

AI

Amir Zare - Summer 2024

Chapter 0: Prologue

Motivation 1

Discovering 30 novel Antimicrobials in matter of days

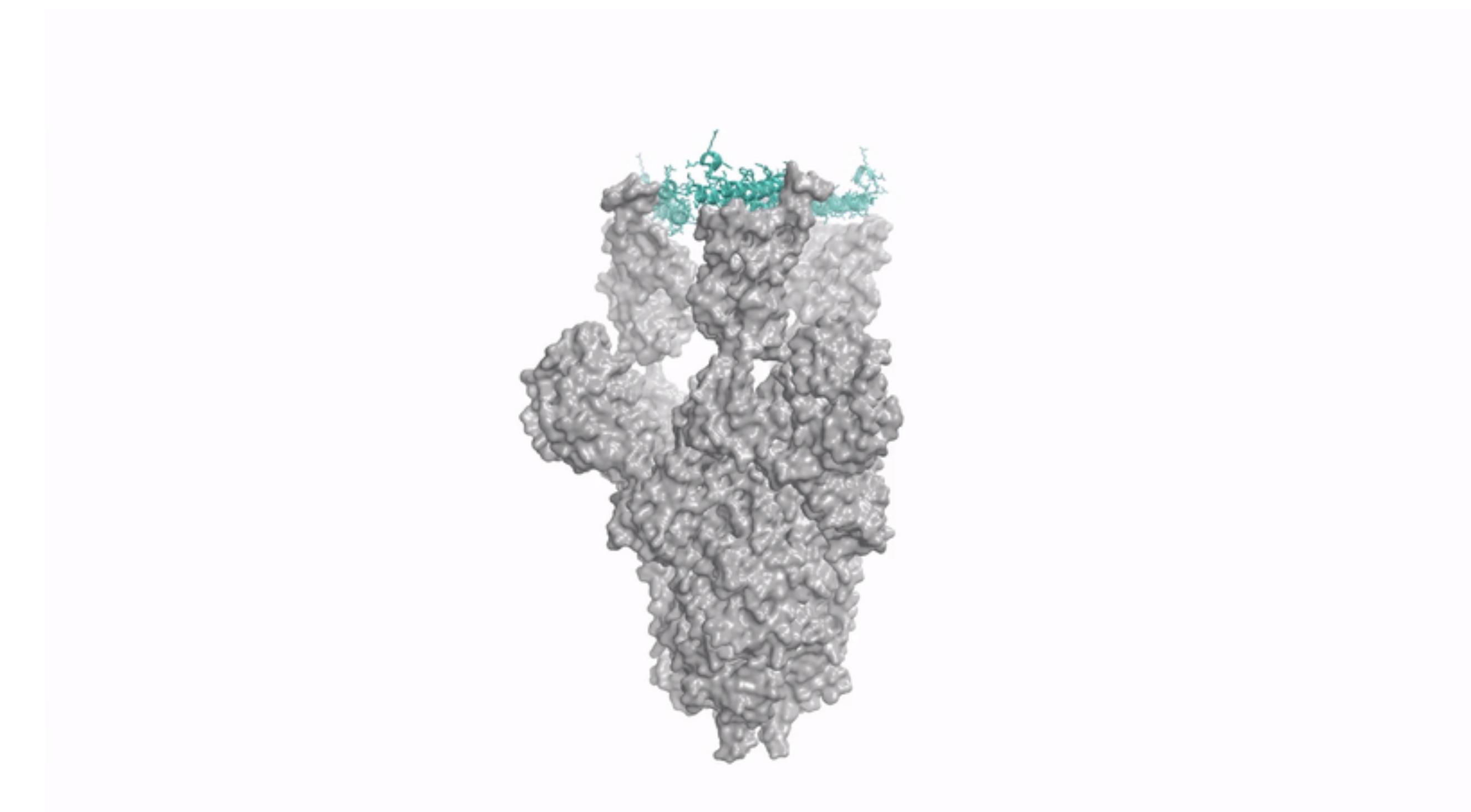
Generative AI

- If you show an AI lots of **images**, it can create new **images** given a prompt.



Generative AI in biology

- If you show an AI lots of **proteins**, it can create new **proteins** given a prompt.





Cell-free biosynthesis combined with deep learning accelerates de novo-development of antimicrobial peptides

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Check for updates

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Bioactive peptides are key molecules in health and medicine. Deep learning holds a big promise for the discovery and design of bioactive peptides. Yet, suitable experimental approaches are required to validate candidates in high throughput and at low cost. Here, we established a cell-free protein synthesis (CFPS) pipeline for the rapid and inexpensive production of antimicrobial peptides (AMPs) directly from DNA templates. To validate our platform, we used deep learning to design thousands of AMPs de novo. Using computational methods, we prioritized 500 candidates that we produced and screened with our CFPS pipeline. We identified 30 functional AMPs, which we characterized further through molecular dynamics simulations, antimicrobial activity and toxicity. Notably, six de novo-AMPs feature broad-spectrum activity against multidrug-resistant pathogens and do not develop bacterial resistance. Our work demonstrates the potential of CFPS for high throughput and low-cost production and testing of bioactive peptides within less than 24 h.

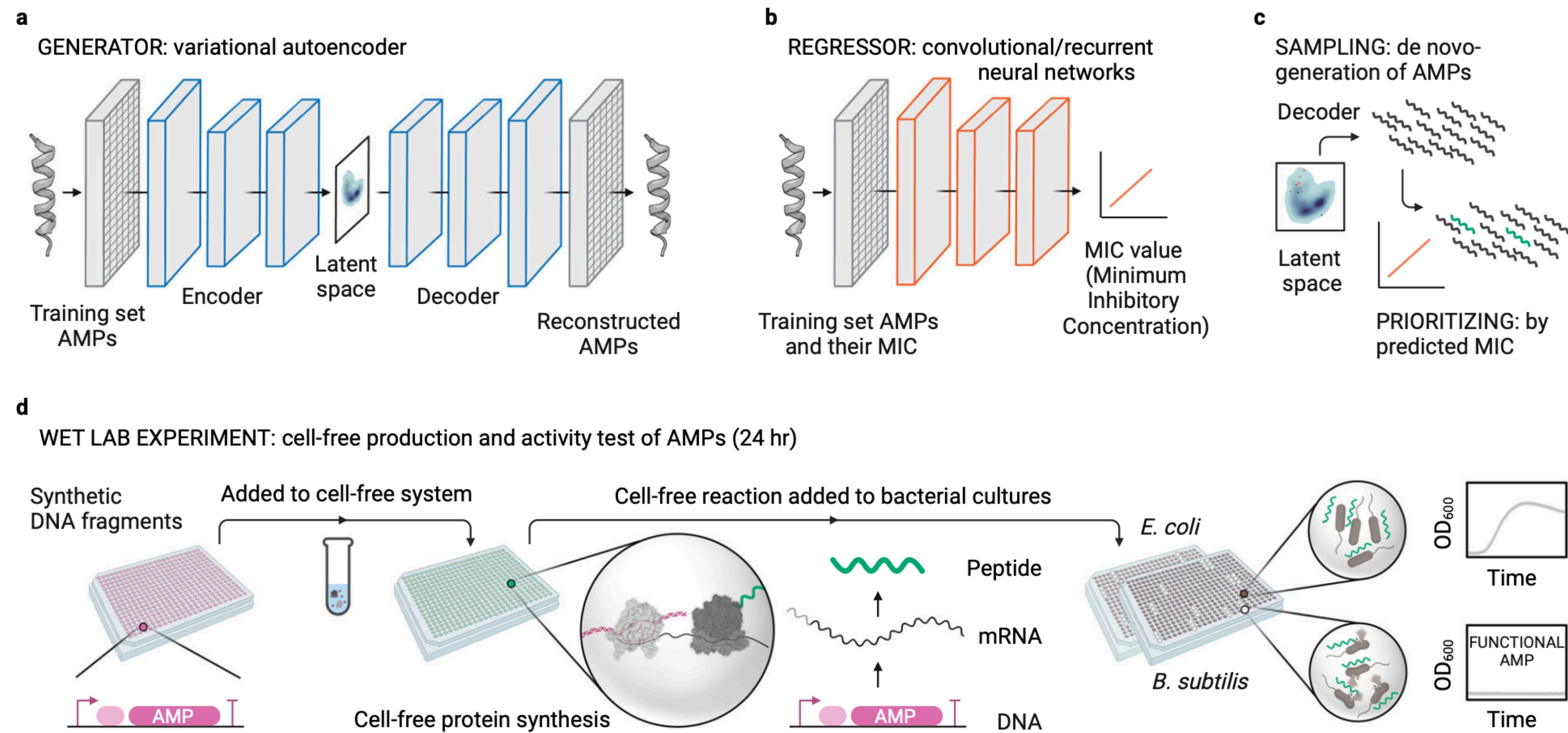
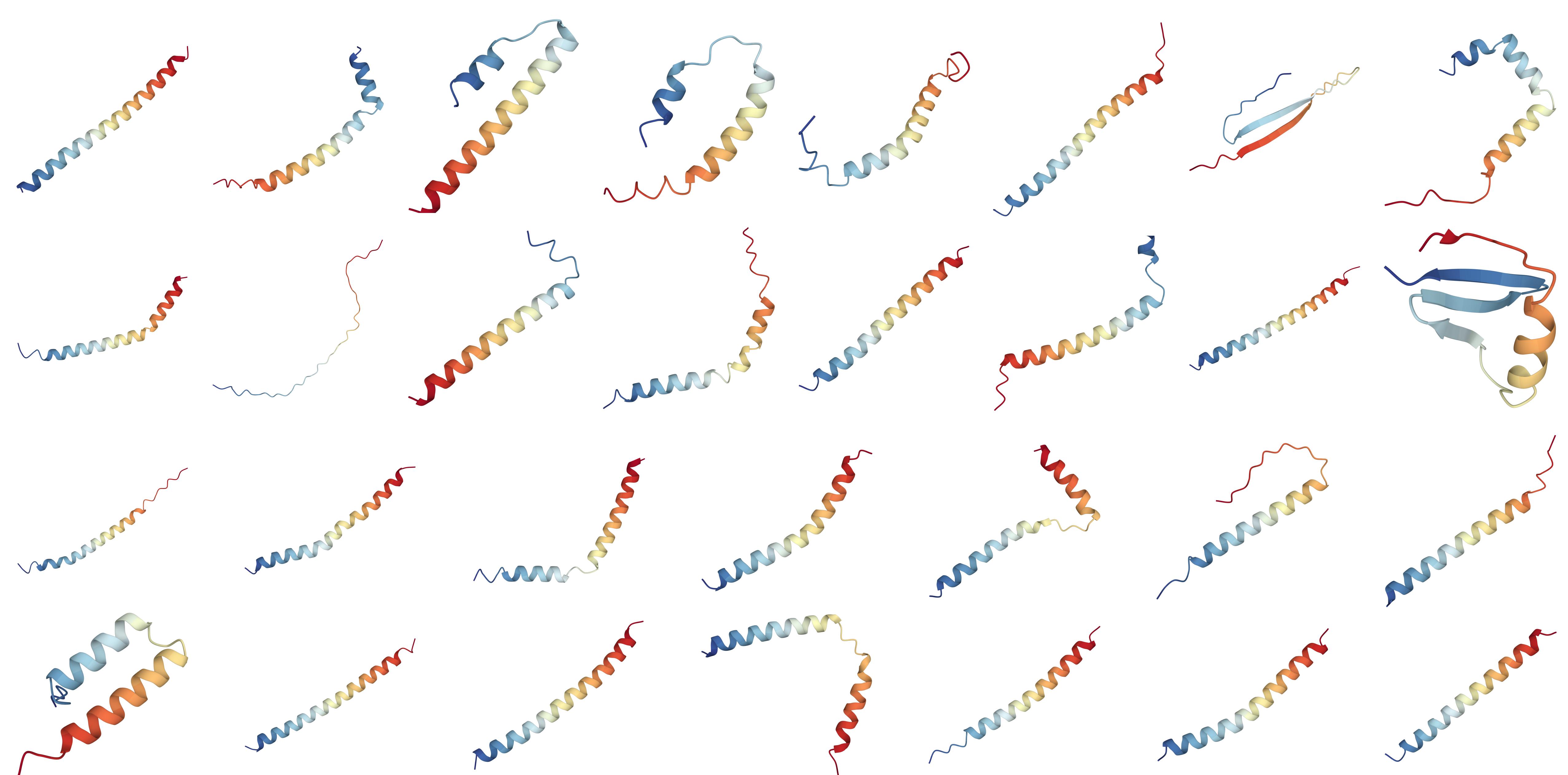


Fig. 1 | The workflow for de novo-development of AMPs via deep learning and cell-free biosynthesis. **a** Generative variational autoencoders (VAE) for de novo-design of AMPs after being trained on known AMP sequences. **b** Predictive convolutional or recurrent neural networks as regressors for the MIC prediction after being trained on known AMPs and their MIC. **c** Trained generative and predictive

