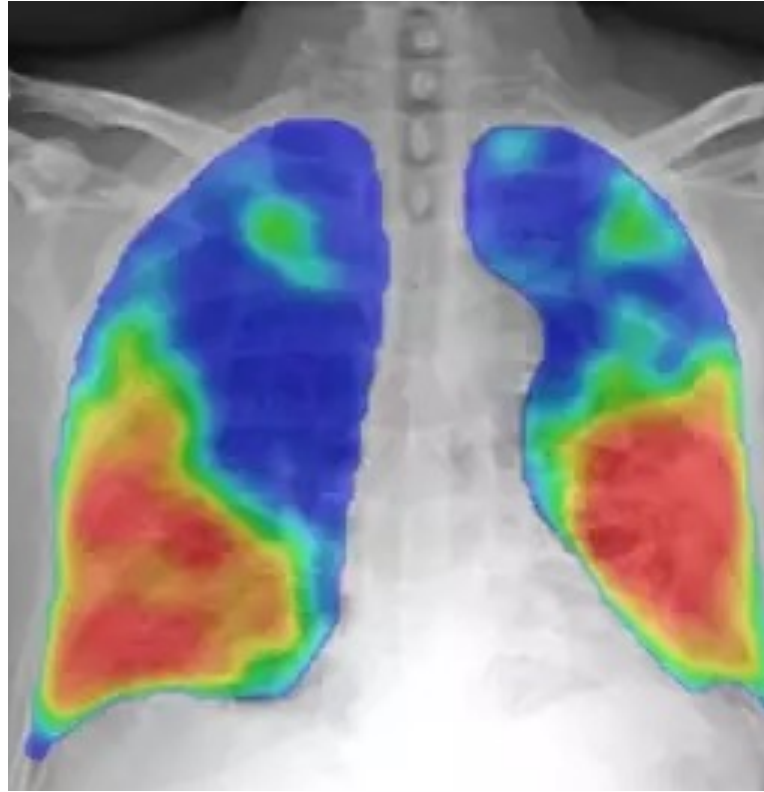
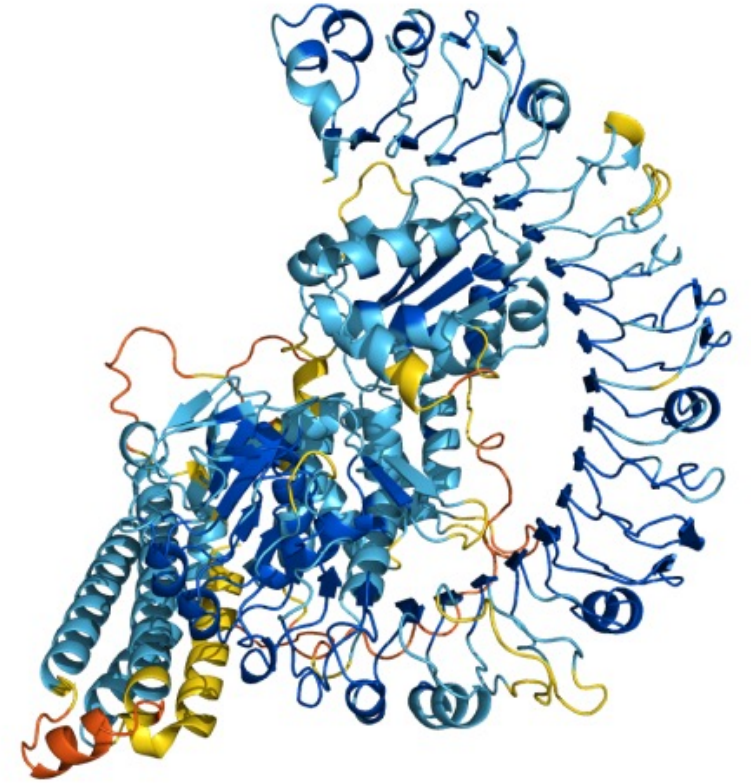


MitoEM



Thirona



AlphaFold2

Artificial Intelligence in Biomedical Sciences

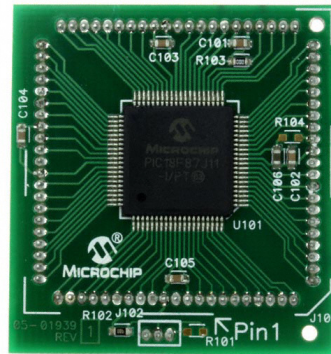
Brian Ondov, Ph.D.

Outline

- What is Artificial Intelligence?
- A brief history of AI
- Domains and applications

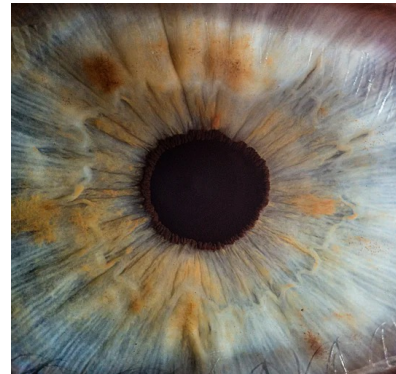
What is Artificial Intelligence?

