Nobel Prizes in Sciences 2024 Roundup

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Science Circle

Medicine

Victor Ambros and Gary Ruvkun

Victor Ambros. Ill. Niklas Elmehed © Nobel Prize Outreach

Gary Ruvkun. Ill. Niklas Elmehed © Nobel Prize Outreach

for the discovery of microRNA and its role in post-transcriptional gene regulation

Medicine

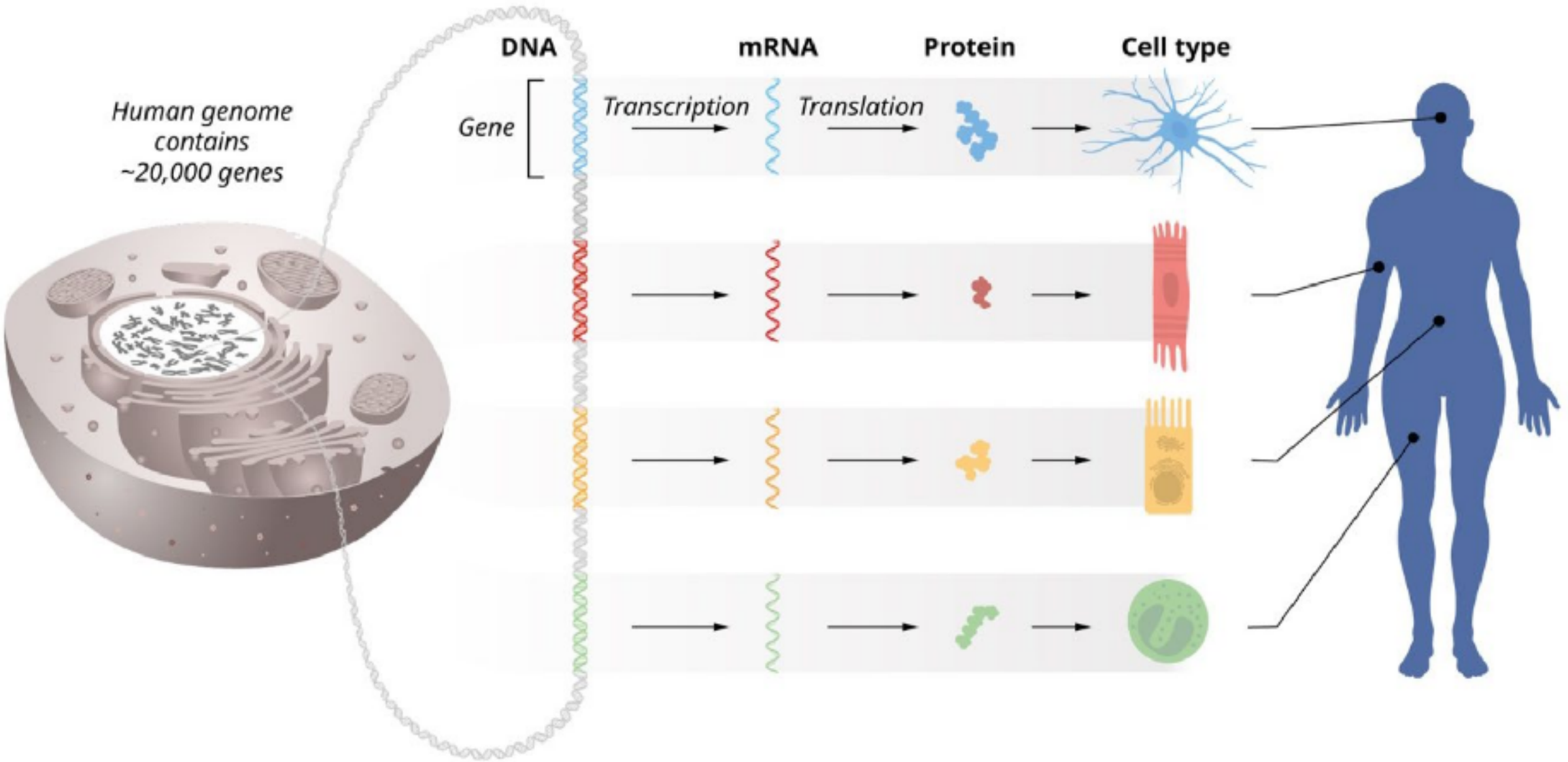


Figure 1. Regulation of cell-type specific functions.
Every cell contains an identical set of chromosomes and therefore, the exact same