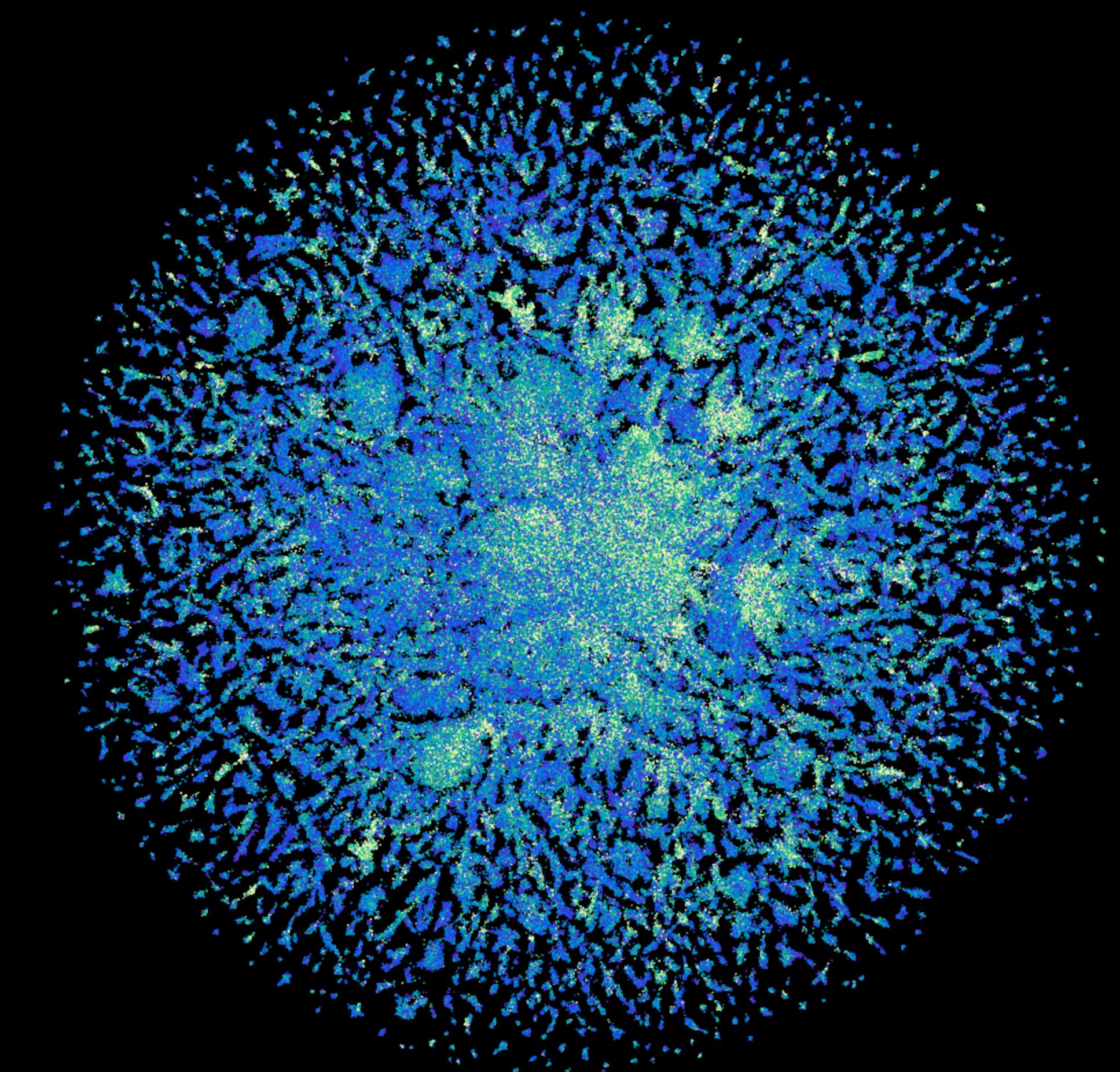
models are used for sampling from the latent space (de novo-design of AMPs) and prioritization of AMPs (predicting their MIC), respectively. **d** Experimental pipeline for rapid cell-free biosynthesis of the designed AMPs from synthetic DNA fragments and direct testing of produced AMPs in the cell-free mix to bacterial cultures followed by overnight continuous growth assay. Created with BioRender.com.



Motivation 2

Protein structure prediction





Drag to pan
Scroll to zoom in/out
Click to select a protein

Exploring 1 million out of 772M proteins

Unknown

Known

- Myoglobin was the first 3D protein structure resolved by John Kendrew in 1958.

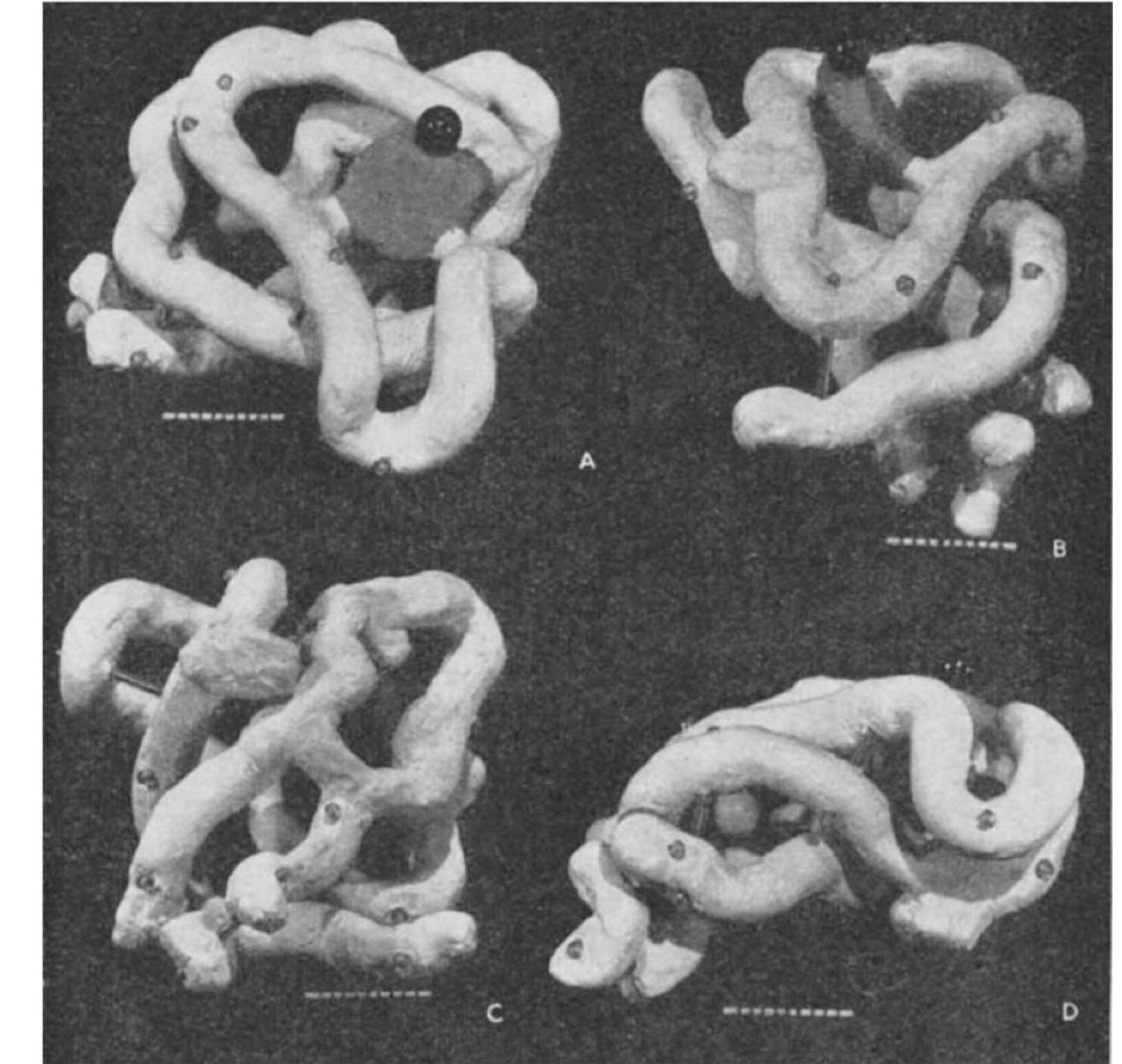


Fig. 2. Photographs of a model of the myoglobin molecule. Polypeptide chains are white; the grey disk is the haem group. The three spheres show positions at which heavy atoms were attached to the molecule (black: Hg of *p*-chloro-mercuri-benzene-sulphonate; dark grey: Hg of mercury diammine; light grey: Au of auri-chloride). The marks on the scale are 1 Å. apart

- Myoglobin structure at 2 Angstrom resolution.