Artificial



Intelligence

“The ability to acquire and apply knowledge and skills” -OED



Visual processing



Language understanding



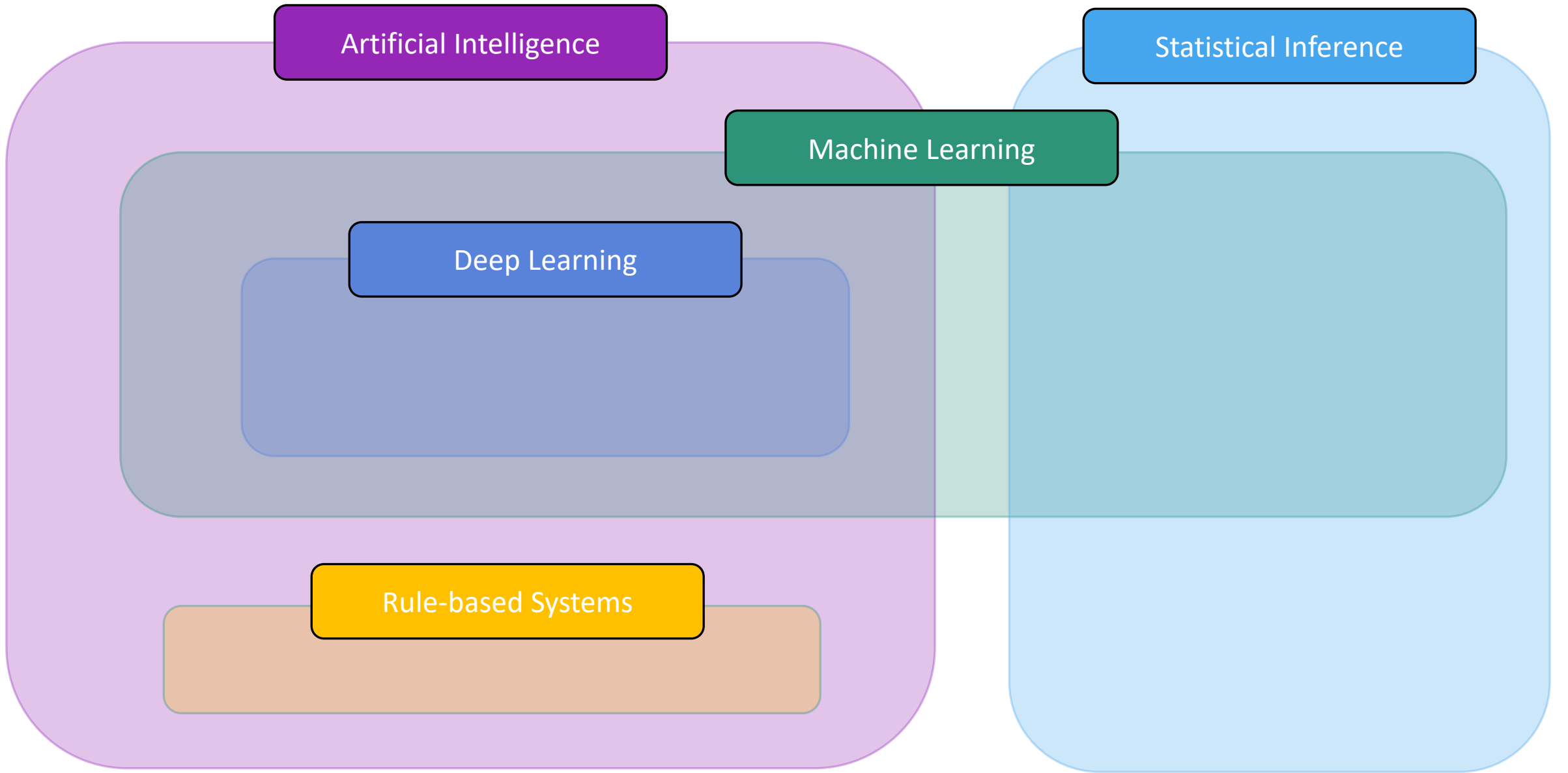
Action planning

Artificial Intelligence

Machine Learning

Deep Learning

Rule-based Systems



Artificial Intelligence

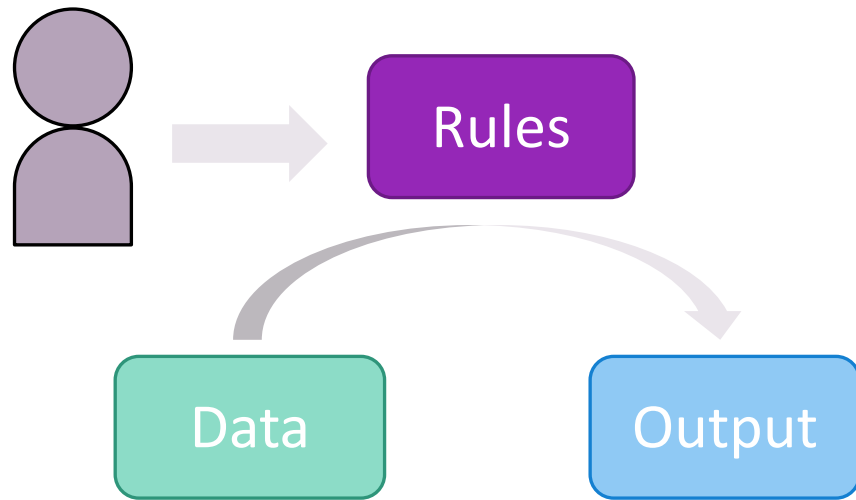
Statistical Inference

Machine Learning

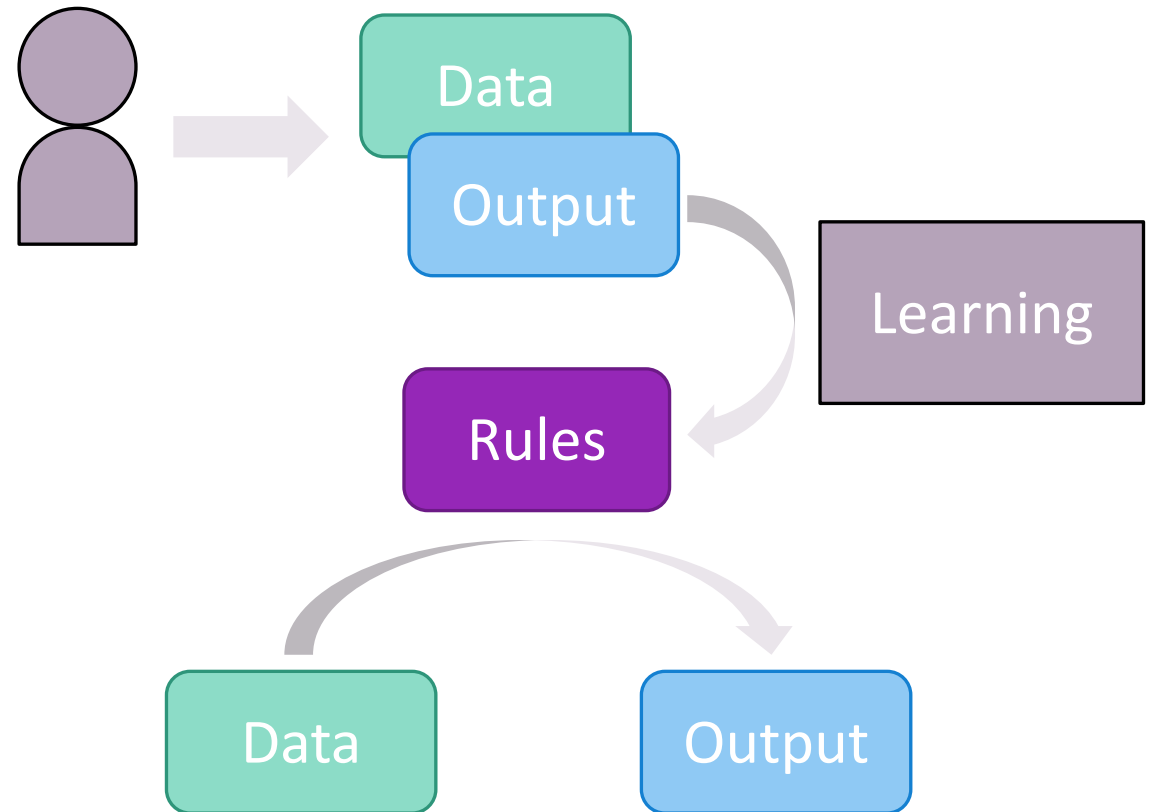
Deep Learning

Rule-based Systems

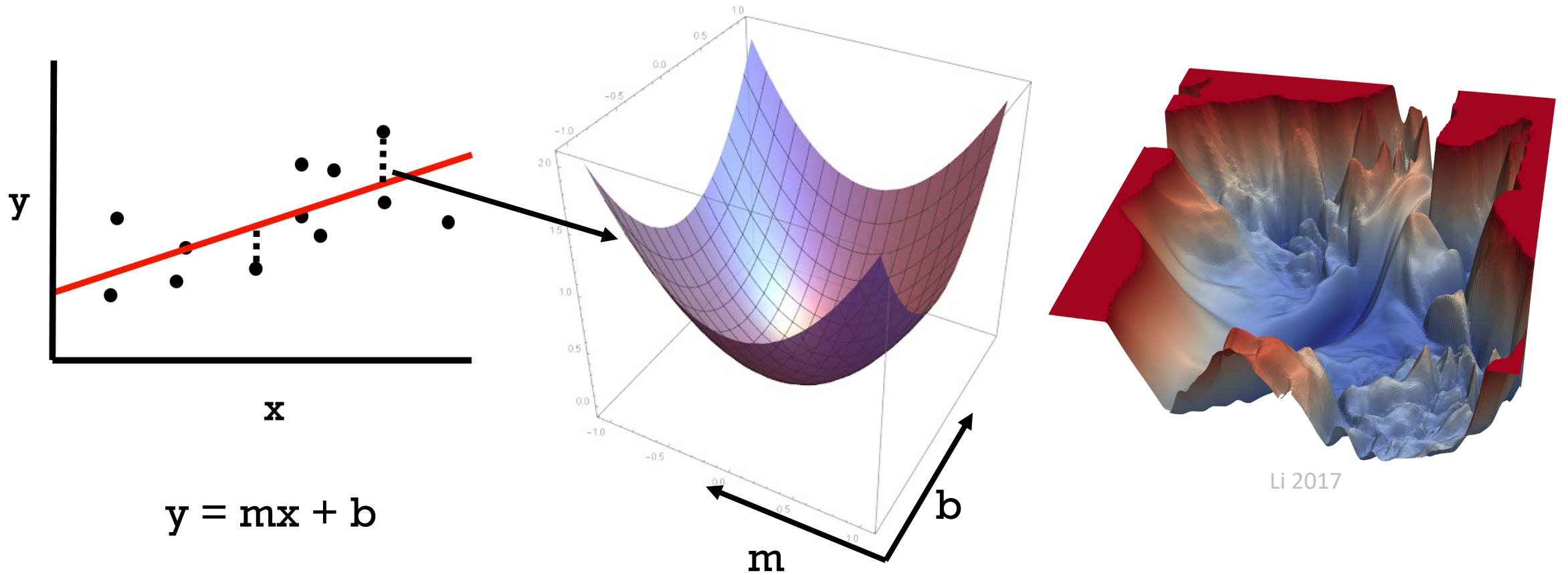
Traditional Computing



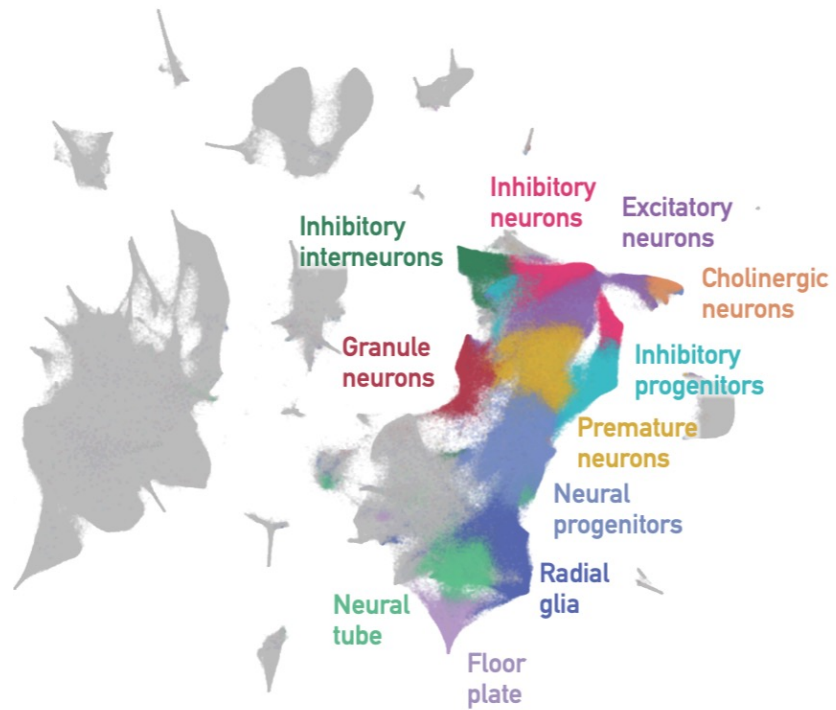
Machine Learning



Machine Learning



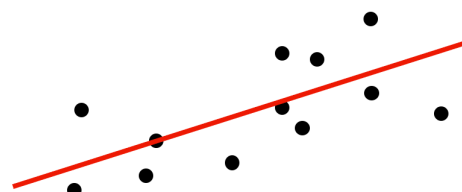
Unsupervised



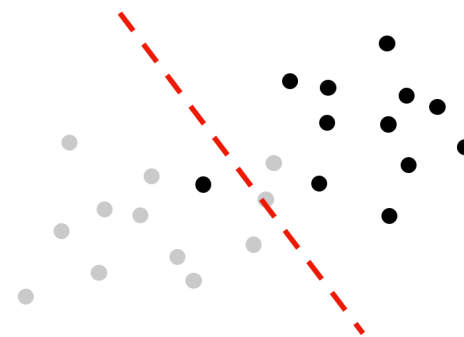
cancer.gov

Supervised

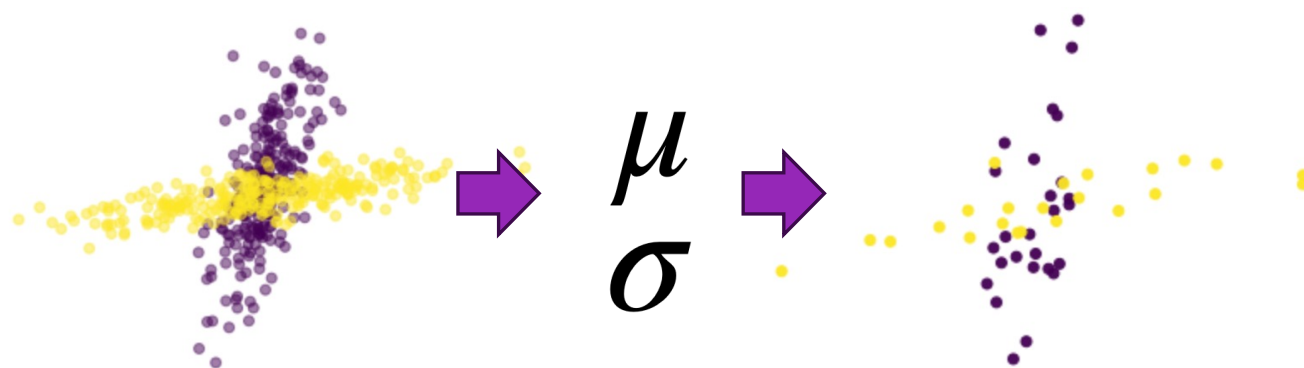
Regression



Classification



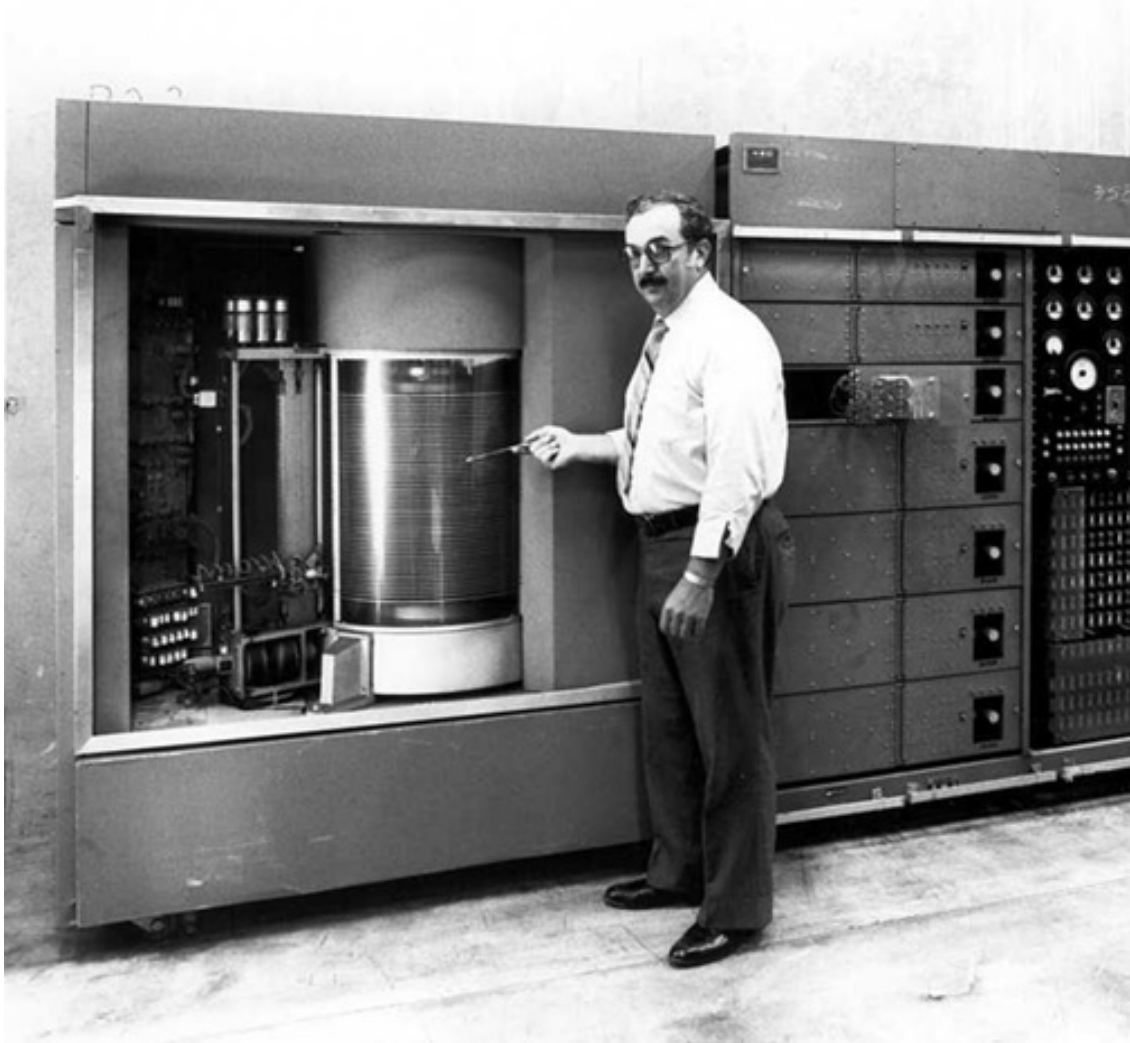
Generative



A brief history of AI

1954

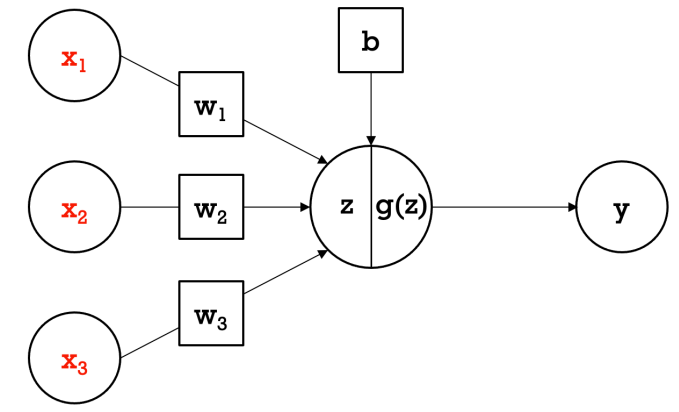
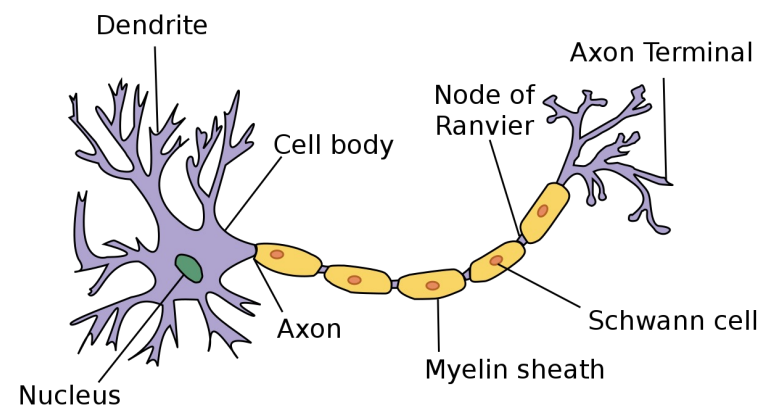
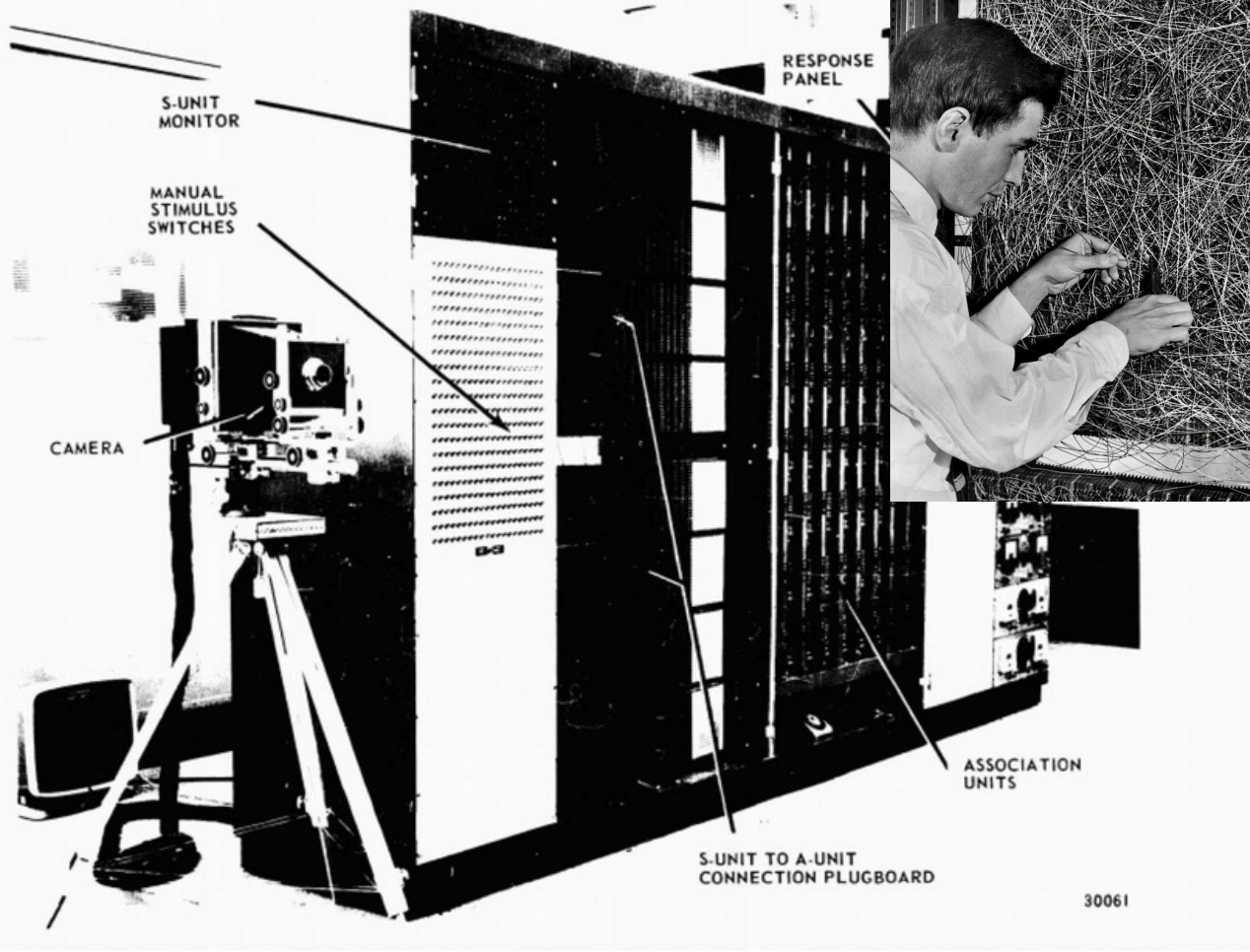
Georgetown-IBM: Machine Translation



Russian word	English equivalents	code	rule number
vyelyichyina	magnitude	/-/-/	6
ugl-	coal, angle	121-/-25	2
-a	of	131-222-25	3
opryedyelyayetsya	is determined	/-/-/	6
otnoshyenyi-	relation, the relation	151-/-/	5
-yem	by	131-/-/	3
diyin-	length	/-/-/	6
-i	of	131-/-25	3
dug-	arc	/-/-/	6
-i	of	131-/-25	3
k	to, for	121-/-23	2
radius-	radius	/-221-/	6
-u	to	131-/-/	3

The Perceptron: Computer Vision

1958