set of genes. Cell-type specific functions arise when only a select subset of these genes is activated within each cell type.

Medicine

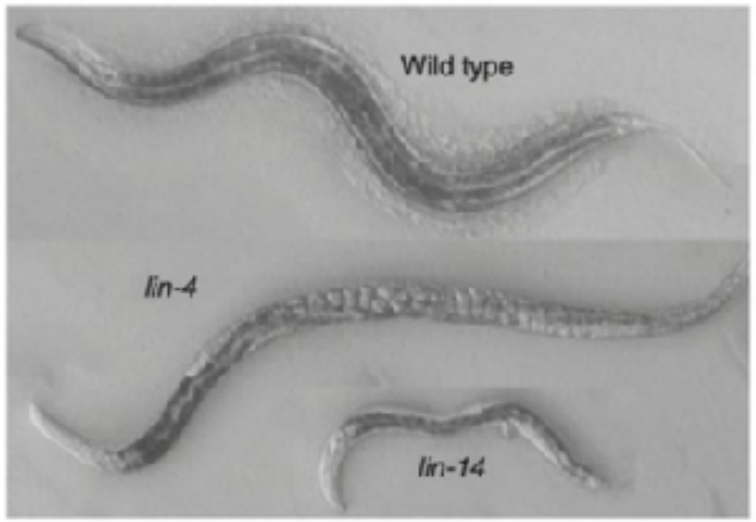


Figure 2. Heterochronic worm mutants with developmental defects. Nematode *lin-4* and *lin-14* mutants with disrupted animal development. Mutant *lin-4* worms reiterate developmental programs for cell lineages to accumulate internal eggs without forming a vulva, while *lin-14* mutants are small and lack larval development. Worms adapted from (Ambros, 2008)