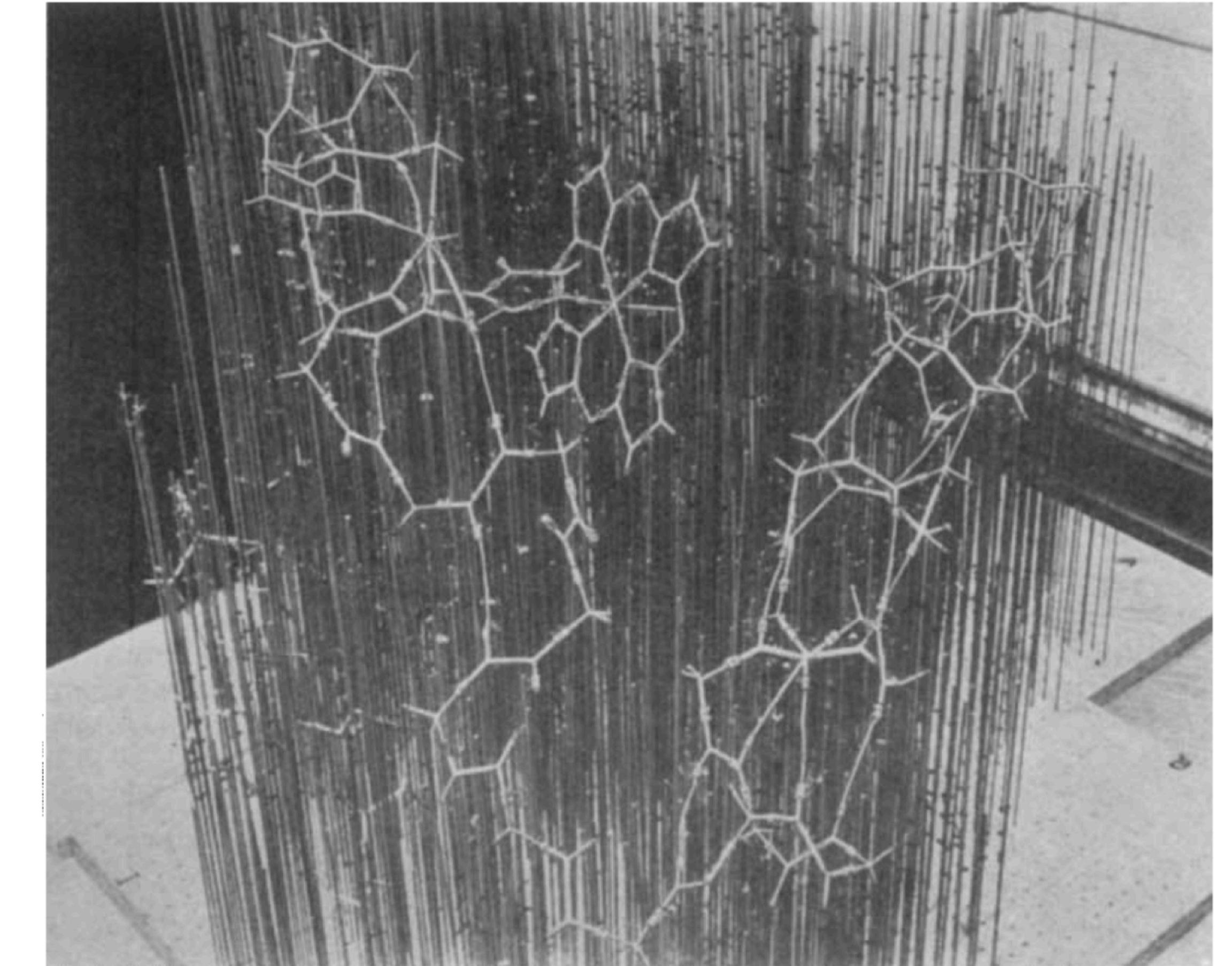
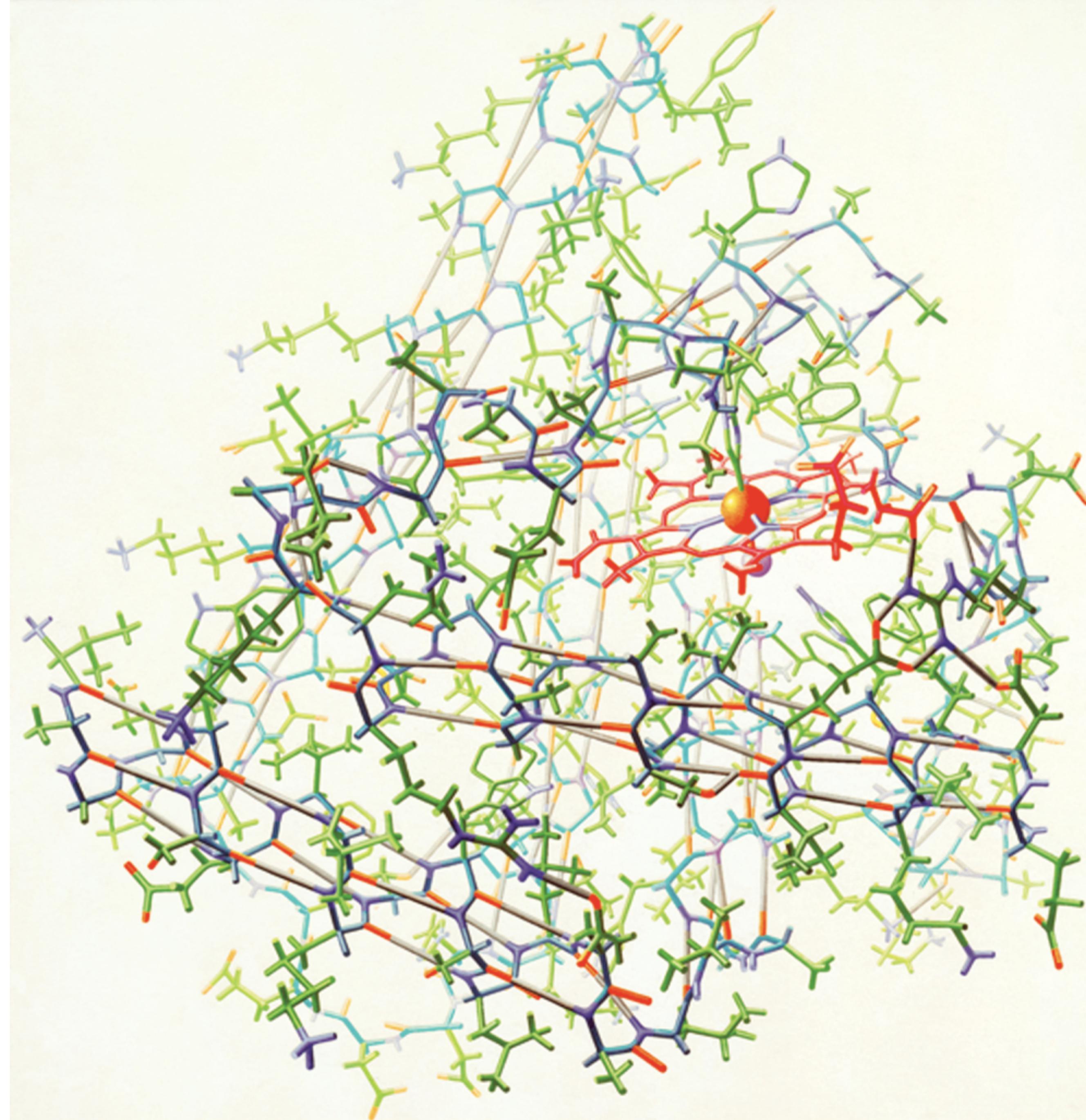
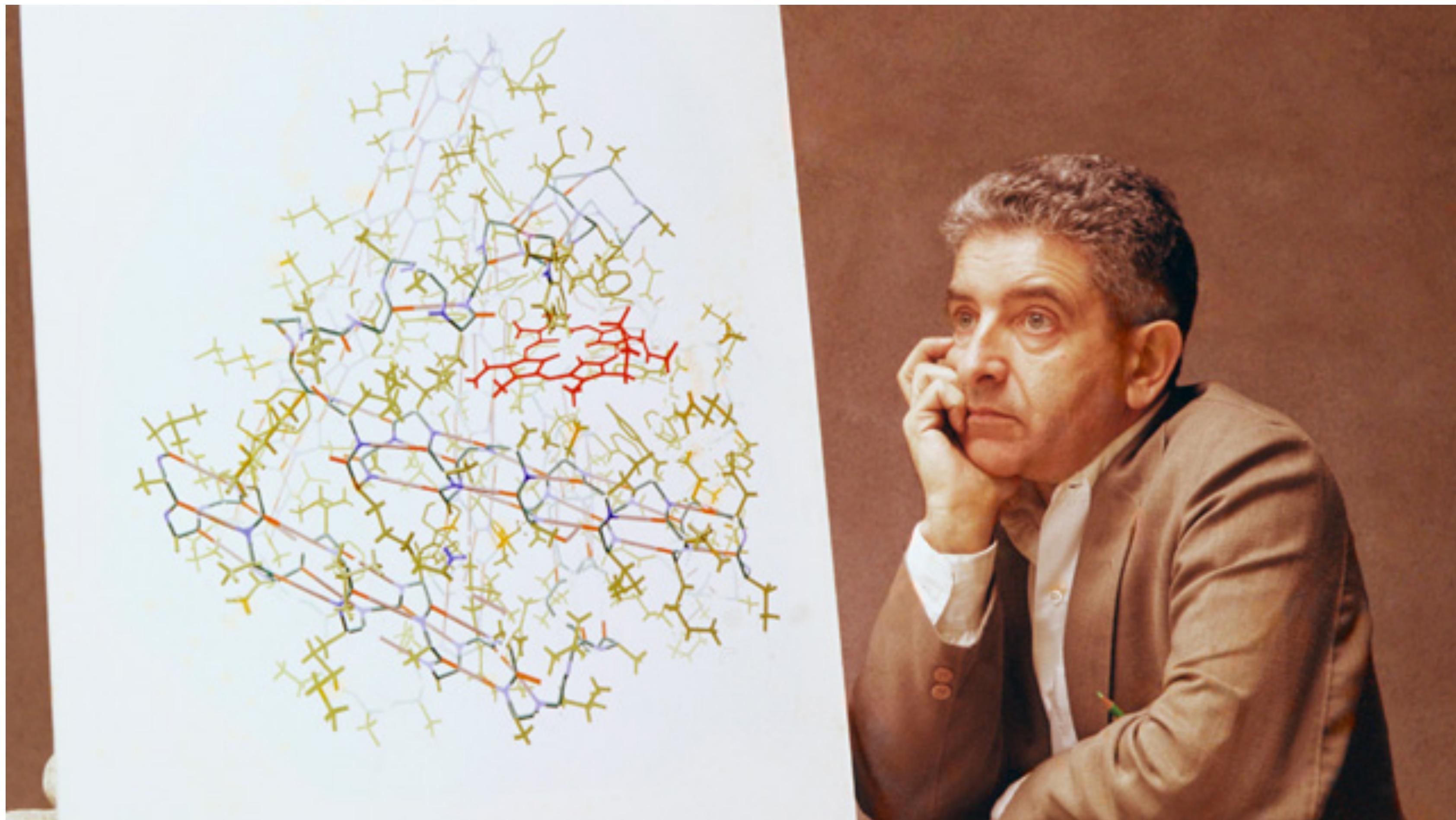


Fig. 4. Photograph of a model of part of the molecule near the haem group, showing the vertical rods and coloured clips which indicate the electron density at each point of the grid, and atomic models of the haem group and neighbouring helices. The terminal carboxyl end of the chain is on the extreme left





Perutz1960

- Haemoglobin structure was resolved by Max Perutz in 1960.