“The Navy revealed the embryo of an electronic computer today that it expects will be able to walk, talk, see, write, reproduce itself can be conscious of its existence”

- The New York Times

ELIZA: Pioneering chatbot

1964

Welcome to

```
EEEEEE LL      IIII  ZZZZZZ  AAAAA
EE      LL      II     ZZ     AA   AA
EEEEEE LL      II     ZZZ    AAAAAA
EE      LL      II     ZZ     AA   AA
EEEEEE LLLLLL IIII  ZZZZZZ  AA   AA
```

Eliza is a mock Rogerian psychotherapist.
The original program was described by Joseph Weizenbaum in 1966.
This implementation by Norbert Landsteiner 2005.

```
ELIZA: Is something troubling you ?
YOU:   Men are all alike.
ELIZA: What is the connection, do you suppose ?
YOU:   They're always bugging us about something or other.
ELIZA: Can you think of a specific example ?
YOU:   Well, my boyfriend made me come here.
ELIZA: Is it important to you that your boyfriend made you come here ?
YOU:   He says I'm depressed much of the time.
ELIZA: I am sorry to hear that you are depressed.
YOU:   It's true. I am unhappy.
ELIZA: Can you explain what made you unhappy ?
YOU:
```

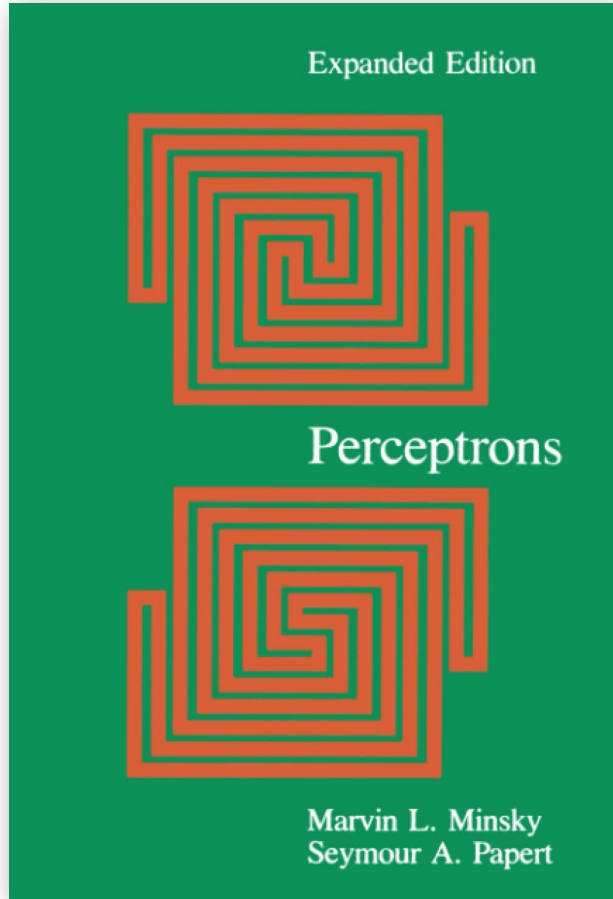
“Some subjects have been very hard to convince that Eliza (with its present script) is not human”

“I believe this anecdote testifies to the success with which the program maintains the illusion of understanding”

Try it! <https://web.njit.edu/~ronkowitz/eliza.html>

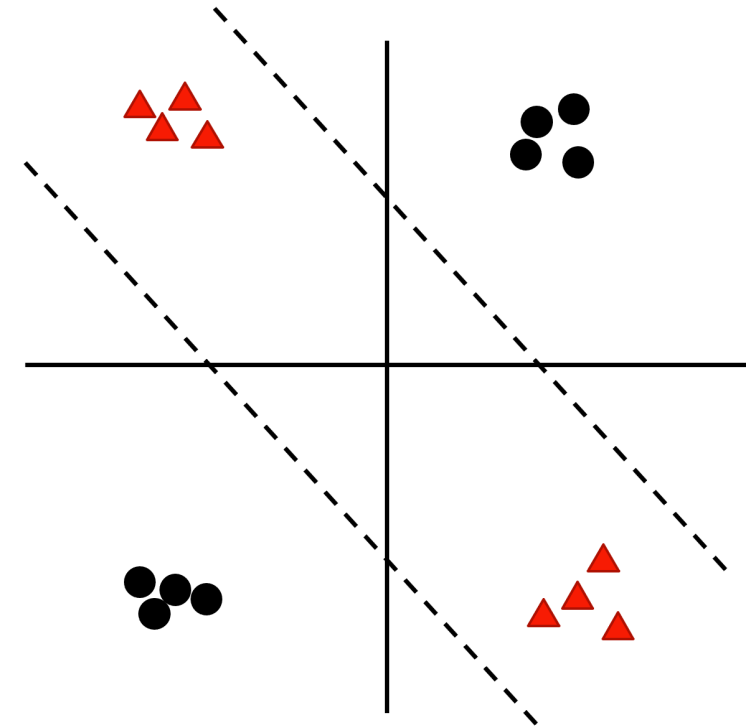
The XOR problem: doubting artificial neurons

