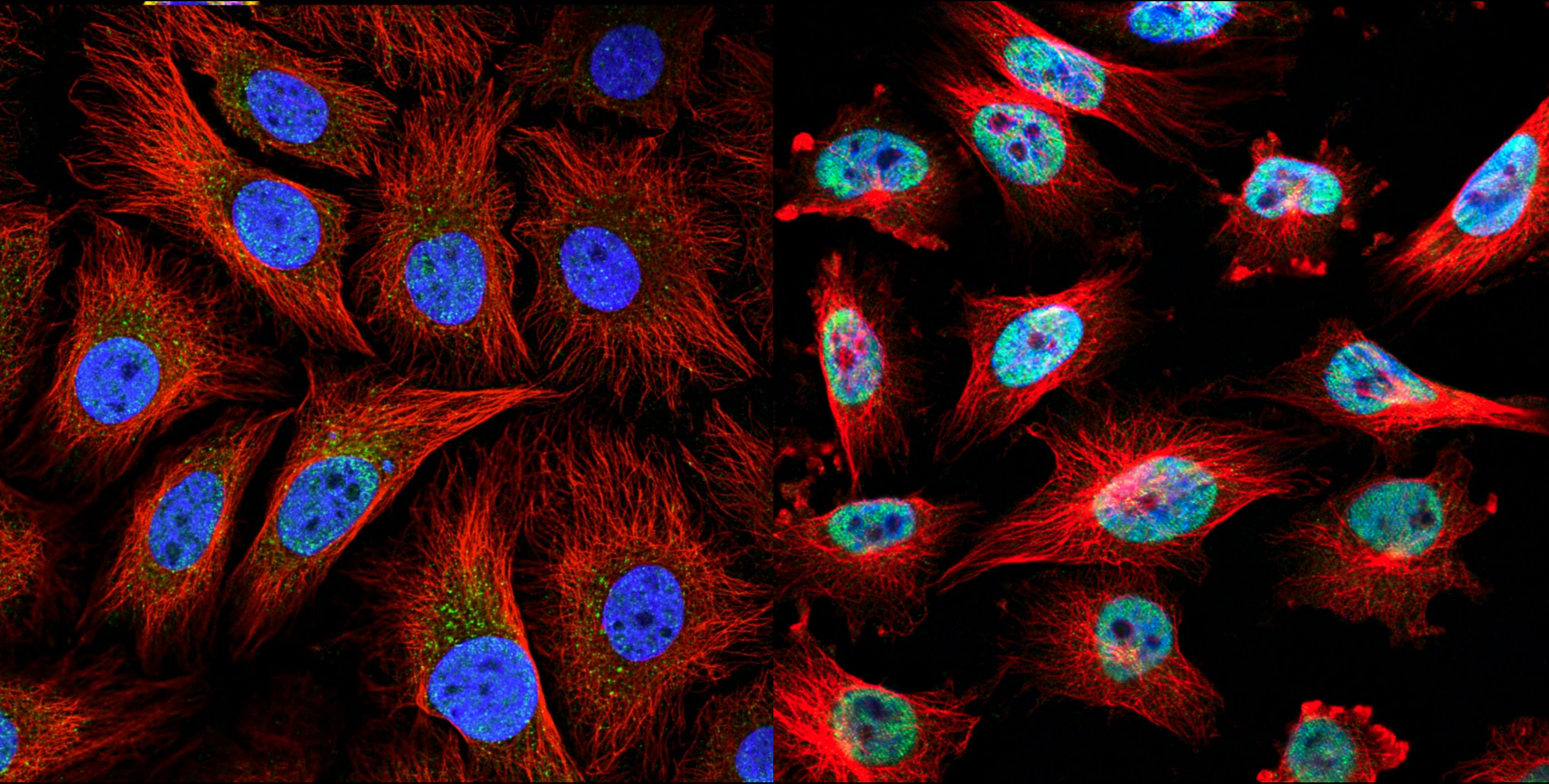
Training styleGAN for HPA images (9 days, 8 GPUs)