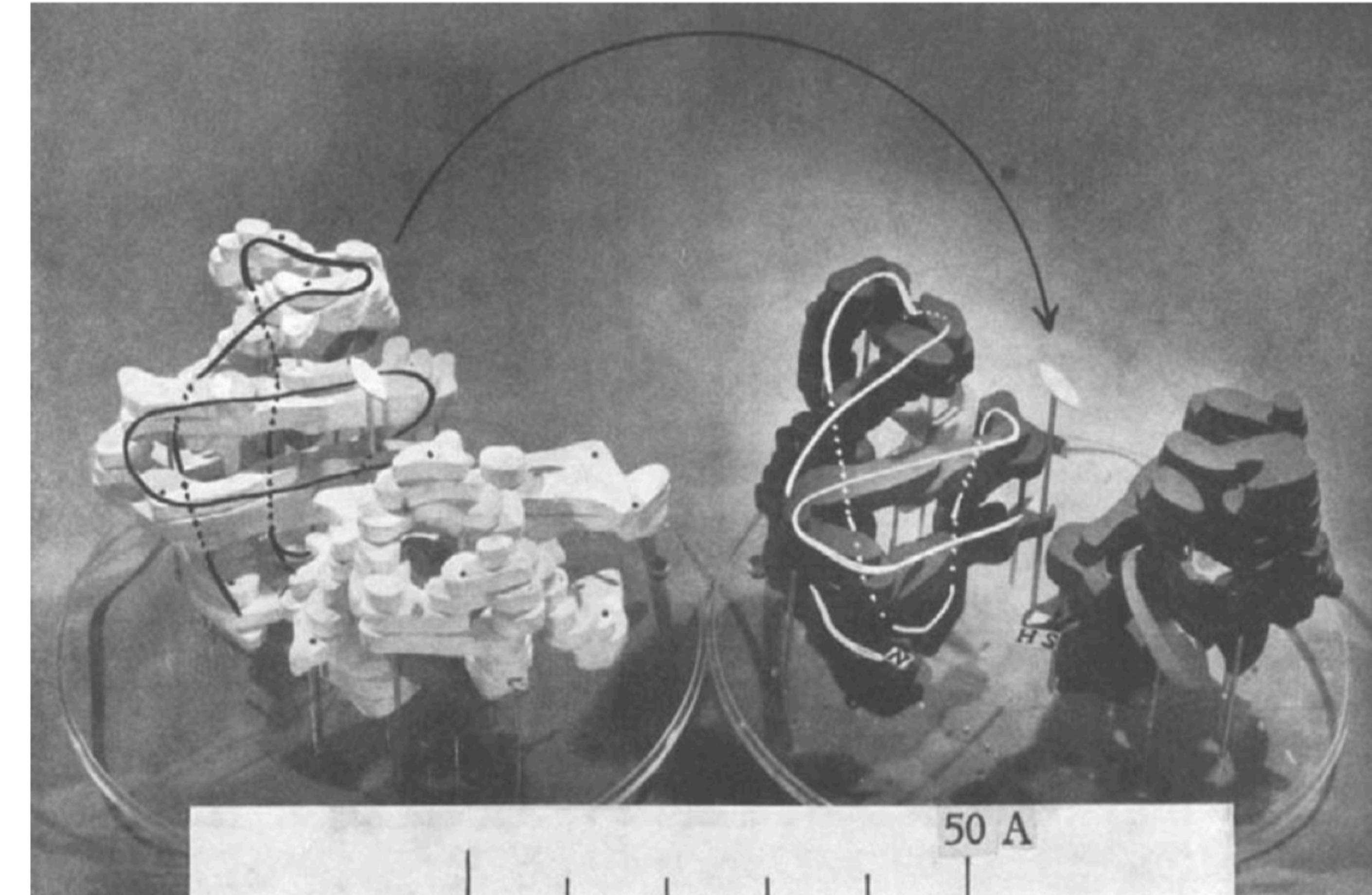
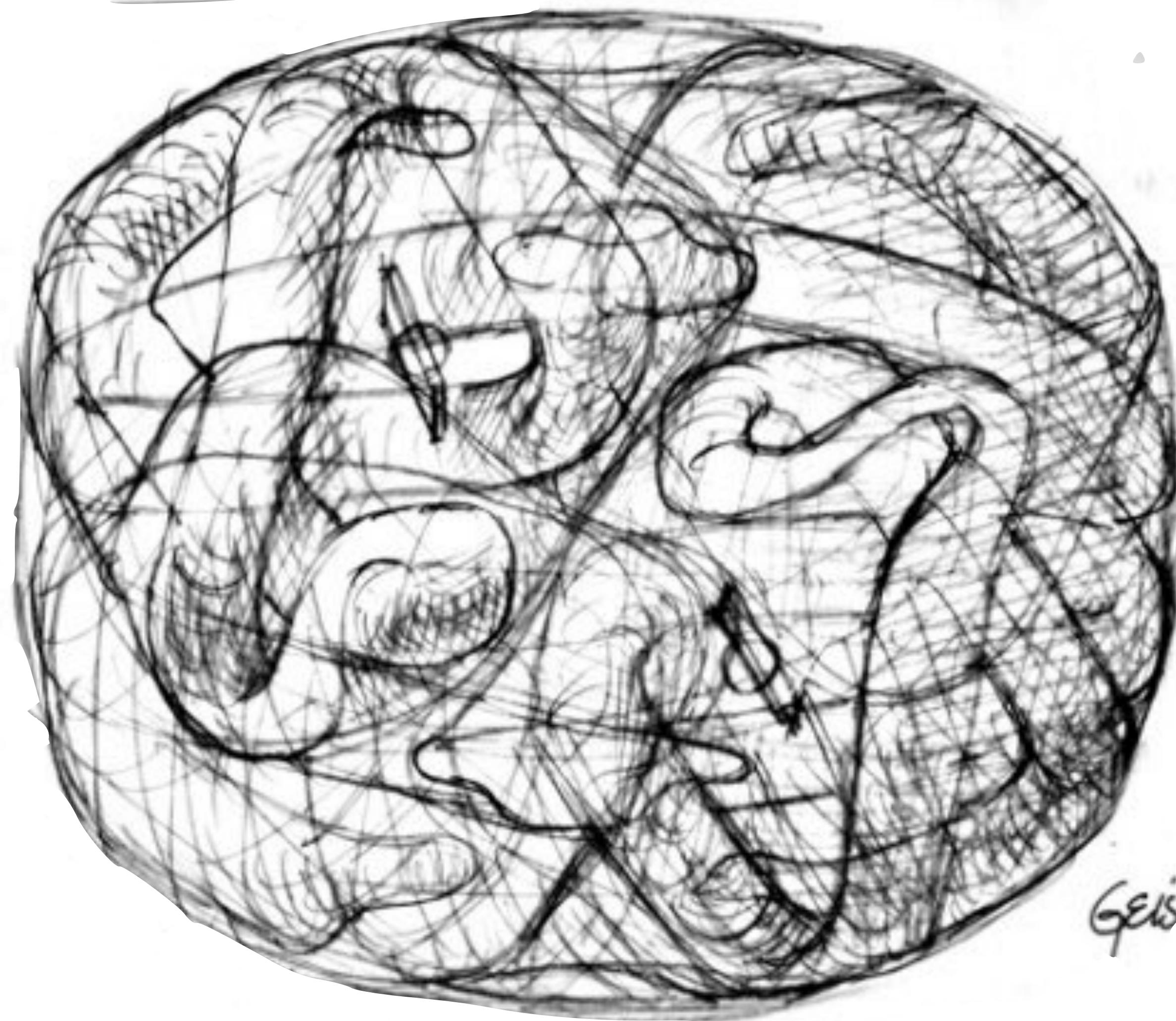
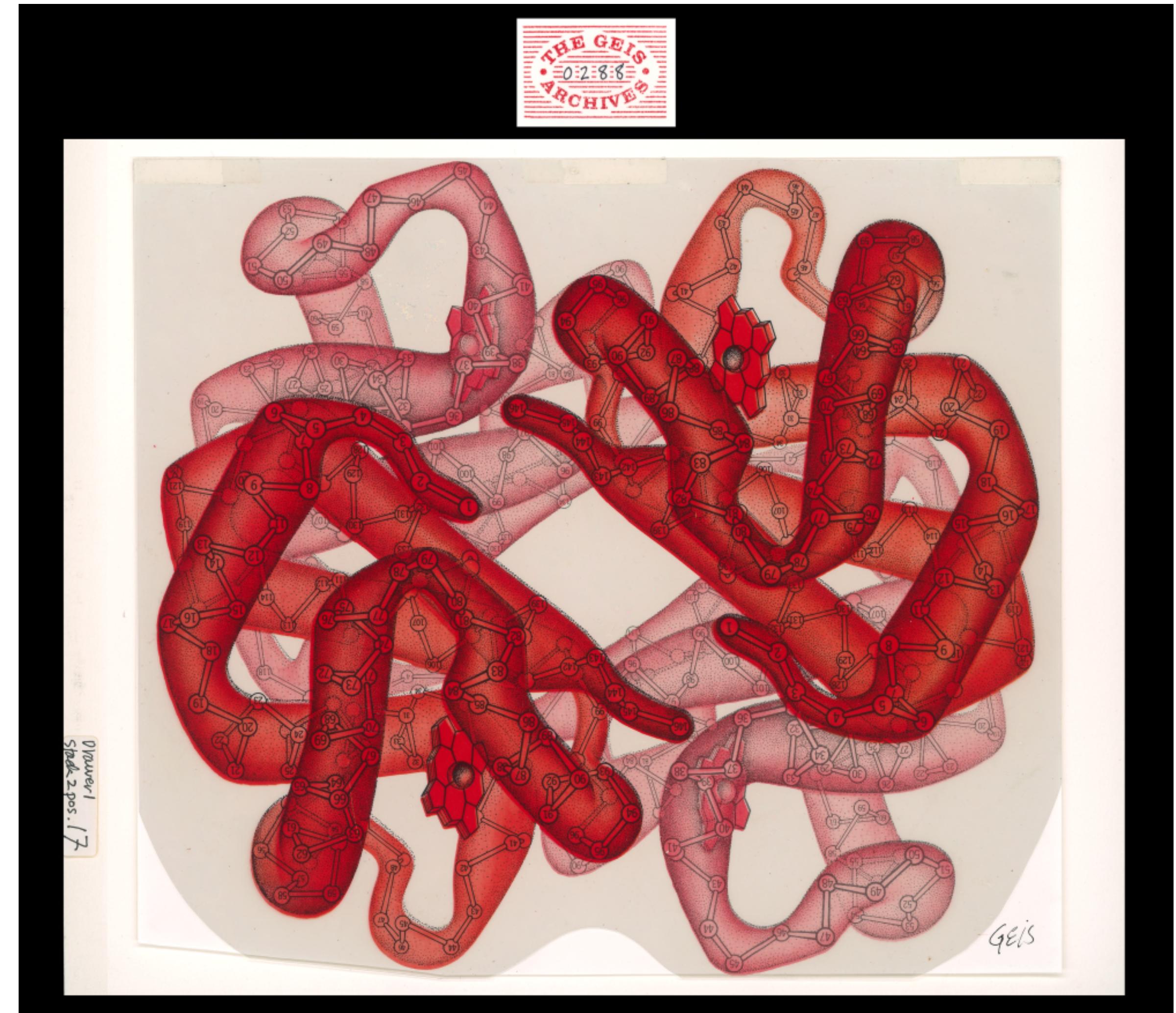
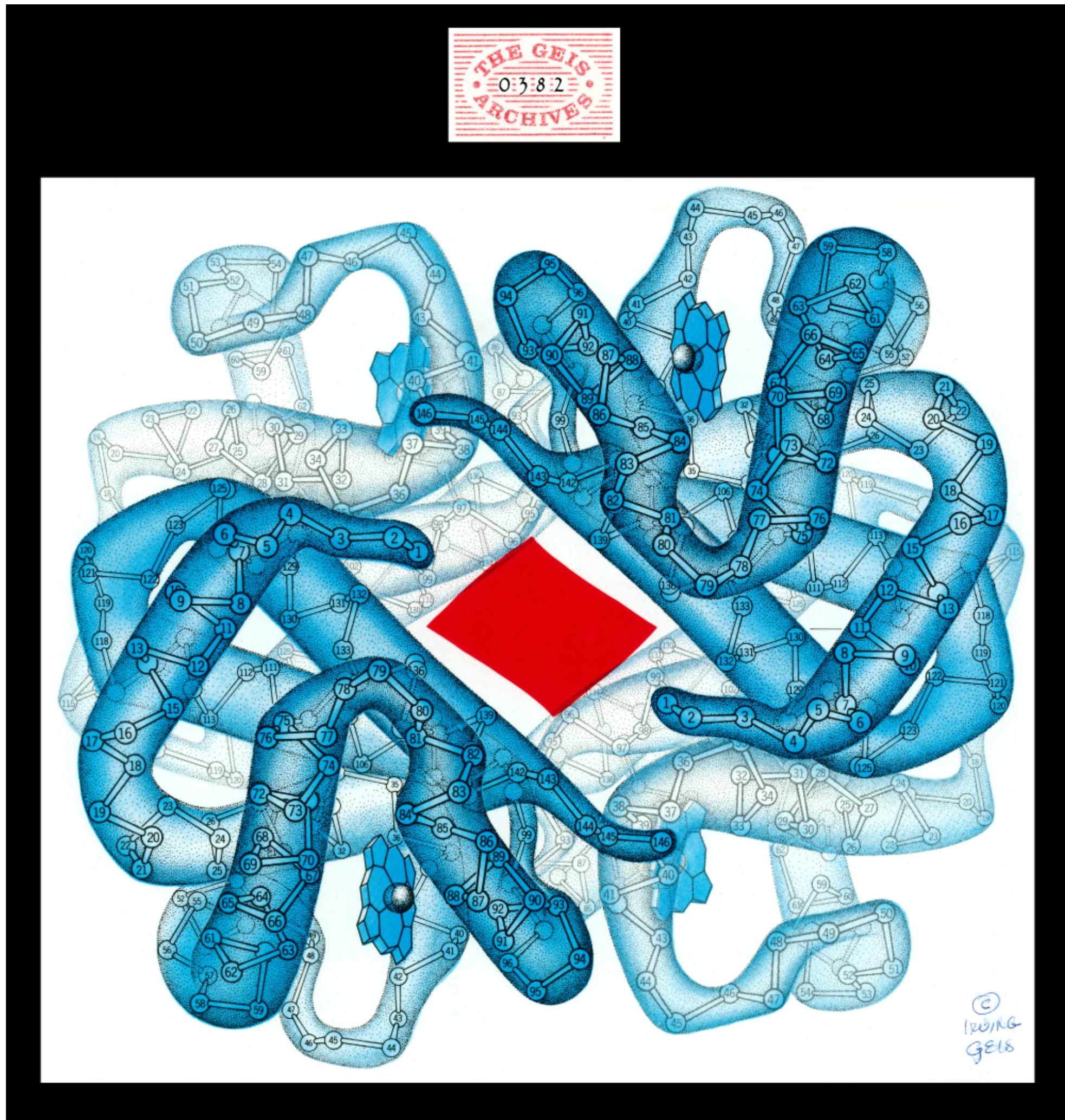


Fig. 6. Two pairs of chains symmetrically related by the dyad axis. The arrow shows how one pair is placed over the other to assemble the complete molecule