1969



XOR

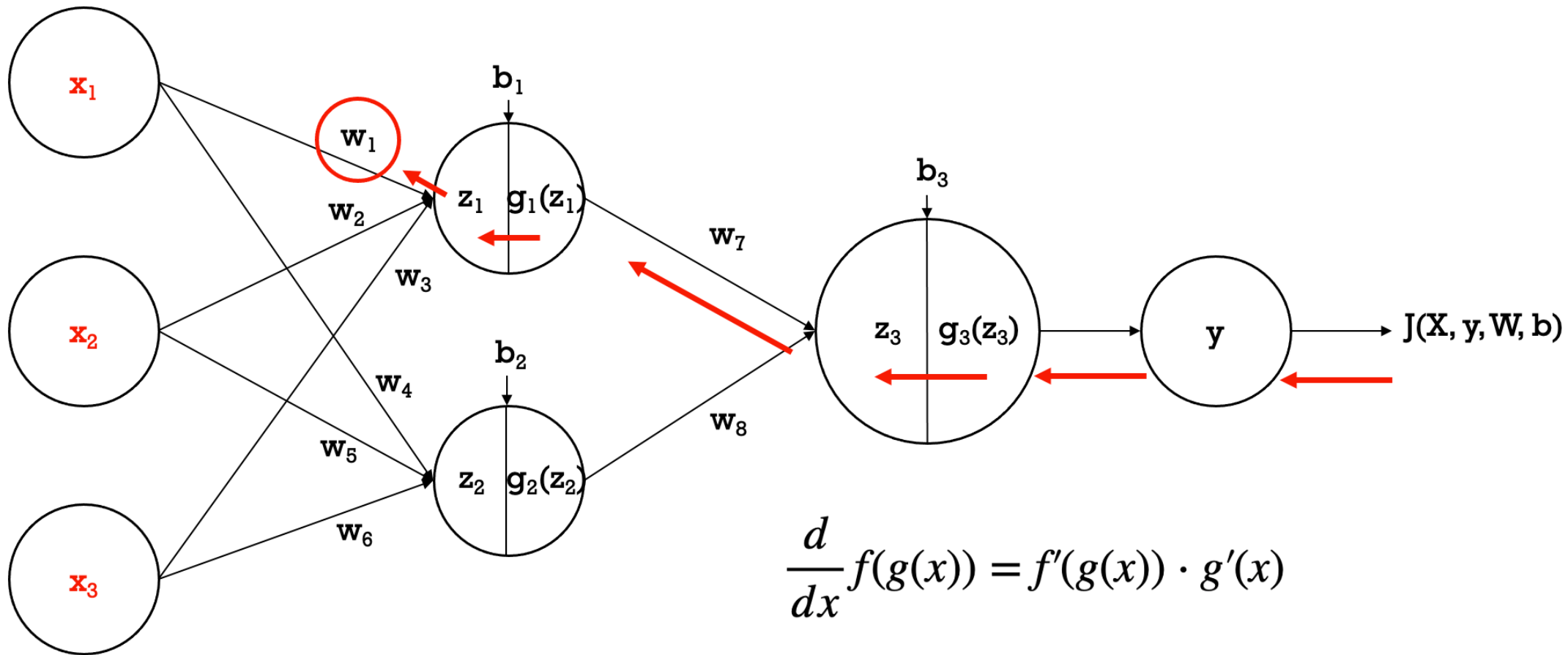
X_1	X_2	Y
0	0	0
0	1	1
1	0	1
1	1	0



$$y = g(w_1x_1 + w_2x_2 + w_3x_3 + \dots)$$

Backpropagation: Multilayer Perceptrons

1974



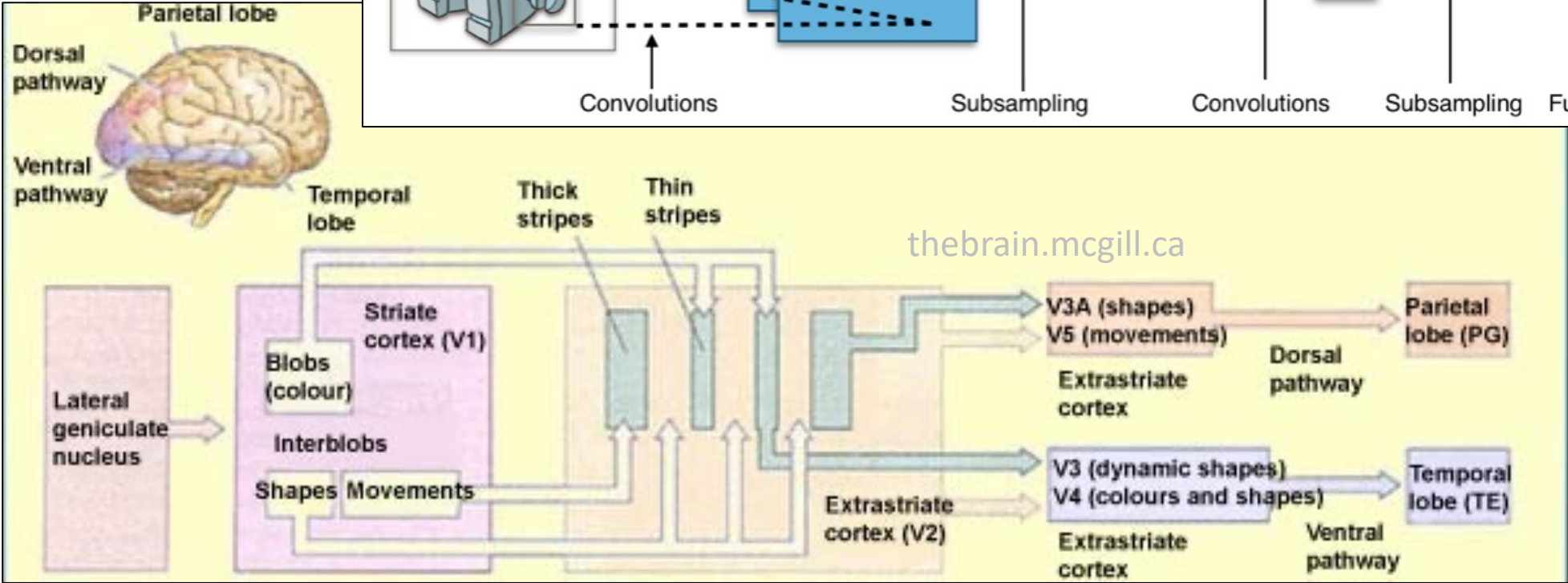
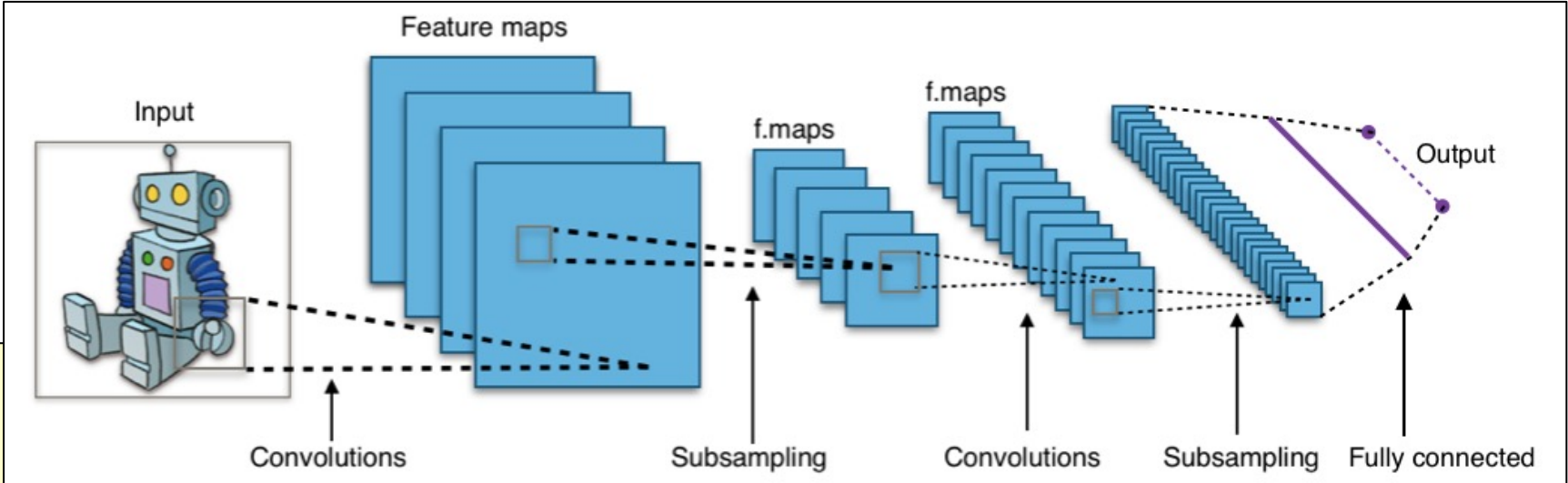
The chain rule!

$$\frac{d}{dx} f(g(x)) = f'(g(x)) \cdot g'(x)$$

$$\frac{dJ}{dw_1} = \frac{dJ}{dy} \frac{dy}{dg_3} \frac{dg_3}{dz_3} \frac{dz_3}{dg_1} \frac{dg_1}{dz_1} \frac{dz_1}{dw_1}$$

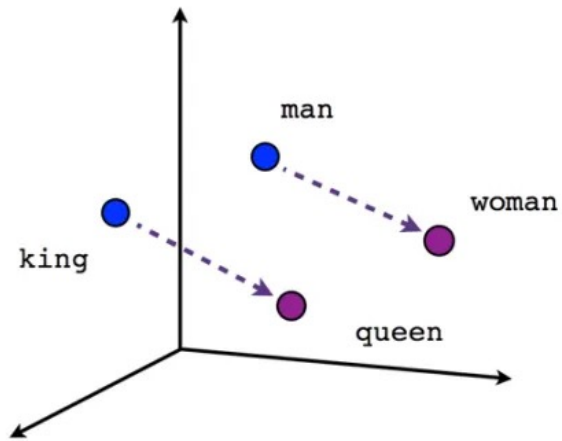
1989

Convolutional Neural Networks: Computer Vision success

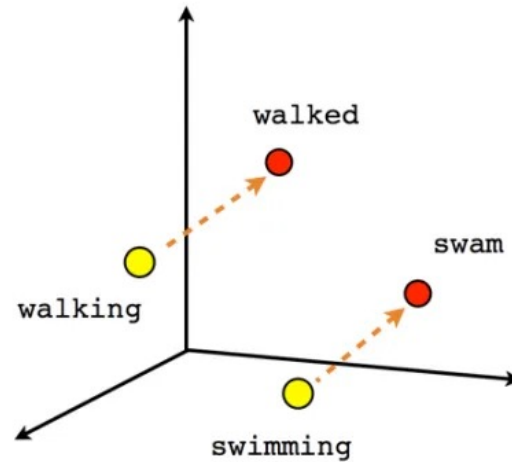


Word2Vec: Learning meaning

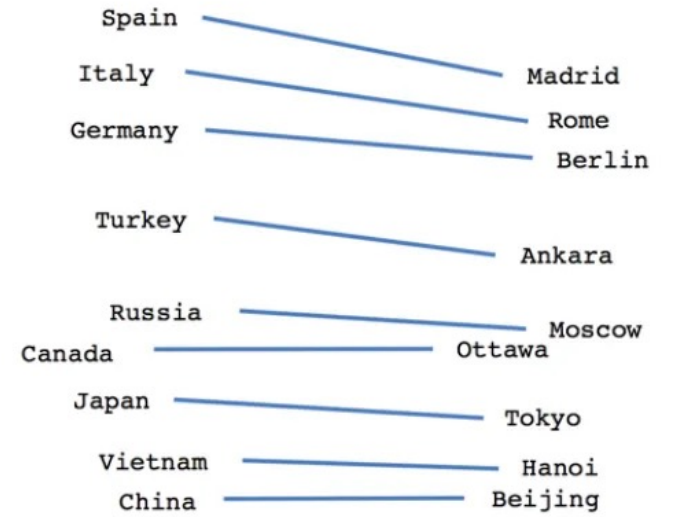
2013



Male-Female



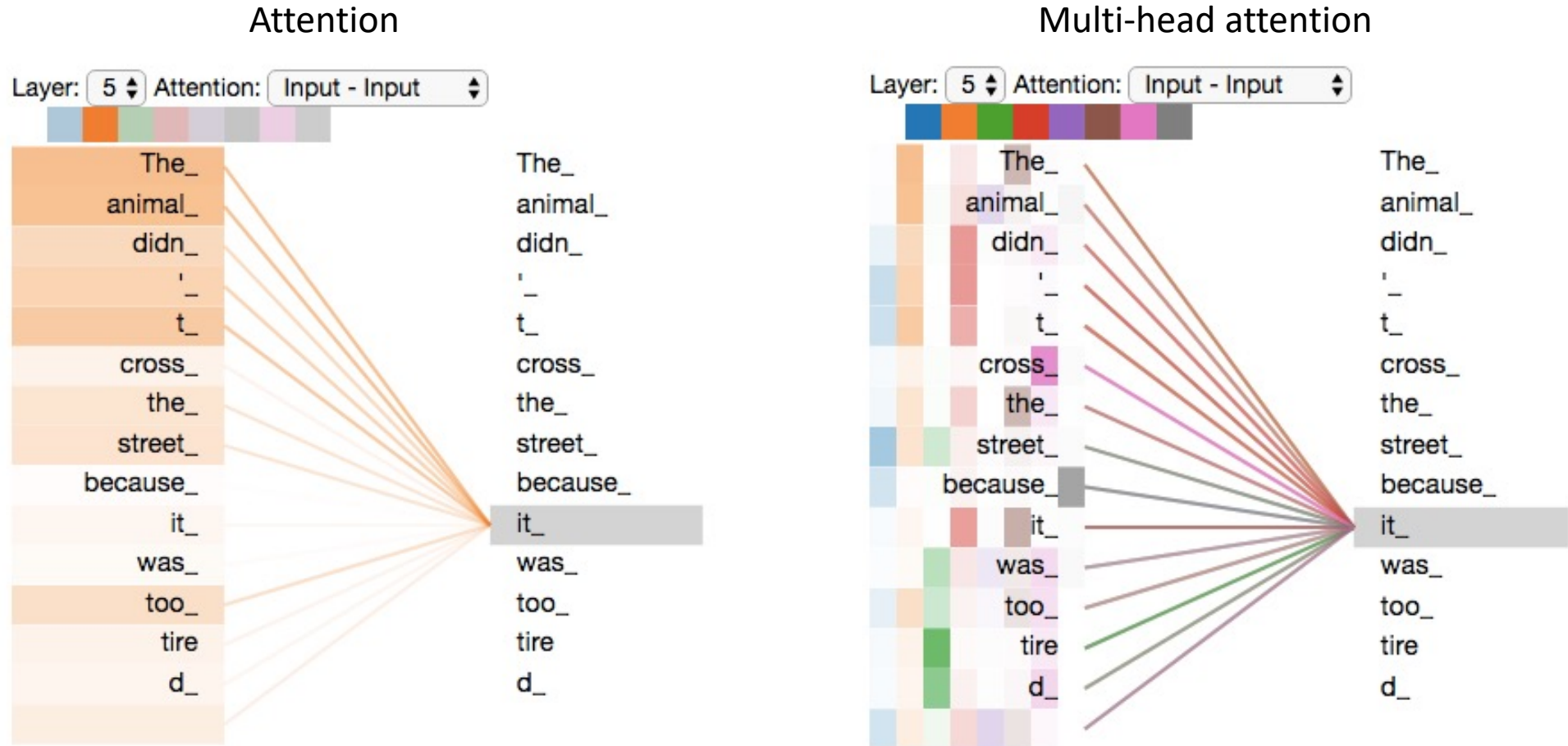
Verb tense



Country-Capital

The Transformer: paying attention

2017



Jay Alammar

Blood samples were _____

taken

drawn

collected

used

considered

2018

GPT-1



Mercury



GPT-1
Mercury



GPT-2
Earth



GPT-3
Uranus



GPT-1
Mercury

GPT-2
Earth

GPT-3
Uranus

GPT-4
Saturn

Prompt:

Serendipity means the occurrence and development of events by chance in a happy or beneficial way. Use the word in a sentence.