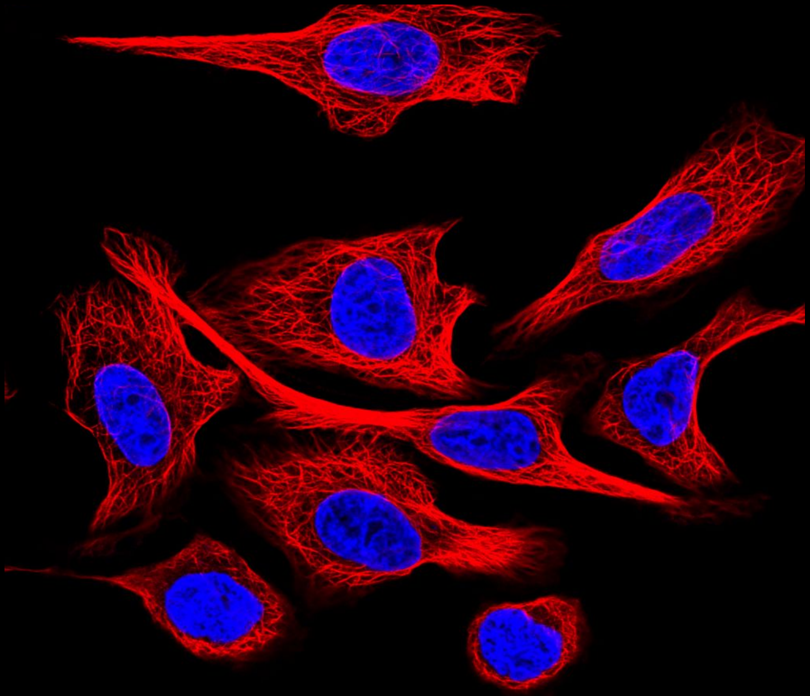
Karras et al. 2019 https://arxiv.org/abs/1812.04948

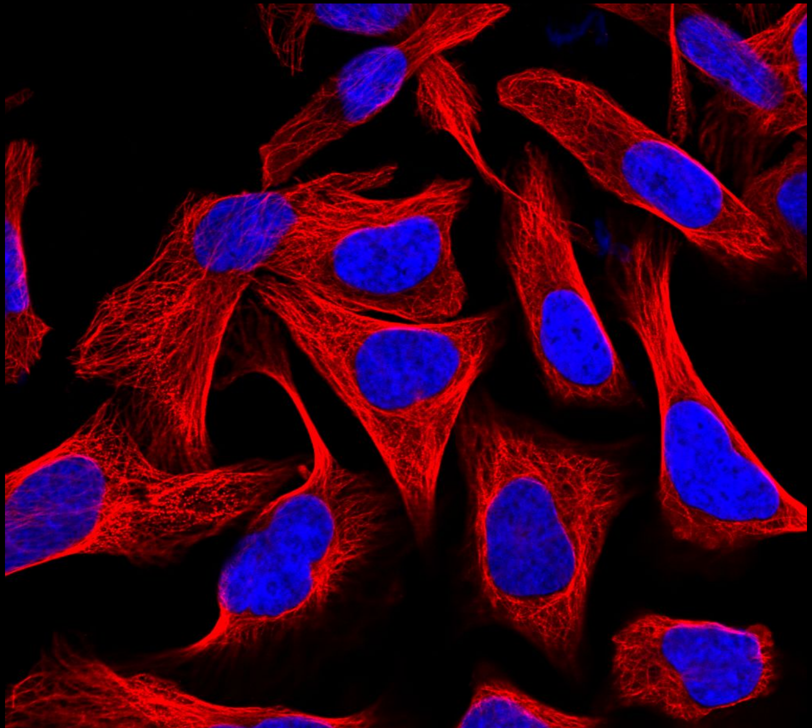
These cells do not exist!





Which one is fake?





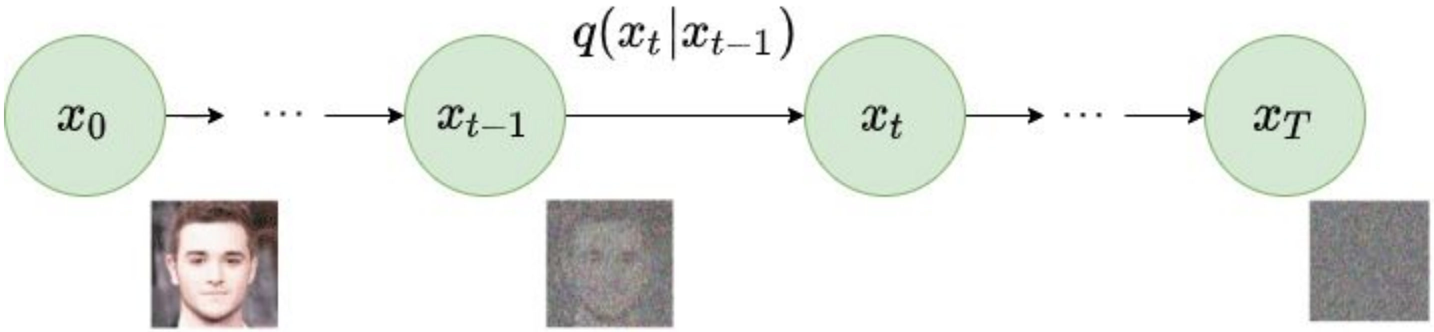
Images provide rich representation of phenotypes