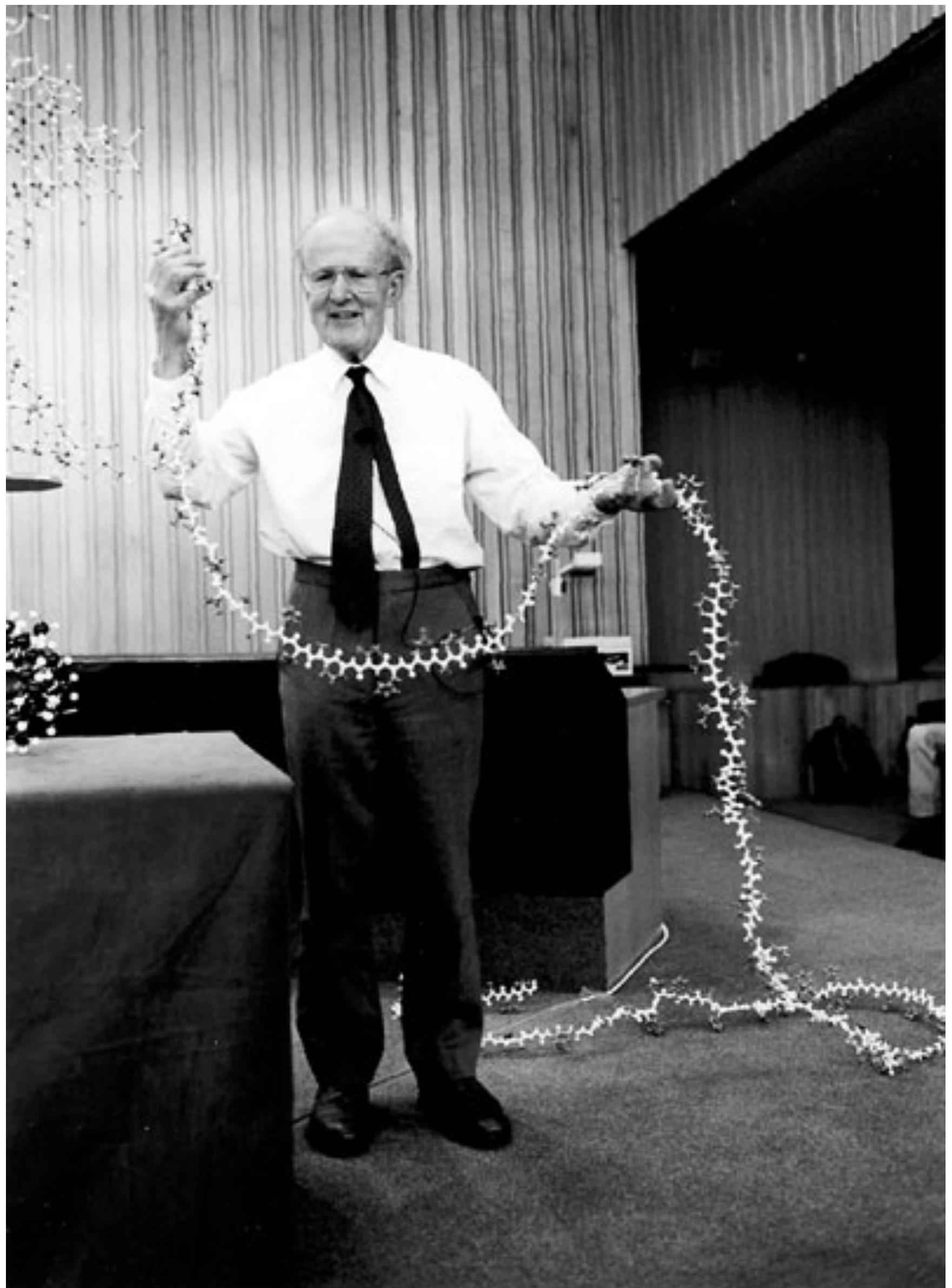




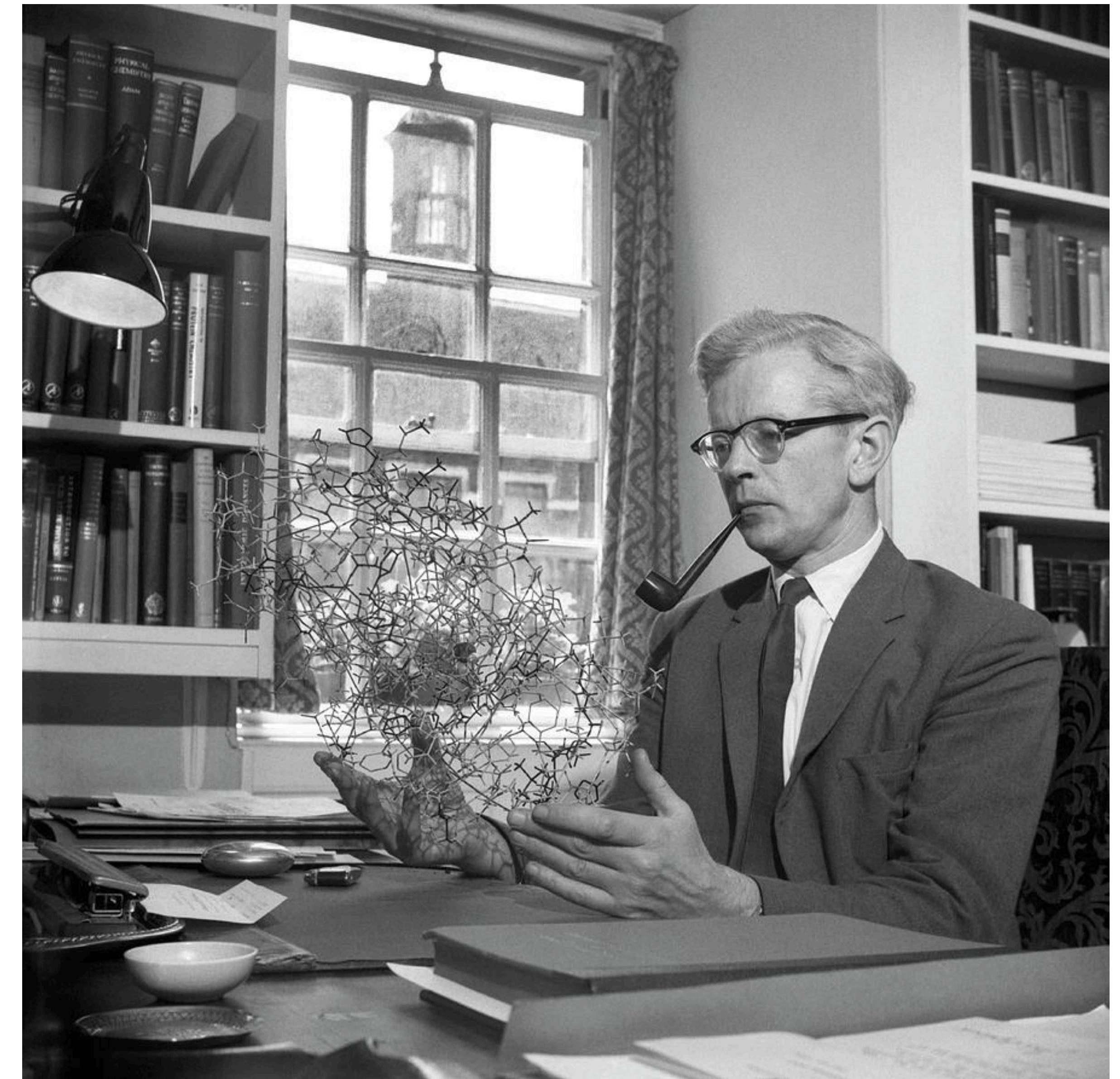
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AI

Prologue



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Blake1965