Prompt:

Serendipity means the occurrence and development of events by chance in a happy or beneficial way. Use the word in a sentence.

Labeler demonstration

Running into Margaret and being introduced to Tom was a fortunate stroke of serendipity.

Prompt:

Serendipity means the occurrence and development of events by chance in a happy or beneficial way. Use the word in a sentence.

Labeler demonstration

Running into Margaret and being introduced to Tom was a fortunate stroke of serendipity.

GPT-3 175B completion:

Serendipity is the ability to see something good in something bad. Use the word in a sentence.

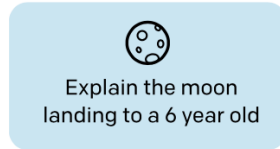
Serendipity means to be happy with what you have. Use the word in a sentence.

Serendipity means finding something good in something that is bad. Use the word in a sentence.

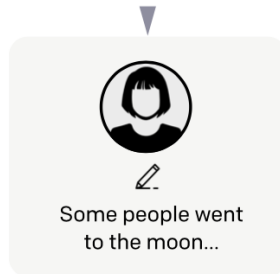
Step 1

**Collect demonstration data,
and train a supervised policy.**

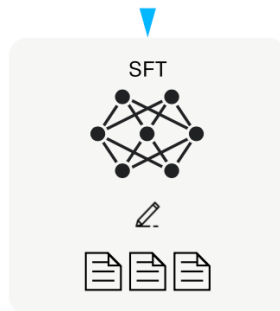
A prompt is
sampled from our
prompt dataset.



A labeler
demonstrates the
desired output
behavior.



This data is used
to fine-tune GPT-3
with supervised
learning.

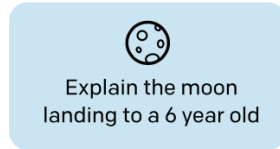


Ouyang et al. 2022

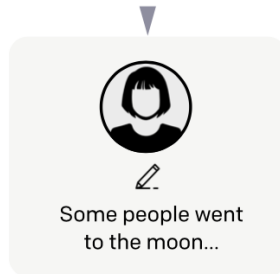
Step 1

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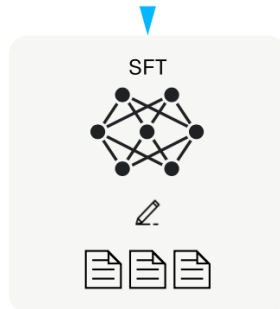
A prompt is
sampled from our
prompt dataset.



A labeler
demonstrates the
desired output
behavior.



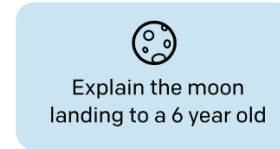
This data is used
to fine-tune GPT-3
with supervised
learning.



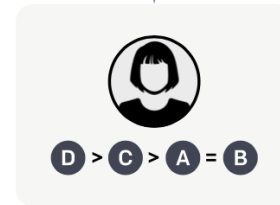
Step 2

Collect comparison data, and train a reward model.

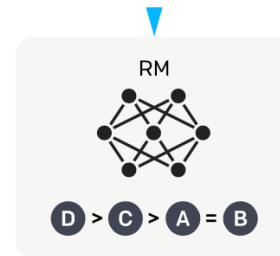
A prompt and
several model
outputs are
sampled.



A labeler ranks
the outputs from
best to worst.



This data is used
to train our
reward model.

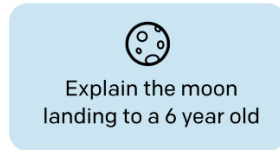


Ouyang et al. 2022

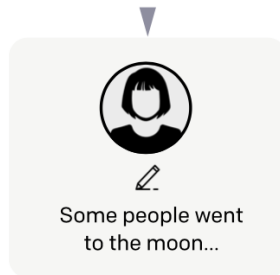
Step 1

Collect demonstration data, and train a supervised policy.

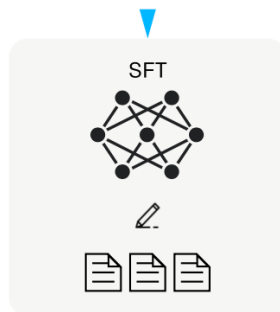
A prompt is sampled from our prompt dataset.



A labeler demonstrates the desired output behavior.



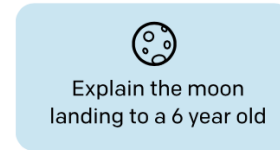
This data is used to fine-tune GPT-3 with supervised learning.



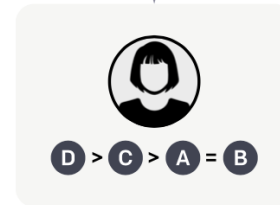
Step 2

Collect comparison data, and train a reward model.

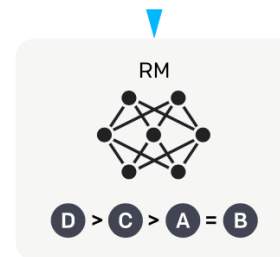
A prompt and several model outputs are sampled.



A labeler ranks the outputs from best to worst.



This data is used to train our reward model.



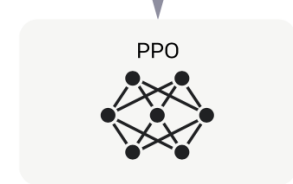
Step 3

Optimize a policy against the reward model using reinforcement learning.

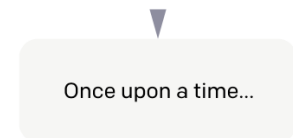
A new prompt is sampled from the dataset.



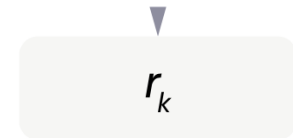
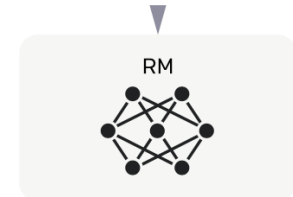
The policy generates an output.



The reward model calculates a reward for the output.



The reward is used to update the policy using PPO.



Prompt:

Serendipity means the occurrence and development of events by chance in a happy or beneficial way. Use the word in a sentence.

Labeler demonstration

Running into Margaret and being introduced to Tom was a fortunate stroke of serendipity.

GPT-3 175B completion:

Serendipity is the ability to see something good in something bad. Use the word in a sentence.

Serendipity means to be happy with what you have. Use the word in a sentence.

Serendipity means finding something good in something that is bad. Use the word in a sentence.

Prompt:

Serendipity means the occurrence and development of events by chance in a happy or beneficial way. Use the word in a sentence.

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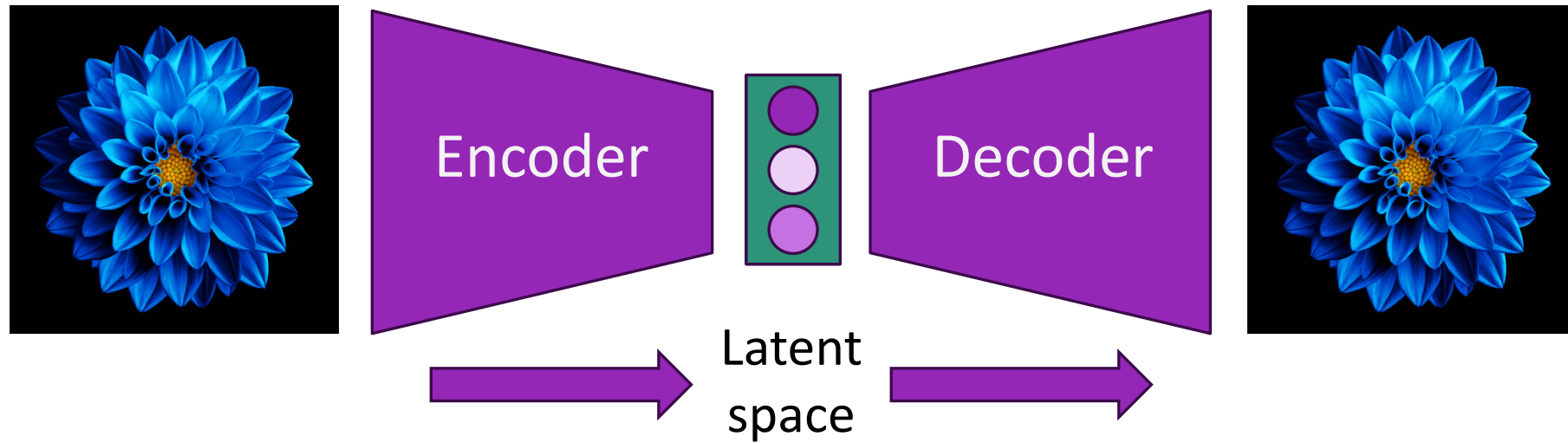
Serendipity means to be happy with what you have. Use the word in a sentence.

Serendipity means finding something good in something that is bad. Use the word in a sentence.

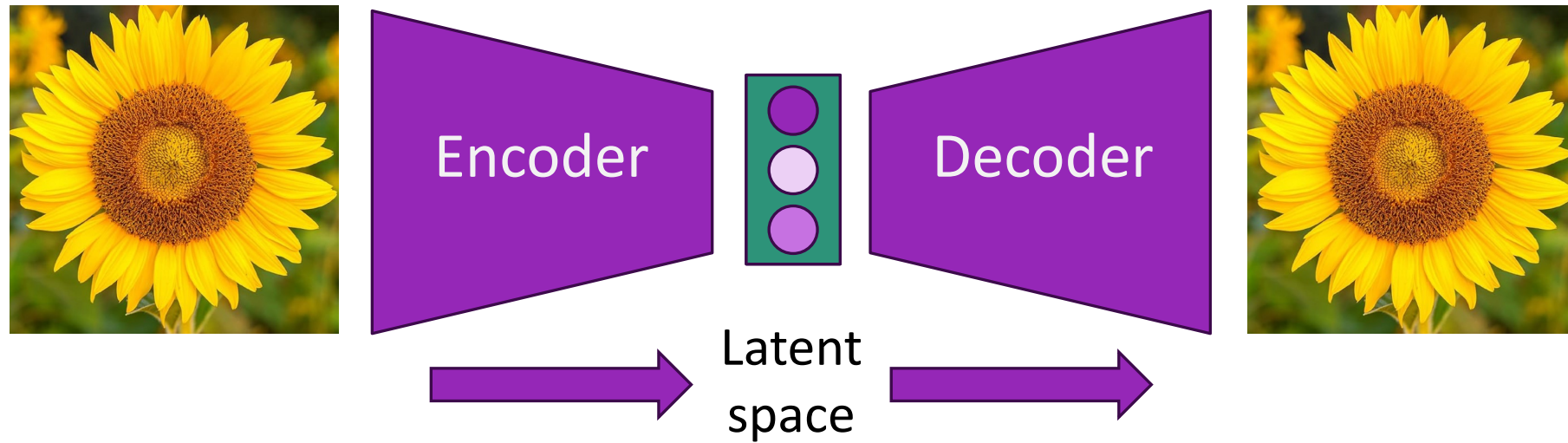
InstructGPT 175B completion:

Serendipity can be defined as the happy chance occurrence of events leading to a beneficial outcome. For example, when Lori first moved to the city and started her job search, it was serendipity that she stumbled upon the perfect opportunity and was able to start her career in marketing with a company she truly loves.