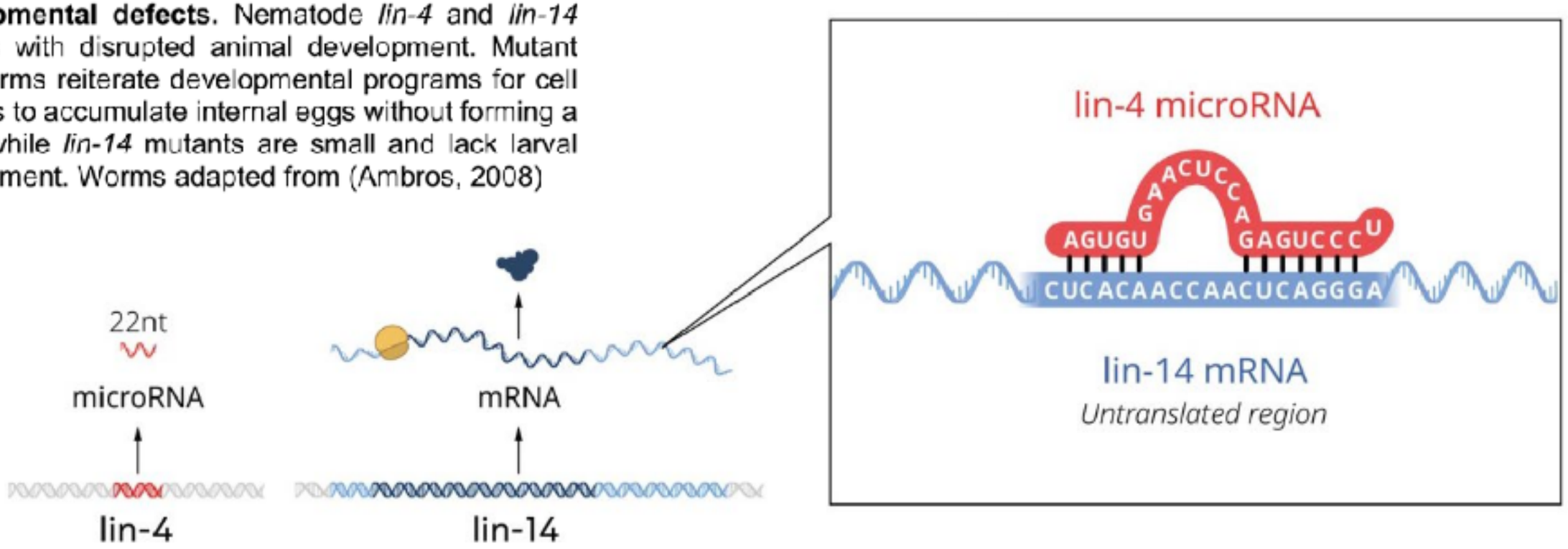


Figure 4. Complementary sequence elements in *lin-4* and *lin-14* RNA. Upon comparing cloned sequences for *lin-4* and *lin-14*, it was revealed that the short 22 nt *lin-4* RNA had partial complementarity to repeated elements in the *lin-14* 3'UTR.