Generative Models Comparisons

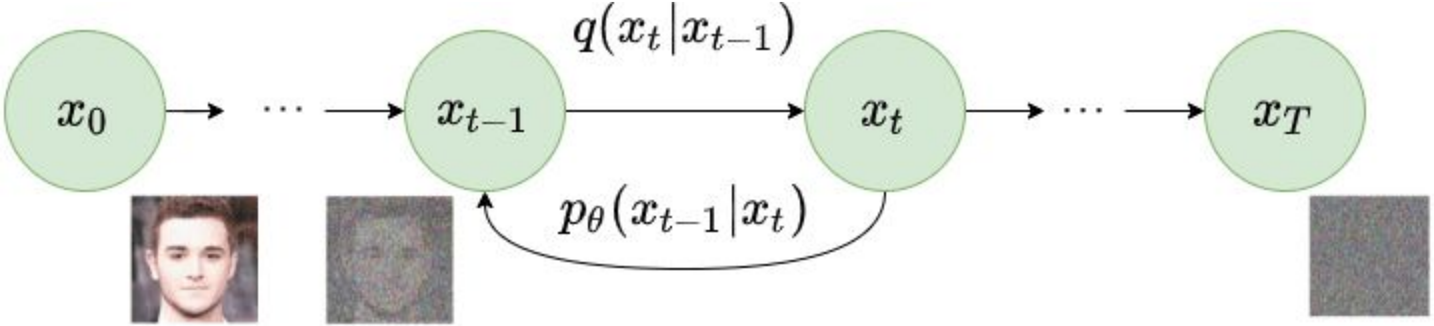
Paradigm	Quality	Diversity	Speed
VAE	✗	✓	✓
GAN	✓	✗	✓
Diffusion	✓	✓	✗