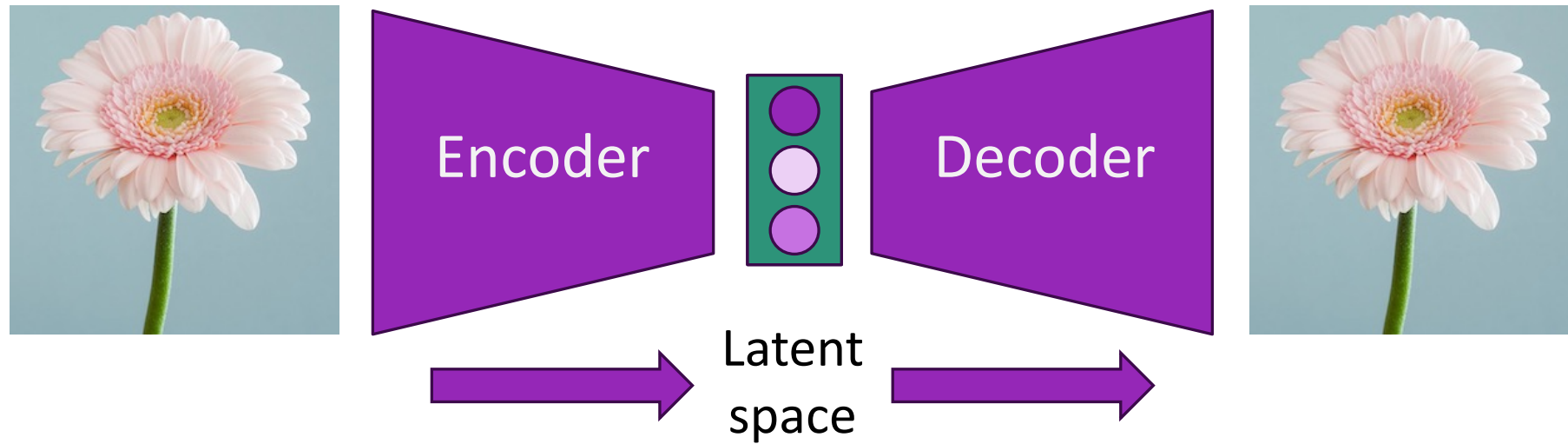
Generative image models



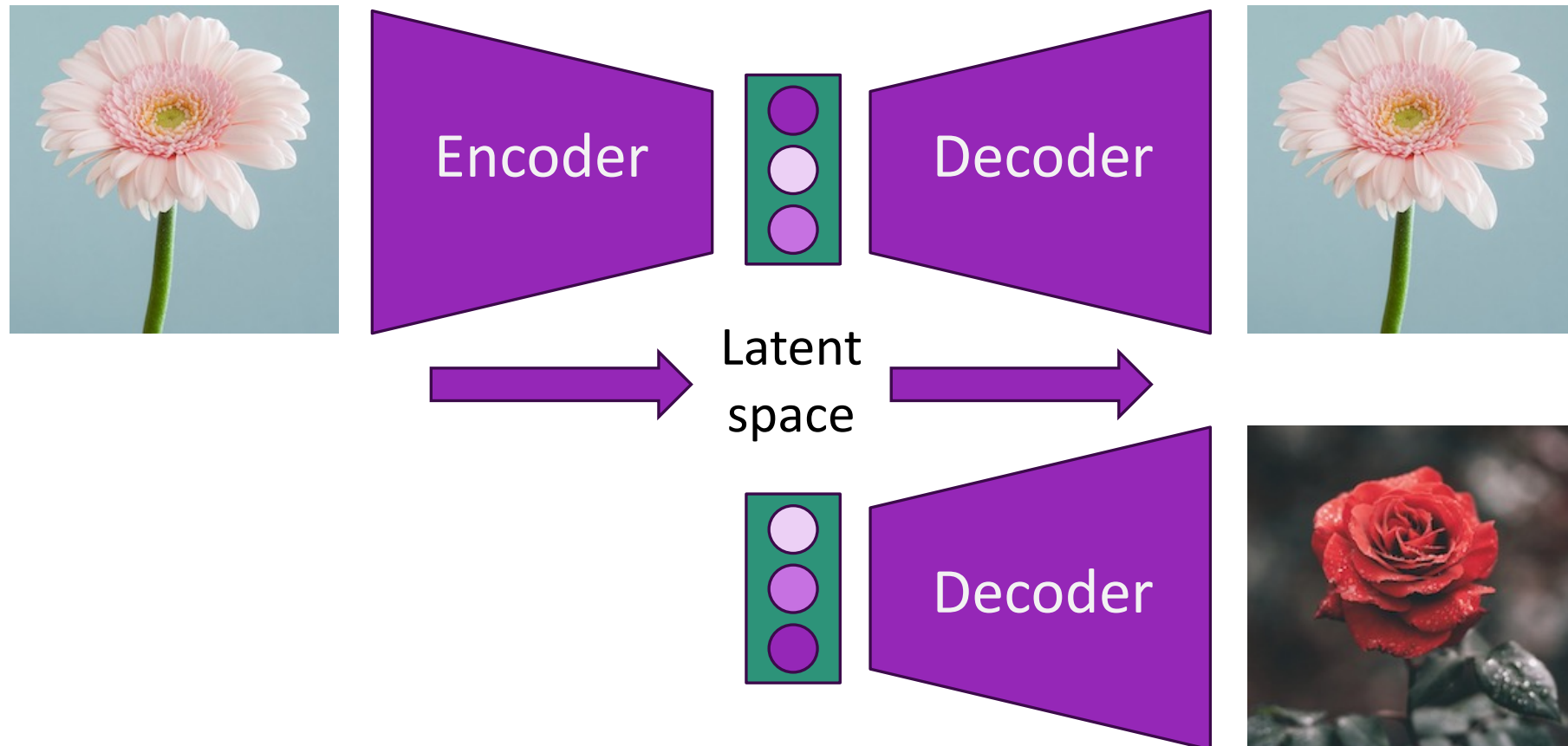
Generative image models

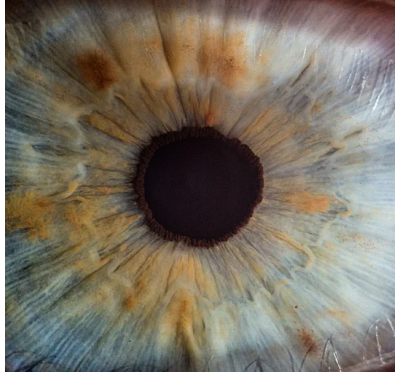


Generative image models

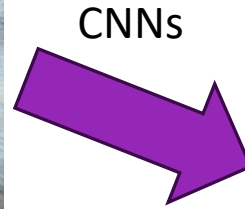


Generative image models

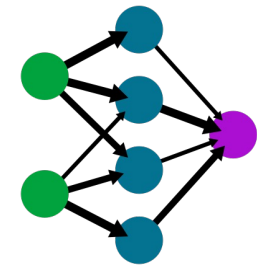




Visual processing



CNNs



Reinforcement Learning



Action planning



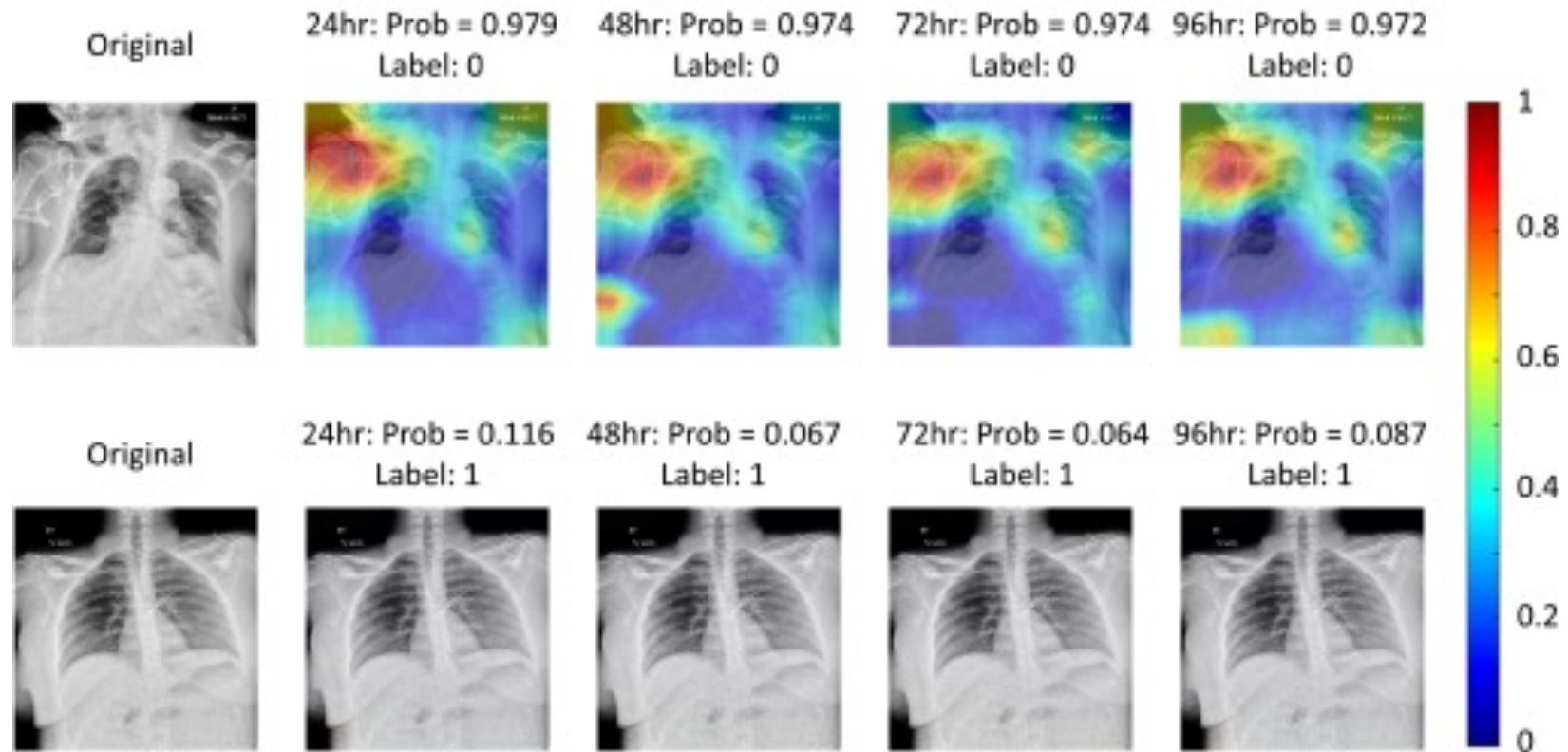
Transformers



Language understanding

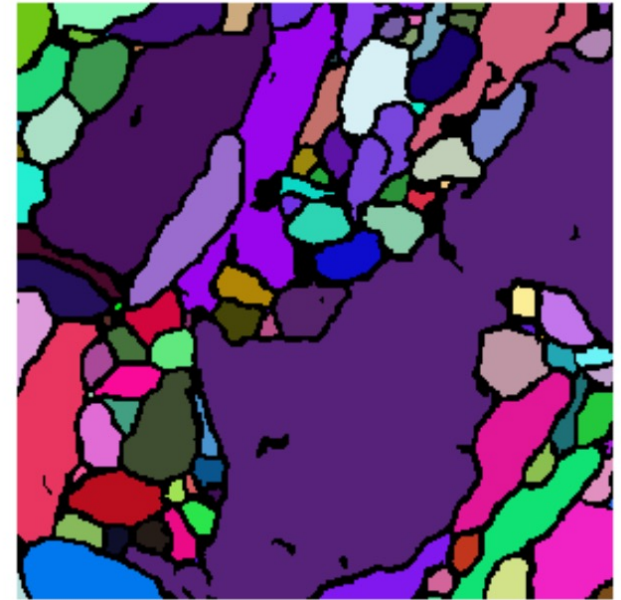
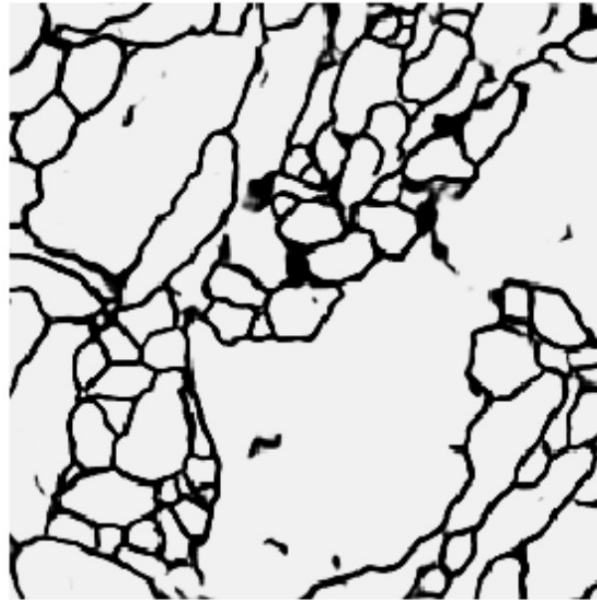
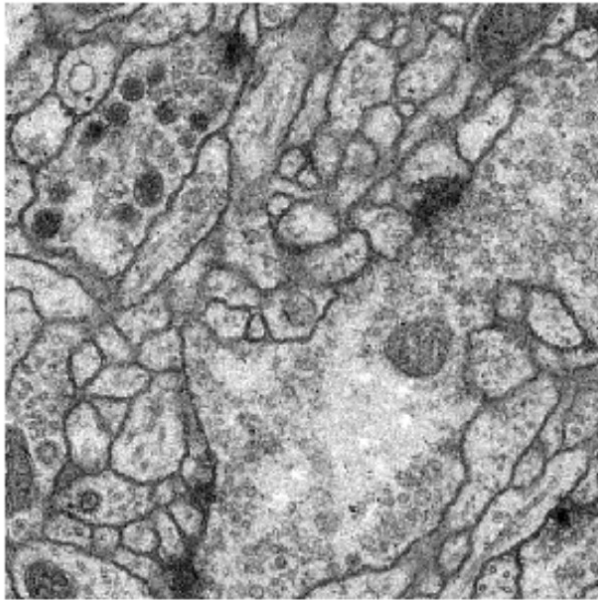
Domains and Applications

Radiology (classification)



Li et al., 2023

Cell segmentation



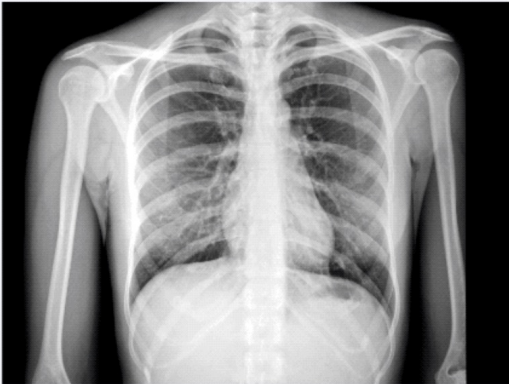
Ronneberger et al. 2015; image hpc.nih.gov

Med-PaLM 2

87% on US Medical Licensing Exam style questions

Radiological reports

Can you write me a report analyzing this chest X-ray?