- Lysozyme was the first enzyme with resolved 3D structure.

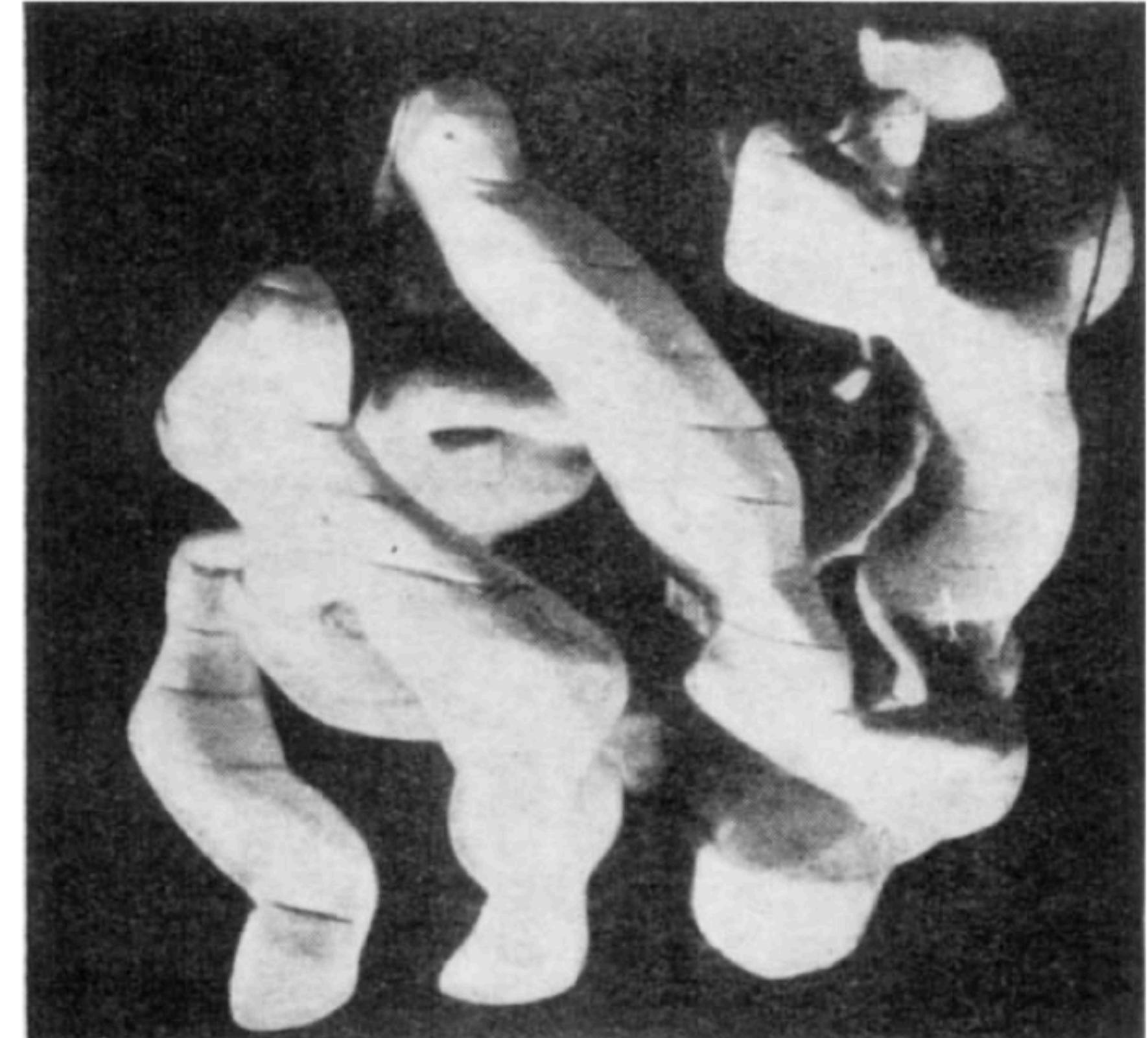
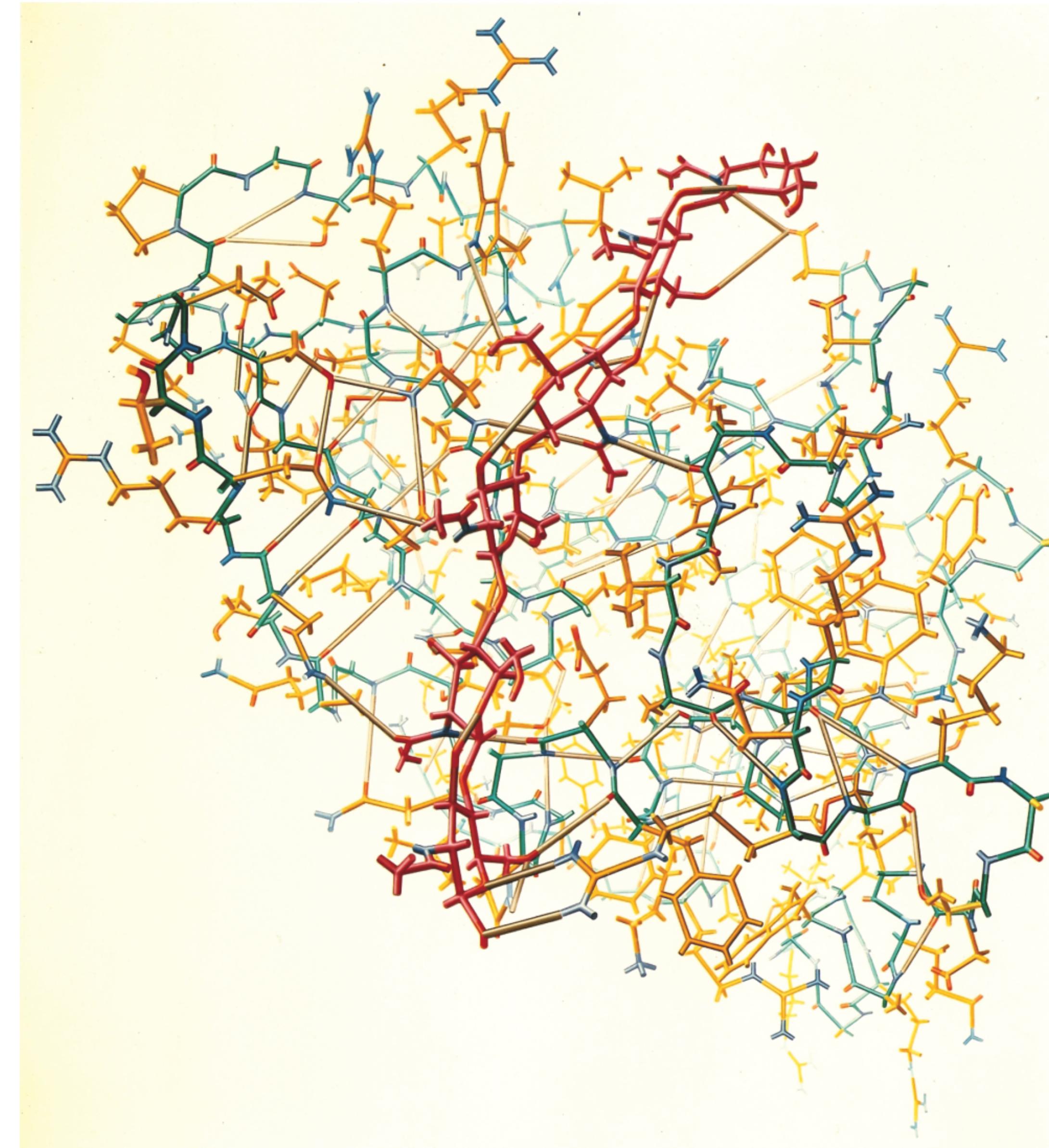
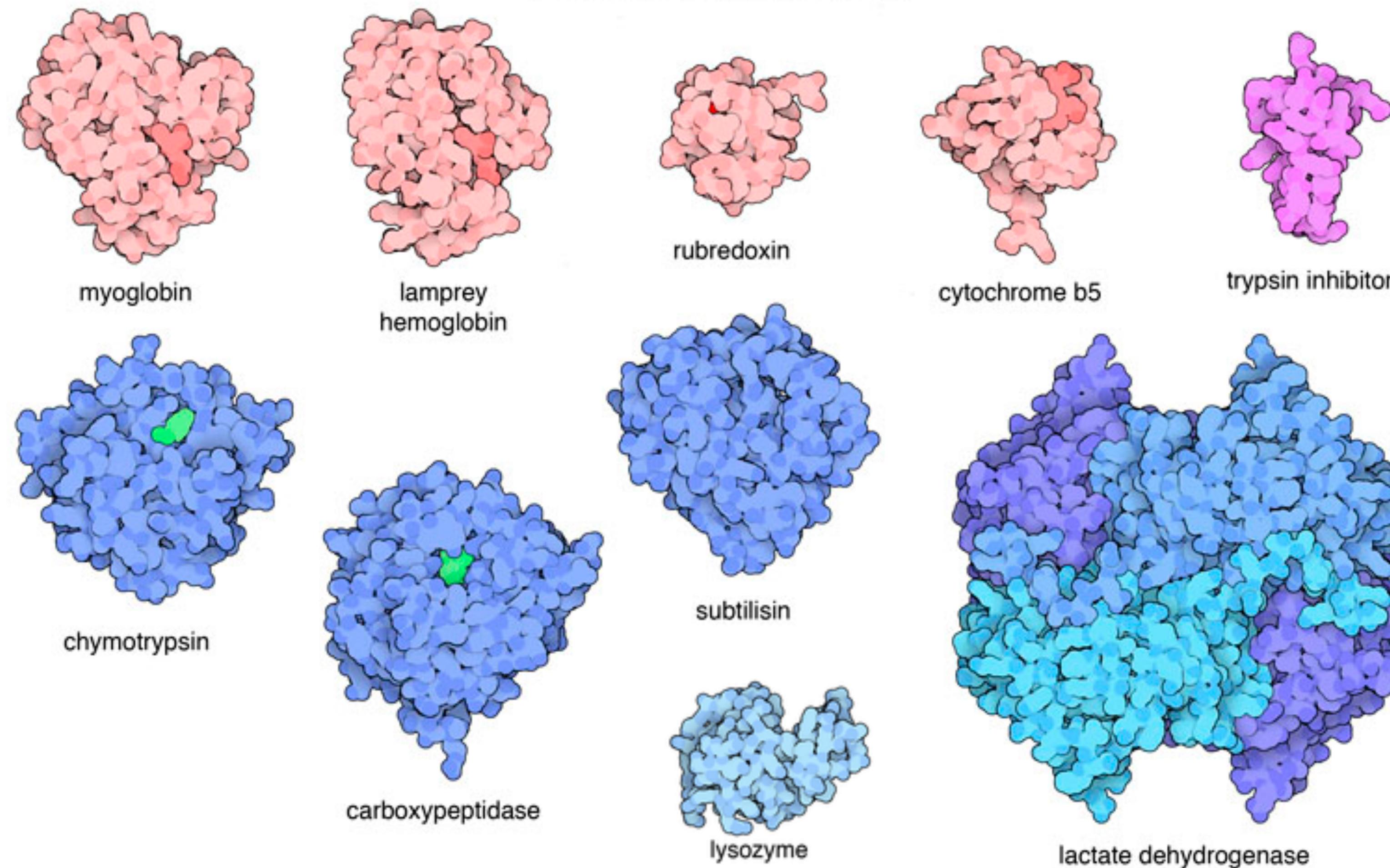
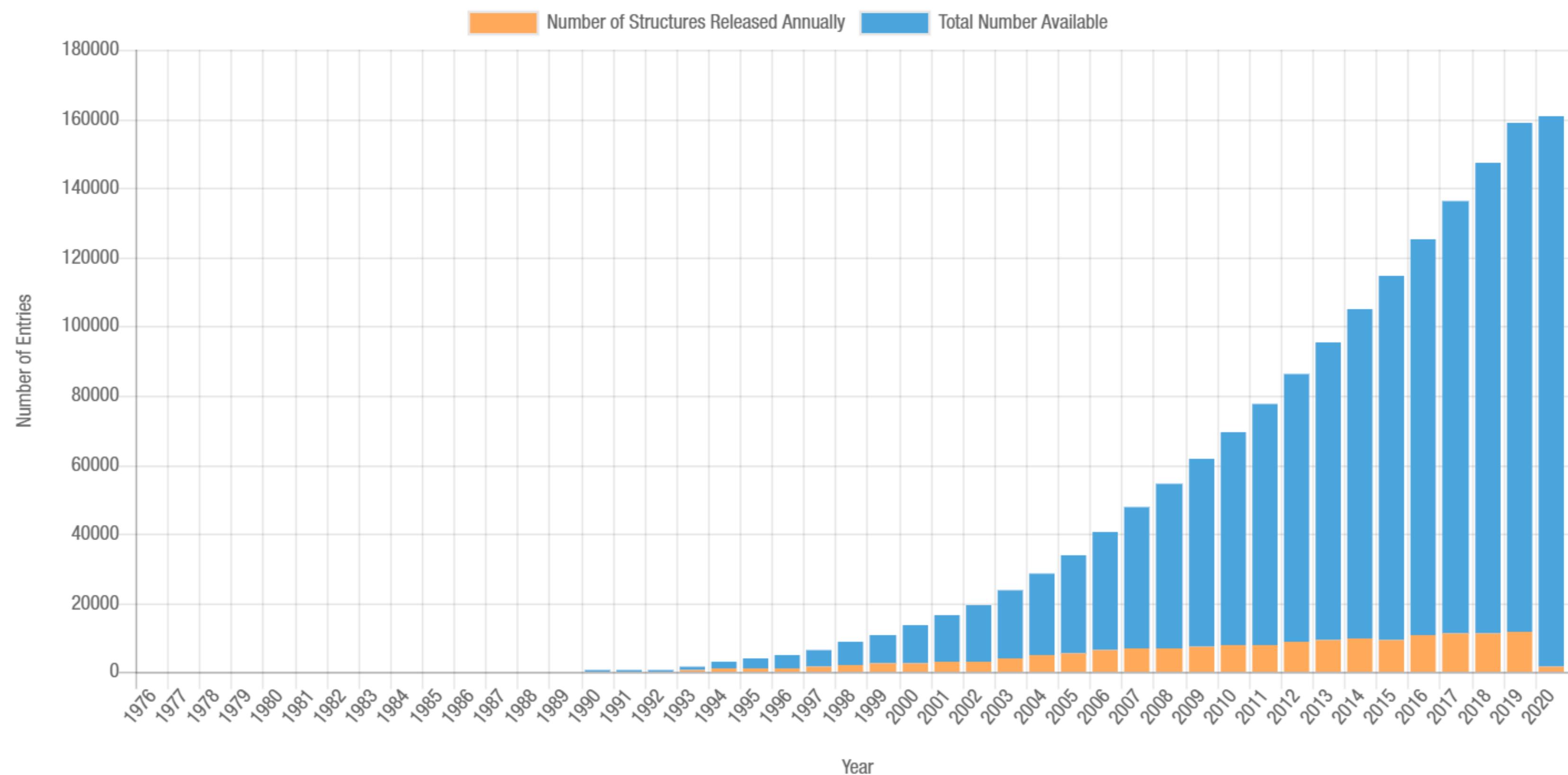