Medicine

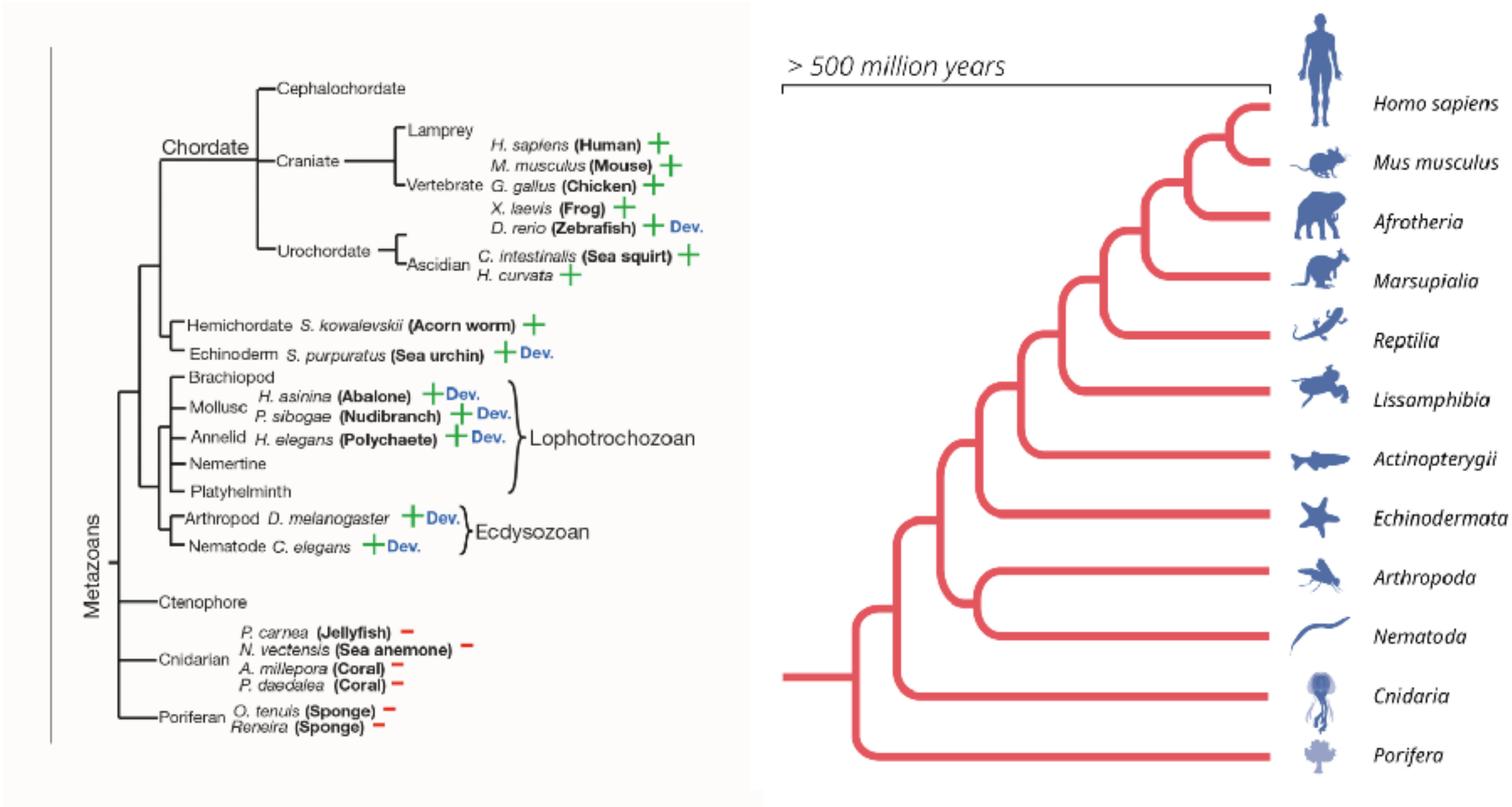


Figure 5. Evolutionary conservation of the *let-7* RNA expression and microRNAs more generally. Left: An evolutionary tree of metazoans, highlighting the branches of the tree with a detectable *let-7* microRNA expression (+) or where no let-7 expression was detected (-). Species with similar developmental pattern of