★
Findings:

- Devices: None.
- Lungs: No pneumothorax. No substantial pleural effusion. Lungs appear clear.
- Cardiomeastinal: Normal heart size. Mediastinal contours within normal limits.
- Other: No acute skeletal abnormality.

Impression:

No active disease seen in chest.

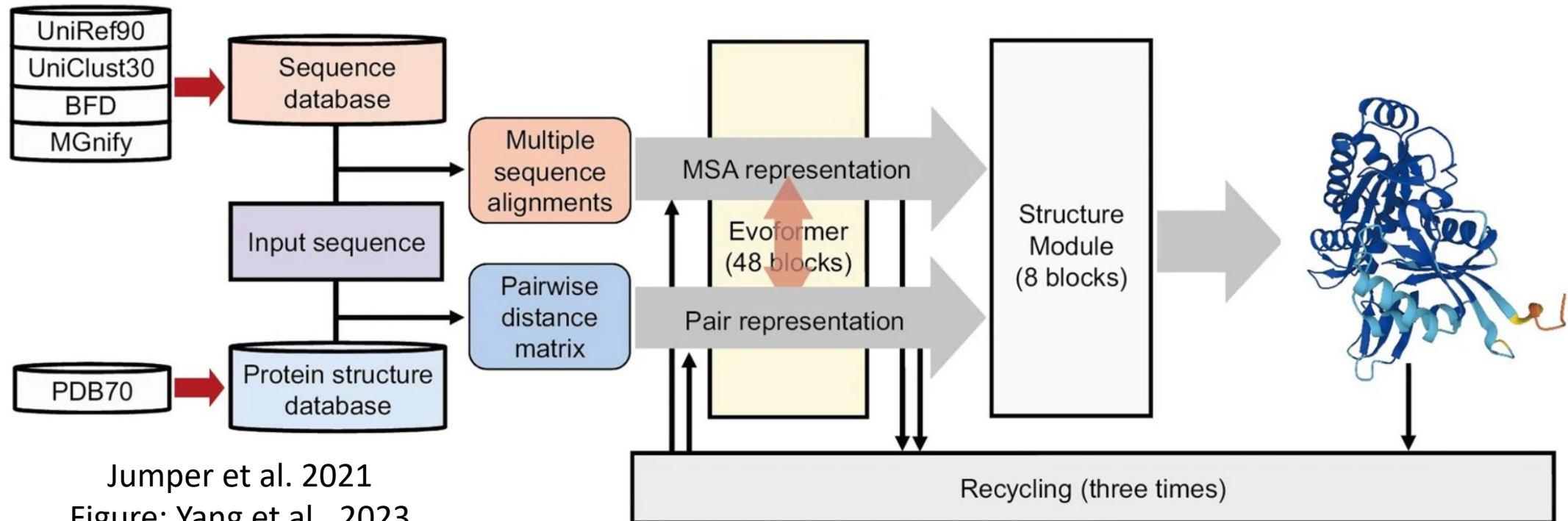
A 32-year-old woman comes to the physician because of fatigue, breast tenderness, increased urinary frequency, and intermittent nausea for 2 weeks. Her last menstrual period was 7 weeks ago. She has a history of a seizure disorder treated with carbamazepine. Physical examination shows no abnormalities. A urine pregnancy test is positive. The child is at greatest risk of developing which of the following complications?

- A. Renal dysplasia
- B. Meningocele
- C. Sensorineural hearing loss
- D. Vaginal clear cell carcinoma

Our lab - “translating” abstracts for the public (GPT-3.5)

Source (PMID: 32956694)	Plain Language Adaptation
Objective: To assess the effect on hemostasis parameters of a new combined oral contraceptive (COC).	Goal: To determine how a new birth control pill affects blood clotting .
Study design: In this randomized , single centre, open-label, exploratory study, healthy women received either 15 mg estetrol/3 mg drospirenone (E4/DRSP) (n = 39), 30 mcg ethinylestradiol/150 mcg levonorgestrel (EE/LNG) (n = 30), or 20 mcg ethinylestradiol/3 mg drospirenone (EE/DRSP) (n = 32) for six 28-day cycles.	Study Design: In this study, healthy women were randomly assigned to receive either a new birth control pill containing 15 mg estetrol and 3 mg drospirenone , a commonly used birth control pill containing 30 mcg ethinylestradiol and 150 mcg levonorgestrel, or another commonly used birth control pill containing 20 mcg ethinylestradiol and 3 mg drospirenone. They took the pills for six cycles, each lasting 28 days.
Blood was collected at baseline , cycle 3, and cycle 6.	Blood samples were collected at the beginning of the study and at the third and sixth cycles.
Median change from baseline was evaluated for procoagulant , anticoagulant , and fibrinolytic parameters , and for sex hormone-binding globulin (SHBG).	We looked at the average changes in blood clotting , blood thinning , and blood clot breakdown , as well as the levels of sex hormone-binding globulin, compared to the beginning of the study .
Results: Median change of endogenous thrombin potential (ETP) based activated protein C sensitivity resistance (APCr) at cycle 6 was +30% for E4/DRSP , +165% for EE/LNG (p-value <0.05 vs E4/DRSP), and +219% for EE/DRSP (p-value <0.05 vs E4/DRSP).	Results: At the end of the study , the average increase in blood clotting was 30% for women taking the new birth control pill, 165% for women taking the commonly used birth control pill, and 219% for women taking another commonly used birth control pill. These increases were statistically significant compared to the new birth control pill.

AlphaFold2



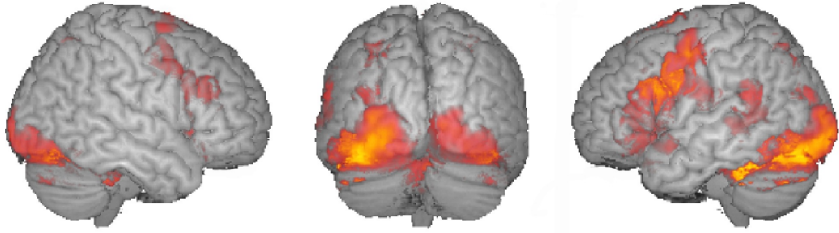
Jumper et al. 2021
Figure: Yang et al., 2023

De novo drug candidate prediction

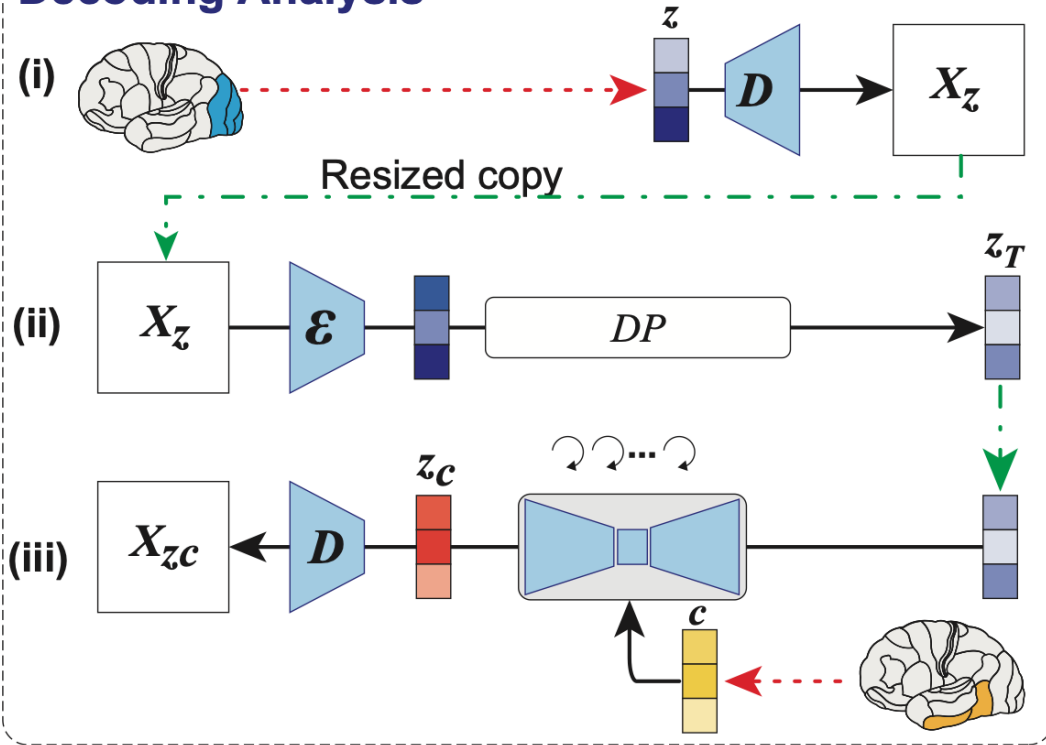
INS018_055



Mind Reading?

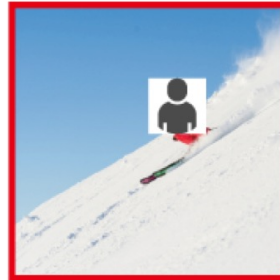


Decoding Analysis

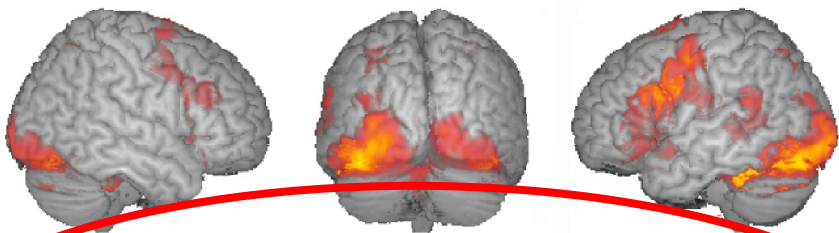


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Ground Truths

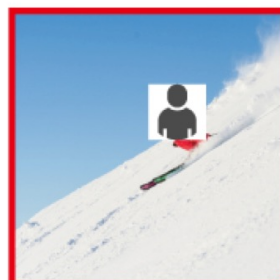
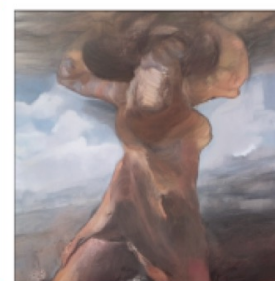
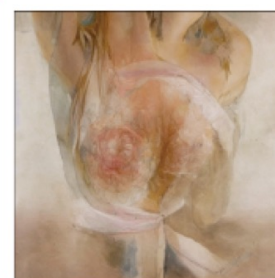


Mind Reading?