Fig. 1. Solid model of the lysozyme electron-density greater than about 0.5 electrons/ \AA^3 at 6 \AA resolution

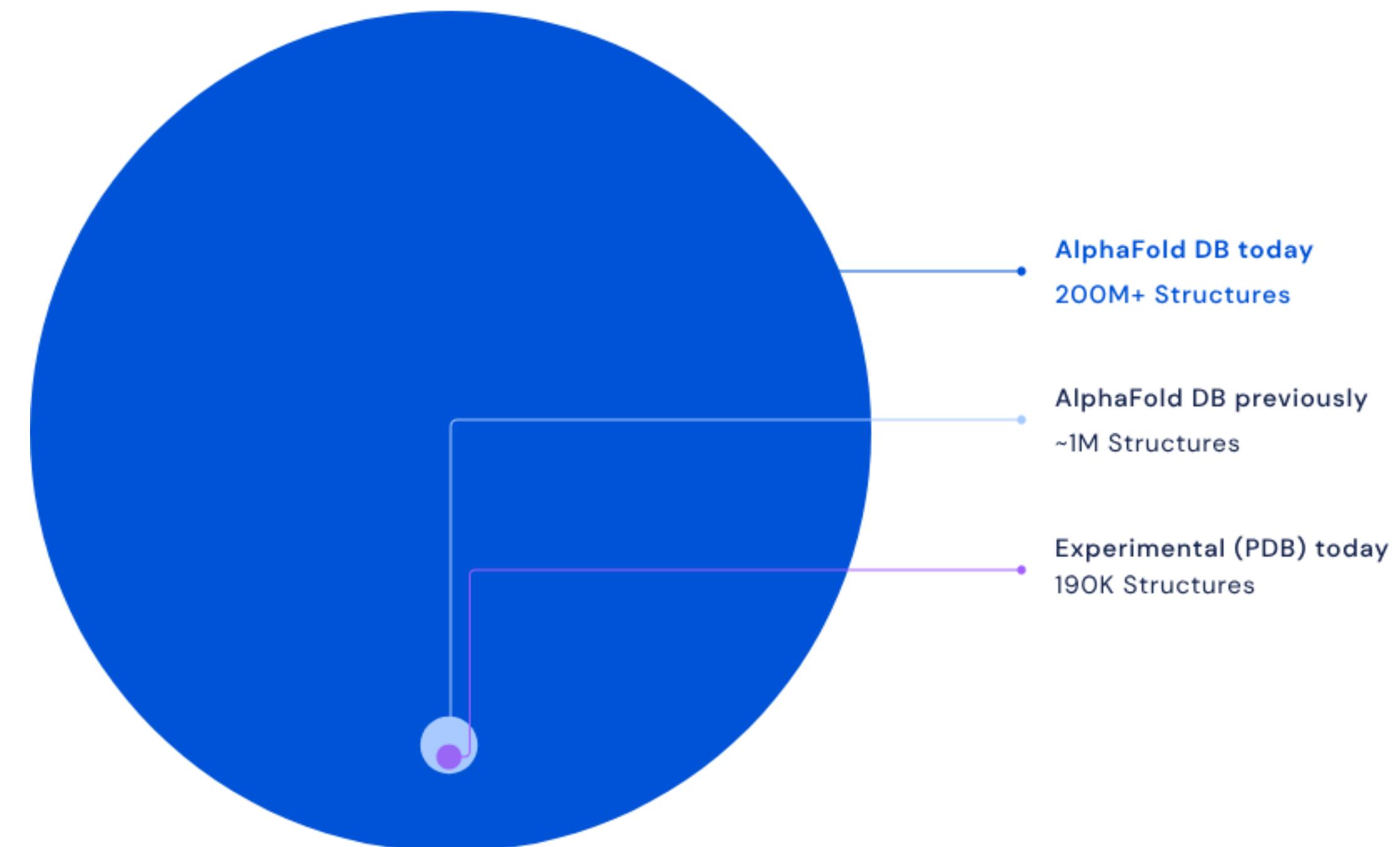


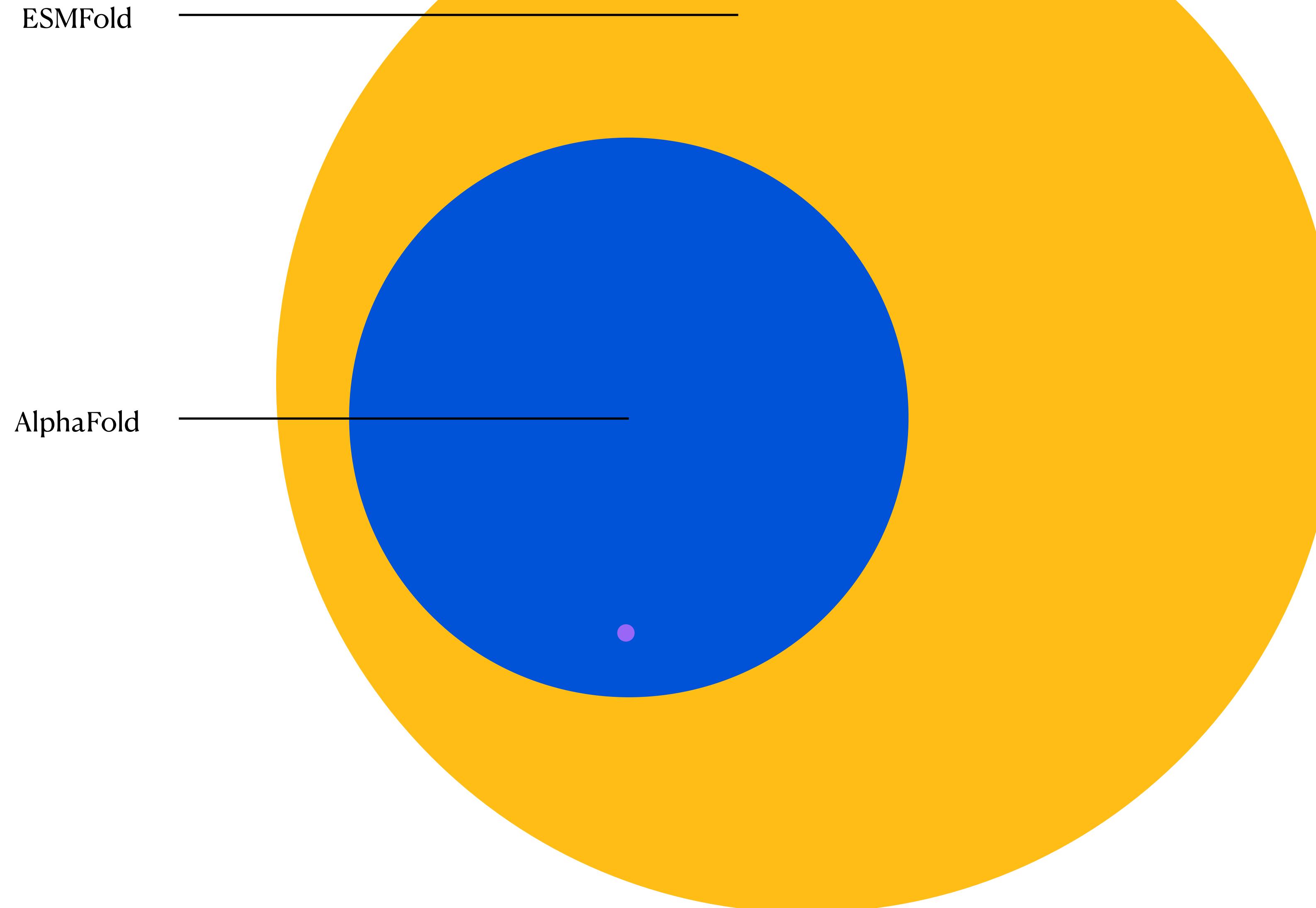
Protein Data Bank in 1973



A

Number of Protein Structures



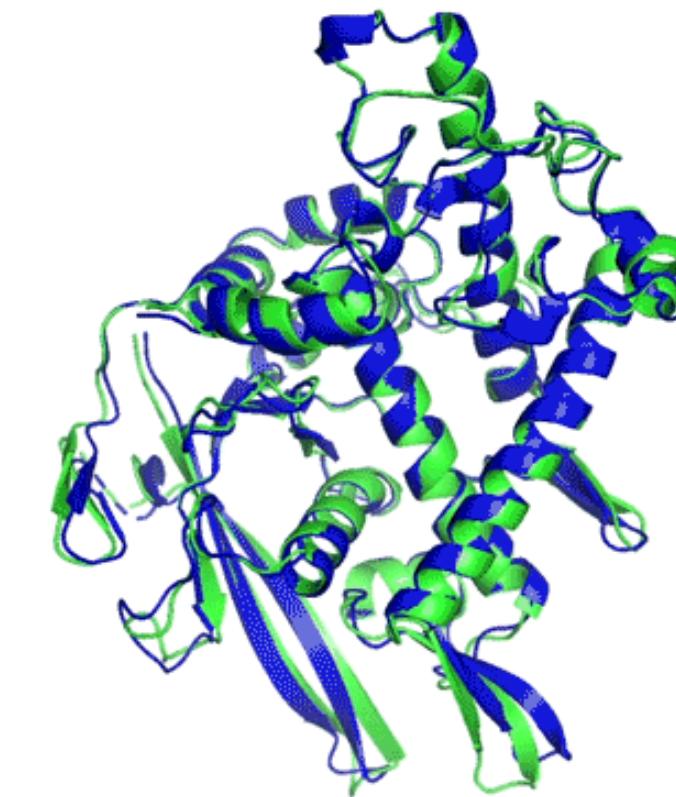


ESMFold

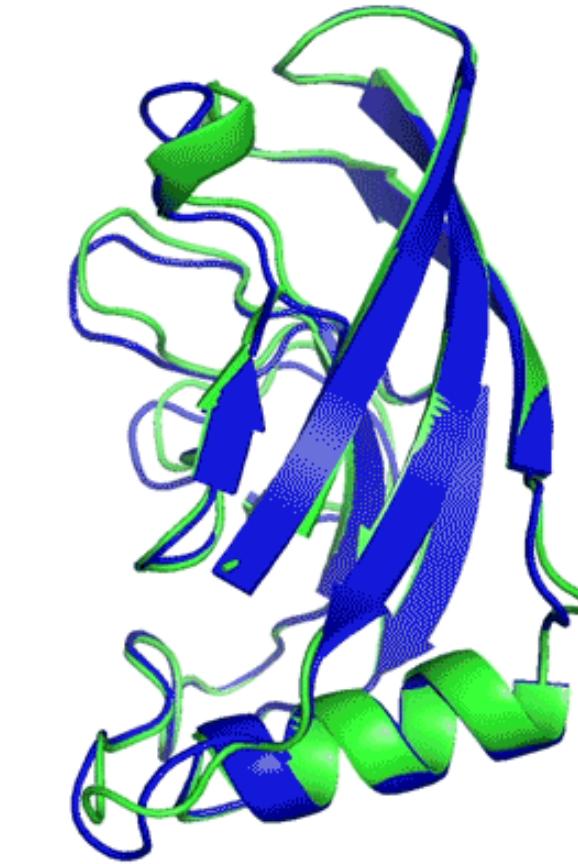
AlphaFold

AlphaFold

- AlphaFold is an AI system developed by Google DeepMind that predicts a protein's 3D structure from its amino acid sequence. It regularly achieves accuracy competitive with experiment.

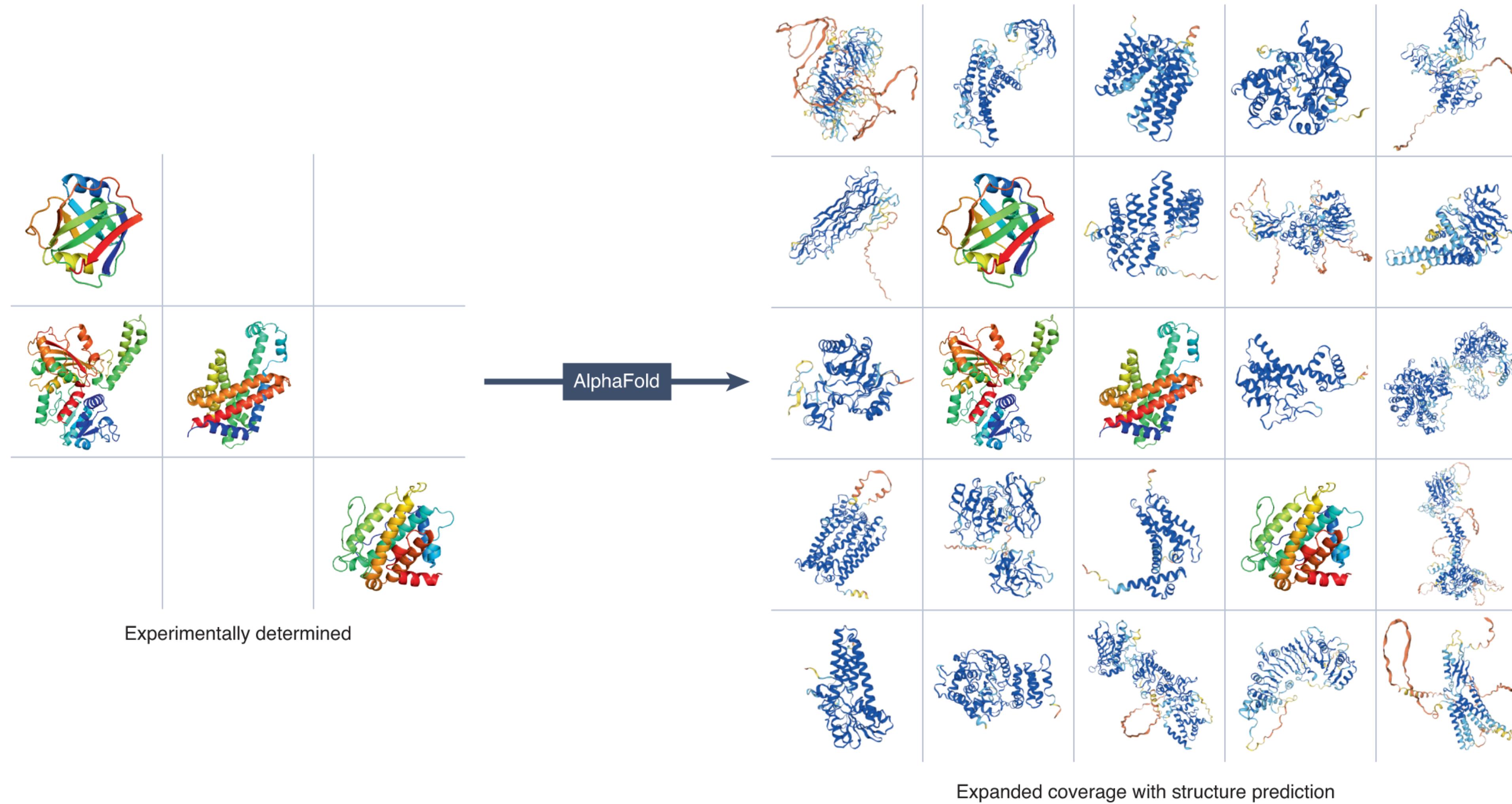


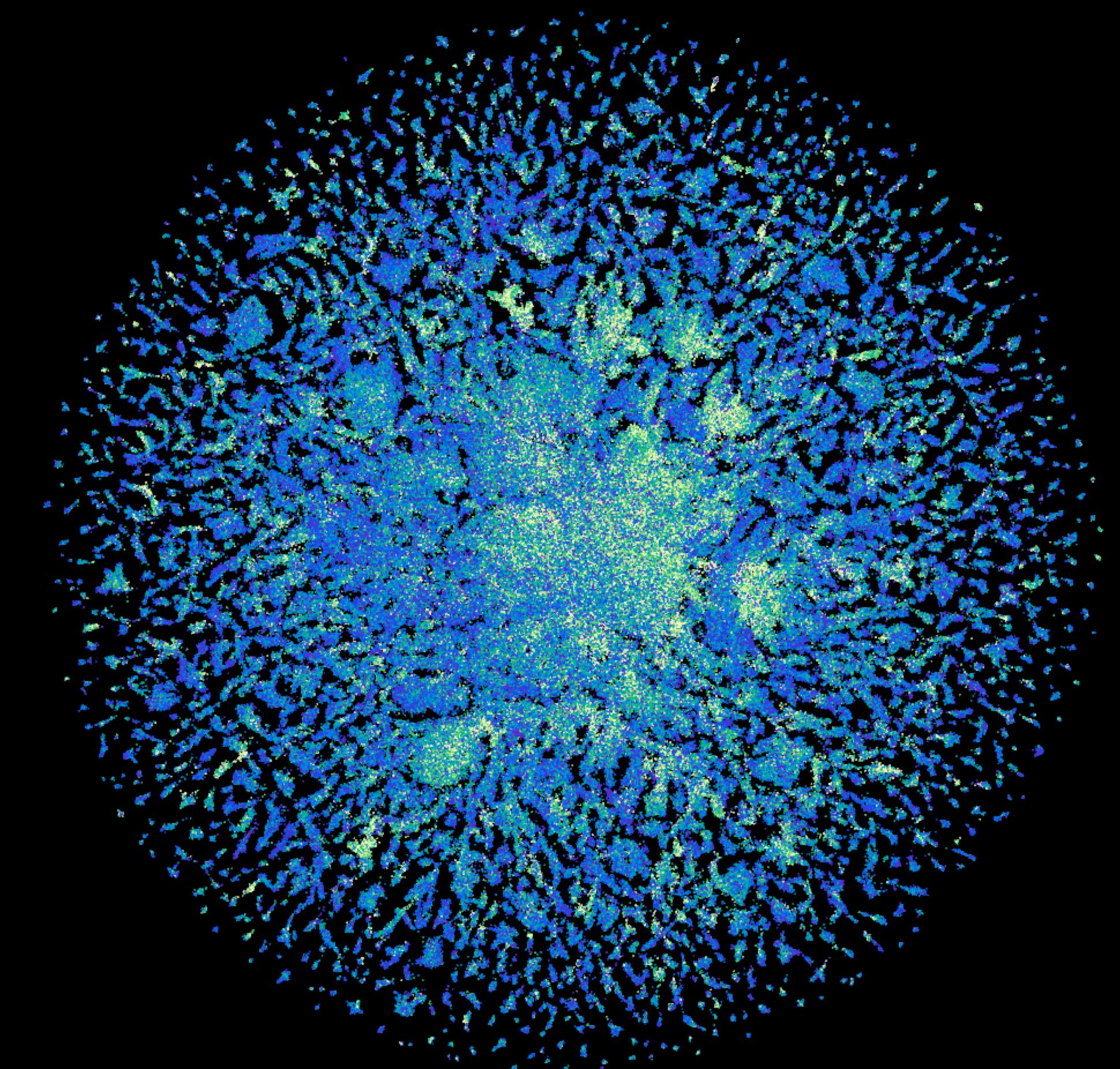
T1037 / 6vr4
90.7 GDT
(RNA polymerase domain)