Diffusion Models

Forward Diffusion

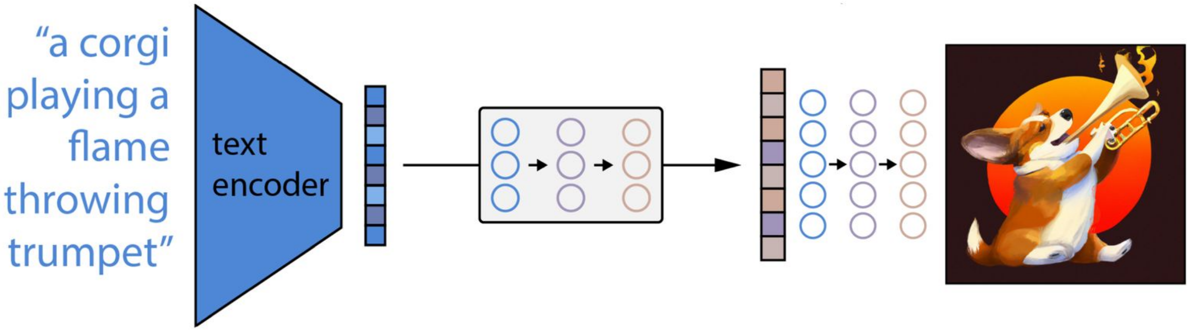


Reverse Diffusion



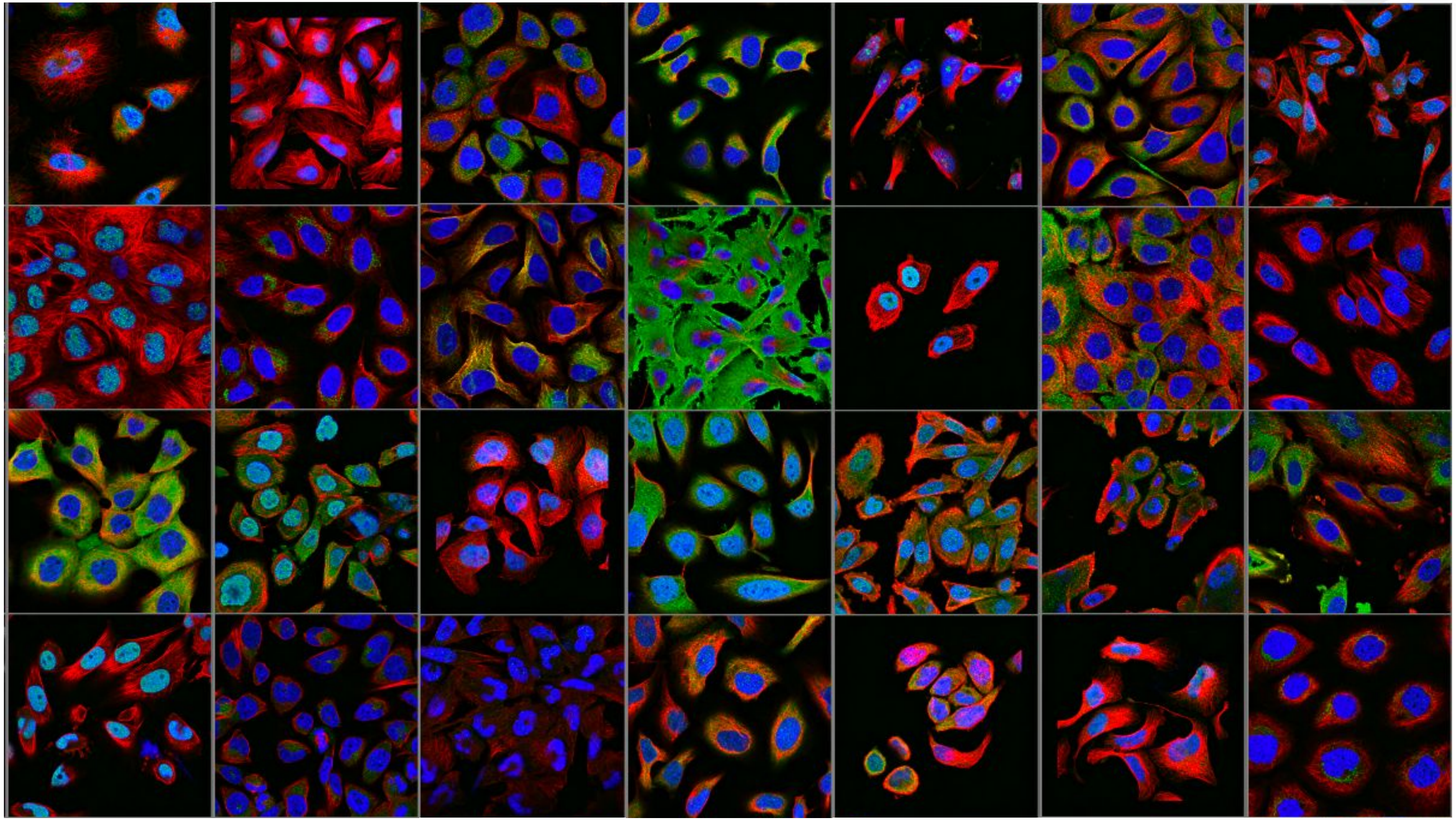
Ho et. al 2020

Diffusion Models for Image Generation



Generated by OpenAI DALL.E

Preliminary results with Diffusion Models



Envisioned Applications

Short-term:

- *In-silico* cell experimentation
- Drug screening
- Tissue and organism modeling

Long-term:

- Understanding the human cell

Foundation Models: Emergence and Homogenization

Bommasani et. al *On the Opportunities and Risks of Foundation Models*, 2022

Challenges in Generative Modeling

- Ours (stable diffusion, 378 million parameters)
  - Training dataset: ~100k images
  - Takes 14 days with 8x NVIDIA A100

- DALL.E 2 (3.5 billion parameters, from OpenAI)
  - Training dataset: > 400 million image-text pairs

- ChatGPT (175 billion parameters, from OpenAI)
  - Training dataset: > 45TB text (data for GPT3)
  - $2-12 million per training

Major Challenges: Data- & Compute-hungry!