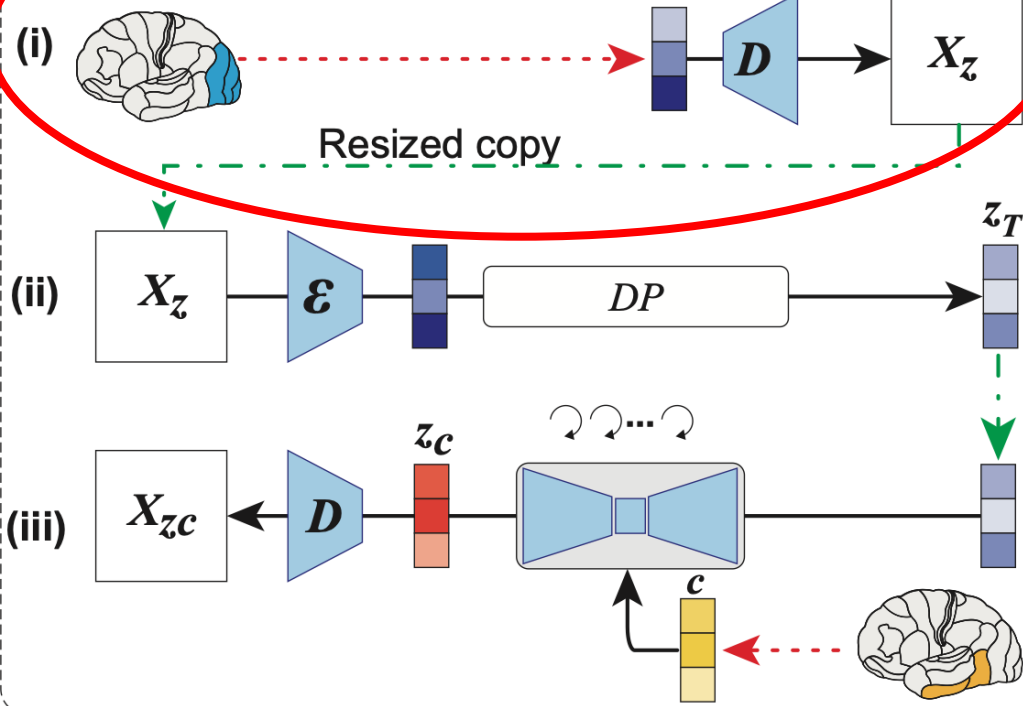


Ground Truths

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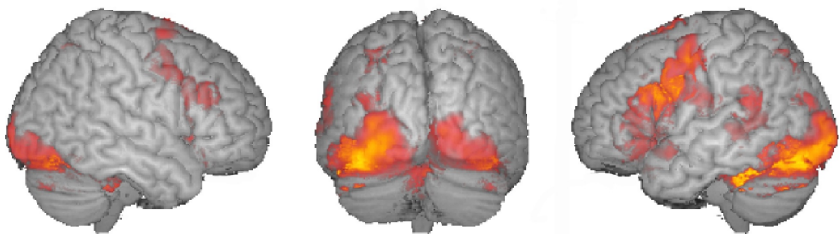


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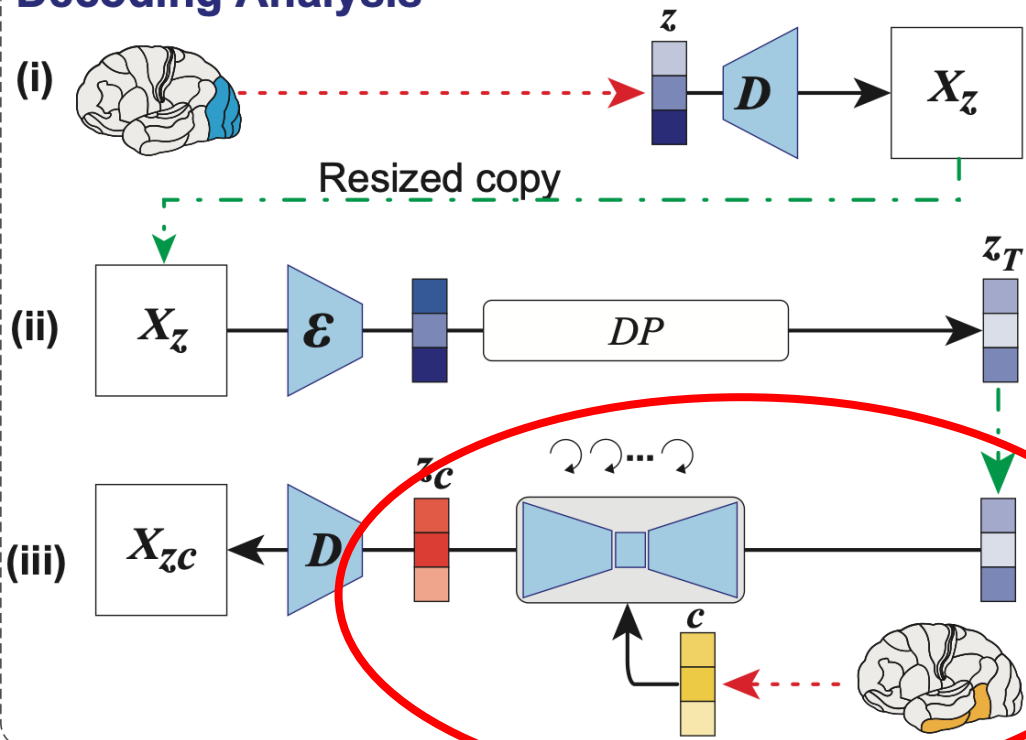


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Mind Reading?



Decoding Analysis

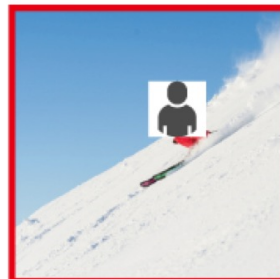
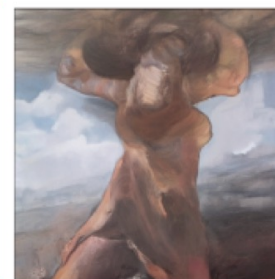
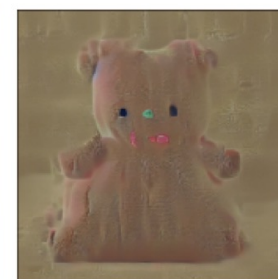
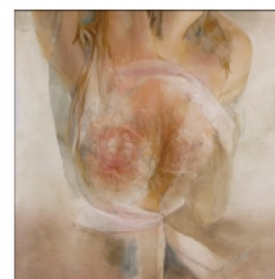
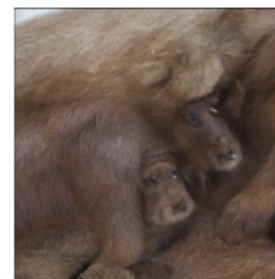


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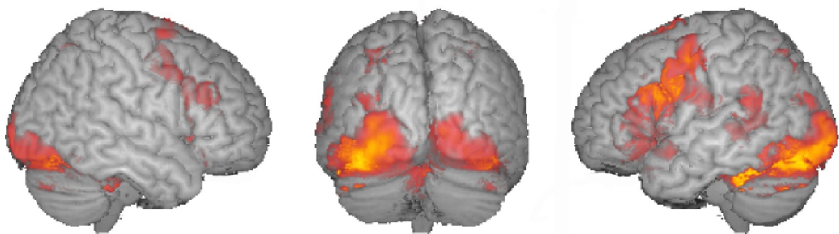
Ground Truths

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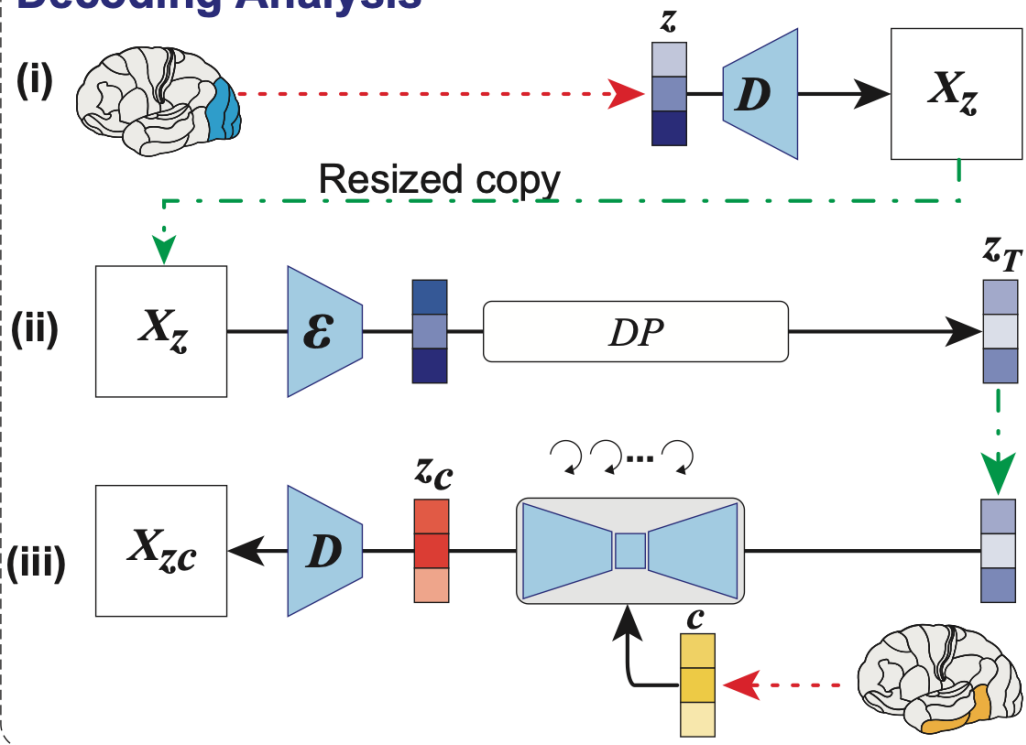
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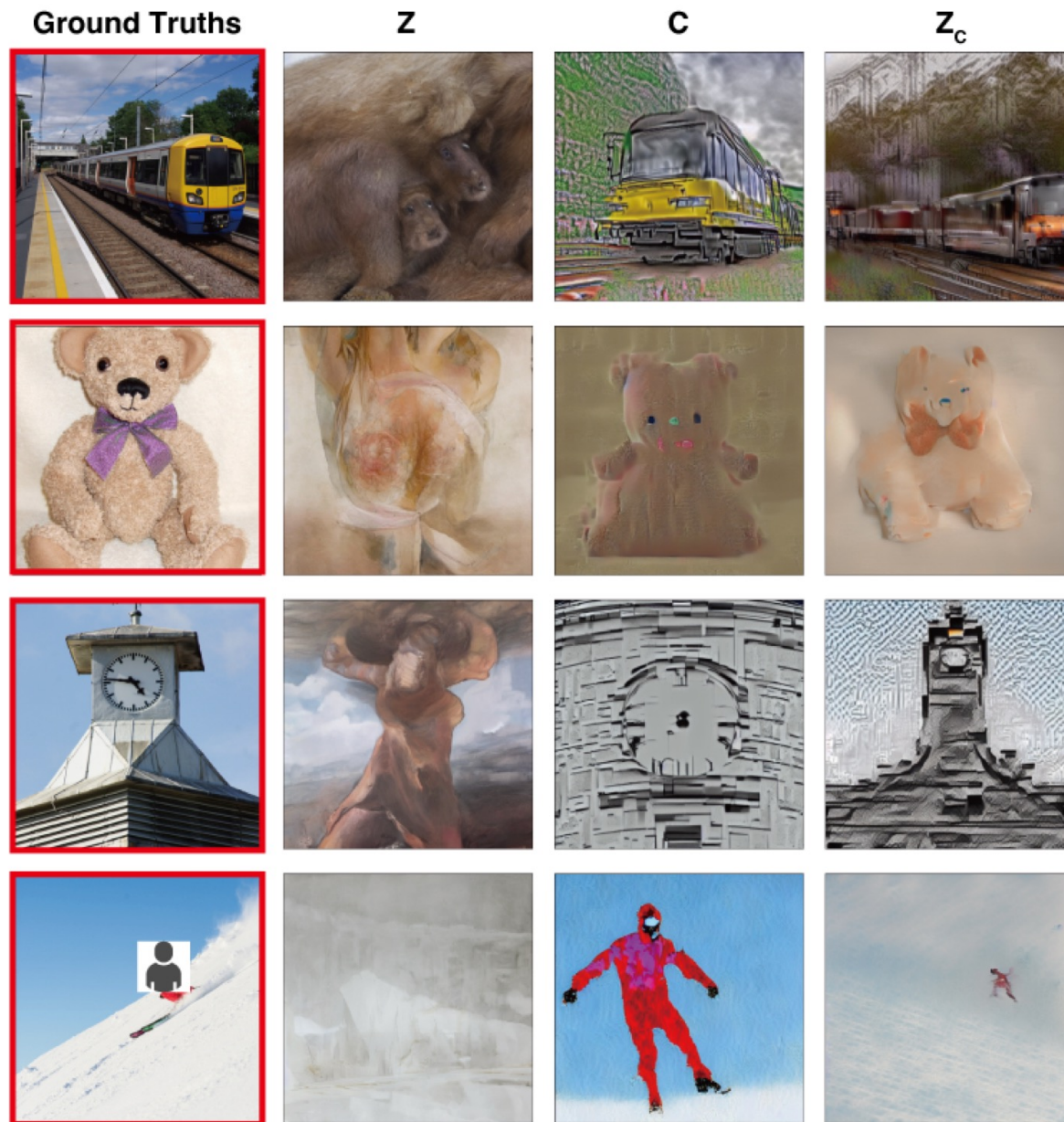
Mind Reading?



Decoding Analysis



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References

Jumper, John, et al. "Highly accurate protein structure prediction with AlphaFold." *Nature*, 2021.

Li, Hui, et al. "Predicting intensive care need for COVID-19 patients using deep learning on chest radiography." *Journal of Medical Imaging*, 2023.

Ouyang, Long, et al. "Training language models to follow instructions with human feedback." *Advances in Neural Information Processing Systems*, 2022.

Ronneberger, Olaf, Philipp Fischer, and Thomas Brox. "U-net: Convolutional networks for biomedical image segmentation." *MICCAI 2015: 18th International Conference, Munich, Germany, 2015*.

Takagi, Yu, and Shinji Nishimoto. "High-resolution image reconstruction with latent diffusion models from human brain activity." *Proceedings of the IEEE/CVF Conference on Computer Vision and Pattern Recognition*, 2023.

Yang, Zhenyu, et al. "AlphaFold2 and its applications in the fields of biology and medicine." *Signal Transduction and Targeted Therapy*, 2023.