T1049 / 6y4f
93.3 GDT
(adhesin tip)

● Experimental result
● Computational prediction





Drag to pan
Scroll to zoom in/out
Click to select a protein

Exploring 1 million out of 772M proteins

Unknown

Known



Drag to pan
Scroll to zoom in/out
Click to select a protein

Exploring 1 million out of 772M proteins
Unknown

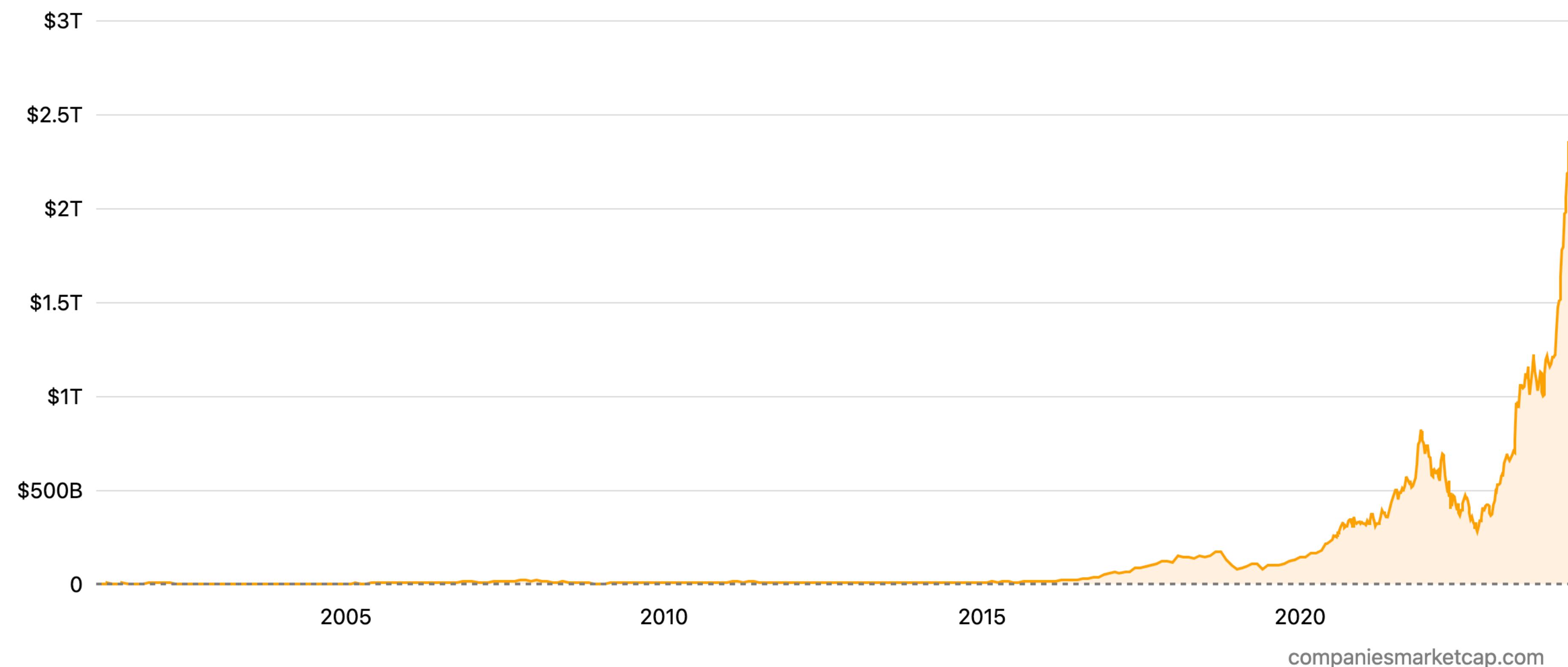
Known

Motivation 3

Is AI the new internet?

Rank	Name	Market Cap	Price	Today	Price (30 days)	Country
1	Microsoft MSFT	\$3.215 T	\$432.68	▲ 1.12%		USA
2	Apple AAPL	\$3.176 T	\$207.15	▲ 7.26%		USA
3	NVIDIA NVDA	\$2.974 T	\$120.91	▼ 0.71%		USA
4	Alphabet (Google) GOOG	\$2.190 T	\$178.19	▲ 0.88%		USA
5	Amazon AMZN	\$1.948 T	\$187.23	▲ 0.09%		USA
6	Saudi Aramco 2222.SR	\$1.820 T	\$7.53	▼ 0.53%		S. Arabia
7	Meta Platforms (Facebook) META	\$1.287 T	\$507.47	▲ 0.97%		USA
8	Berkshire Hathaway BRK-B	\$881.22 B	\$408.50	▼ 0.56%		USA
9	TSMC TSM	\$859.49 B	\$165.71	▼ 1.46%		Taiwan
10	Eli Lilly LLY	\$822.87 B	\$865.82	▲ 0.09%		USA

Market cap history of NVIDIA from 2001 to 2024



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Aptos (Body) 11 I U A ...

Create content with Copilot

draft a proposal from yesterday's meeting notes

To create a game like the one shown in the image (similar to the classic "Breakout" or "Arkanoid" game) in Python, you can use the `pygame` library. Below is a simple implementation of the game. You need to have `pygame` installed, which you can do by running `pip install pygame`.

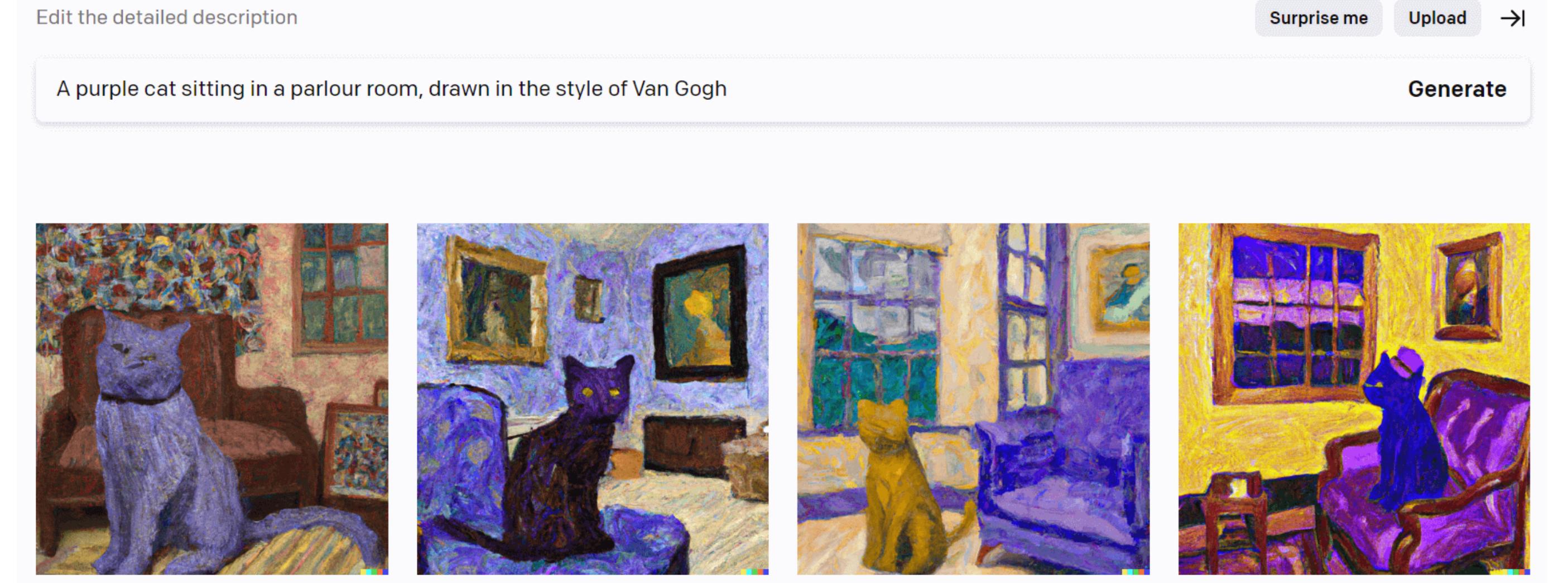
Here is a basic example code:

```
python
import pygame
import sys
import random

# Initialize Pygame
pygame.init()

# Set up the screen
screen_width = 800
screen_height = 600
screen = pygame.display.set_mode((screen_width, screen_height))
pygame.display.set_caption("Breakout")
```

I want to make this game. code this in python.

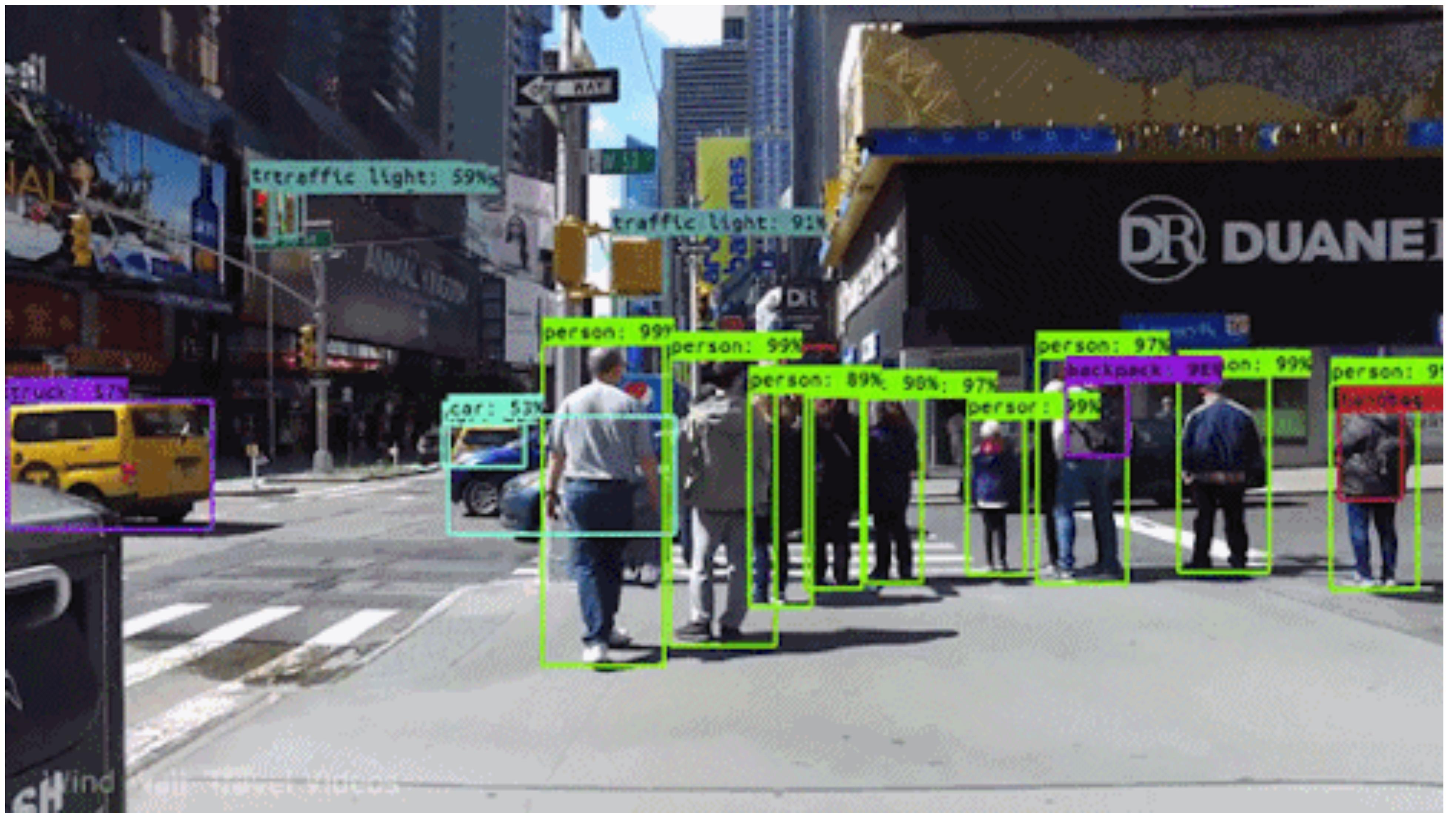


can you critique my final design to make it more accurate?

Sure, I can critique the design of your paper airplane. Here are a few things you can do to improve it:

- The wings are too small. This will make the airplane unstable in flight.
- The tail is too small. This will make it difficult to control the airplane.
- The folds are not sharp enough. This will make the airplane fly less smoothly.
- The paper is too light. This will make the airplane more susceptible to wind.

View other drafts



Chapter 1: History of AI