let-7 RNA expression is (no let-7 in early stages; but let-7 expression by adulthood) are indicated by 'Dev.'. (Pasquinelli et al., 2000). Right: MicroRNA genes have evolved and expanded within the genomes of multicellular organisms for over 500 million years.

Medicine 2006 Flashback

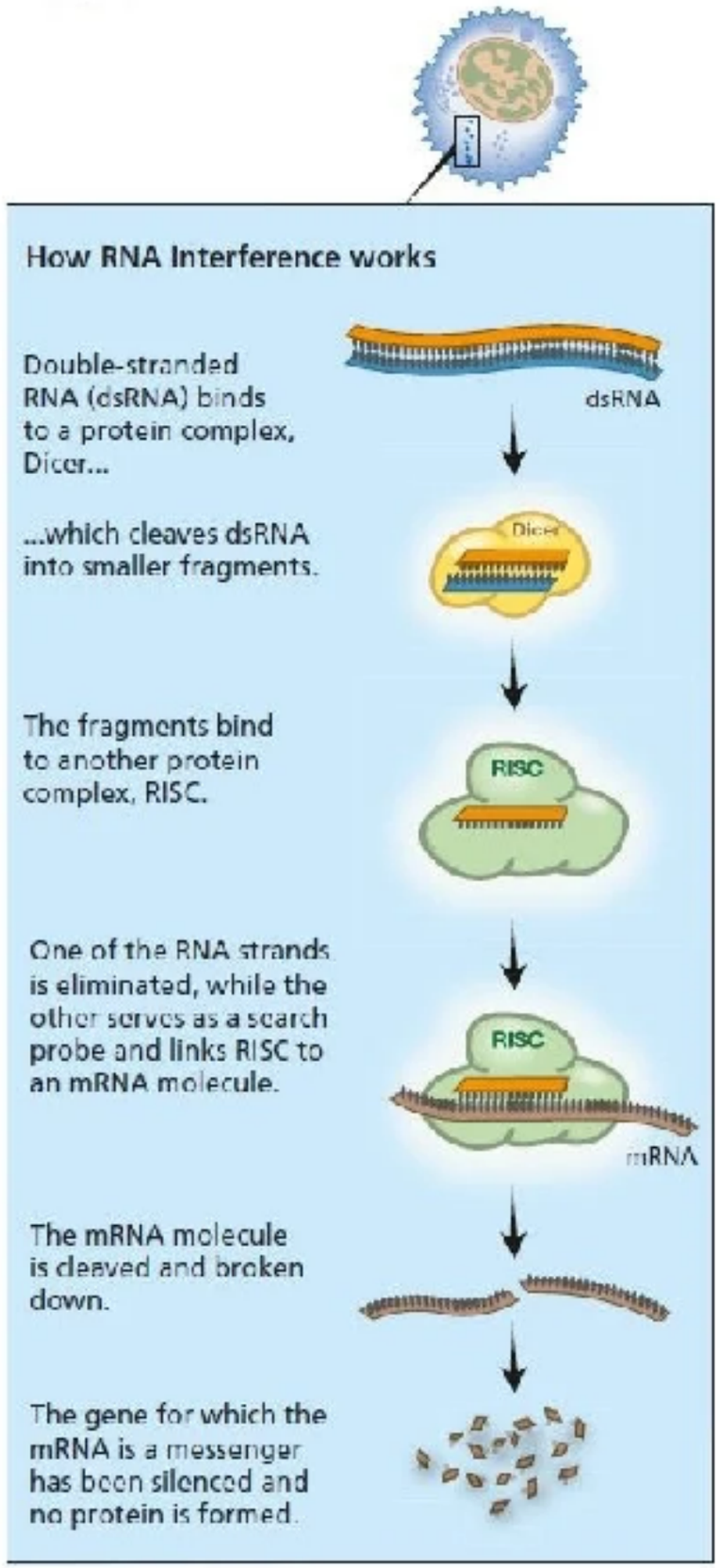
attempting to make the flower MORE RED!

The Nobel Prize in Physiology or Medicine 2006 was awarded jointly to Andrew Z. Fire and Craig C. Mello "for their discovery of RNA interference - gene silencing by double-stranded RNA"

Photo: L. Cicero
Andrew Z. Fire

Photo: J. Mottern
Craig C. Mello

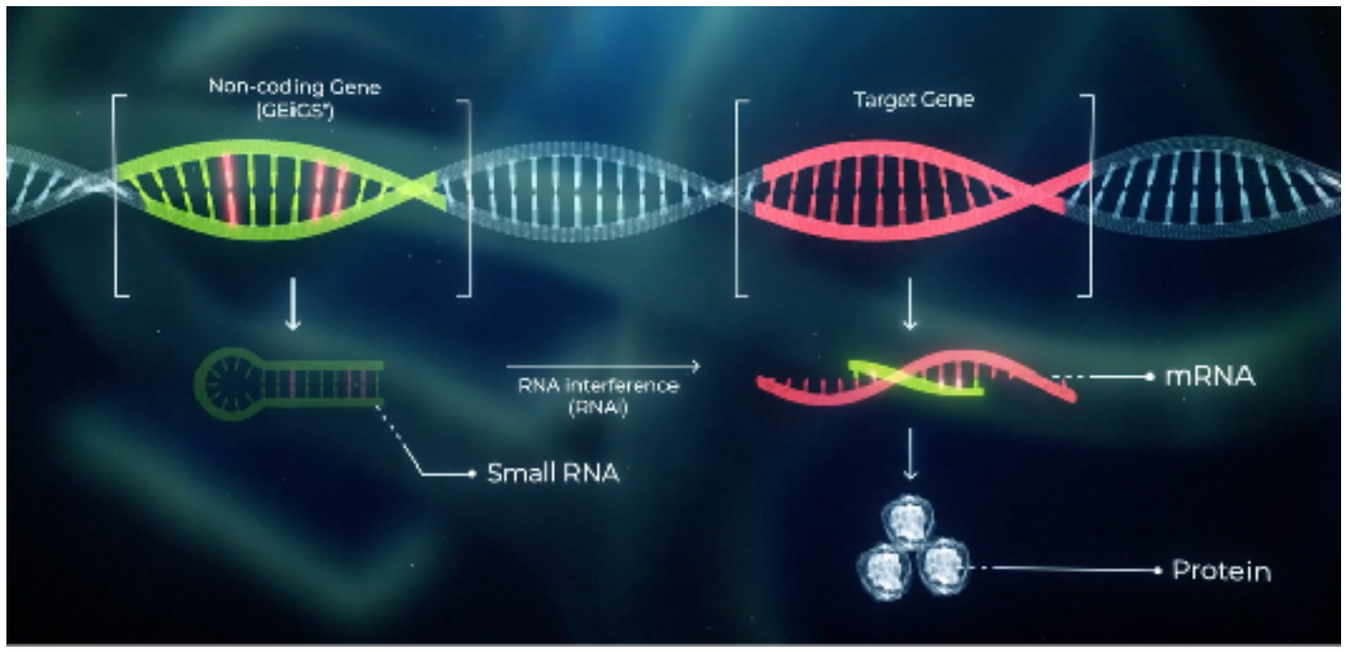
C. elegans



Medicine

Implications

- Understanding expression at fundamental level
- Reminder that our definition of a “gene” is not limited to things that make proteins
- Lab tool for controlling expression
- Useful in plant and human biotechnology



Tropic

A way to enhance plants for disease resistance via CRISPR

Physics

John J. Hopfield and Geoffrey E. Hinton

John Hopfield. Ill. Niklas Elmehed © Nobel Prize Outreach

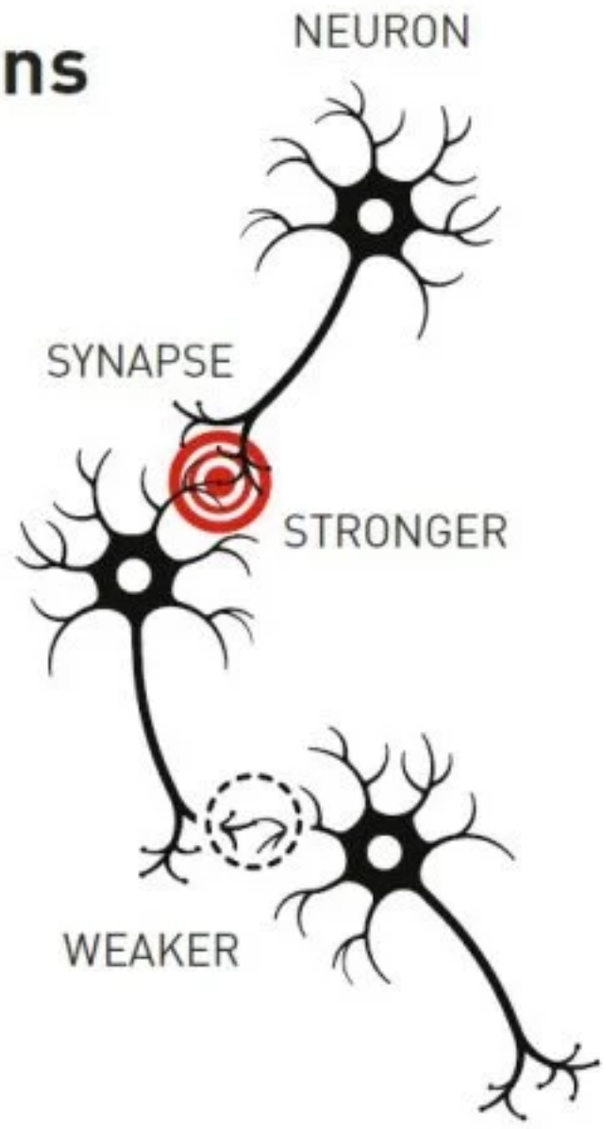
Geoffrey Hinton. Ill. Niklas Elmehed © Nobel Prize Outreach

for foundational discoveries and inventions that enable machine learning with artificial neural networks

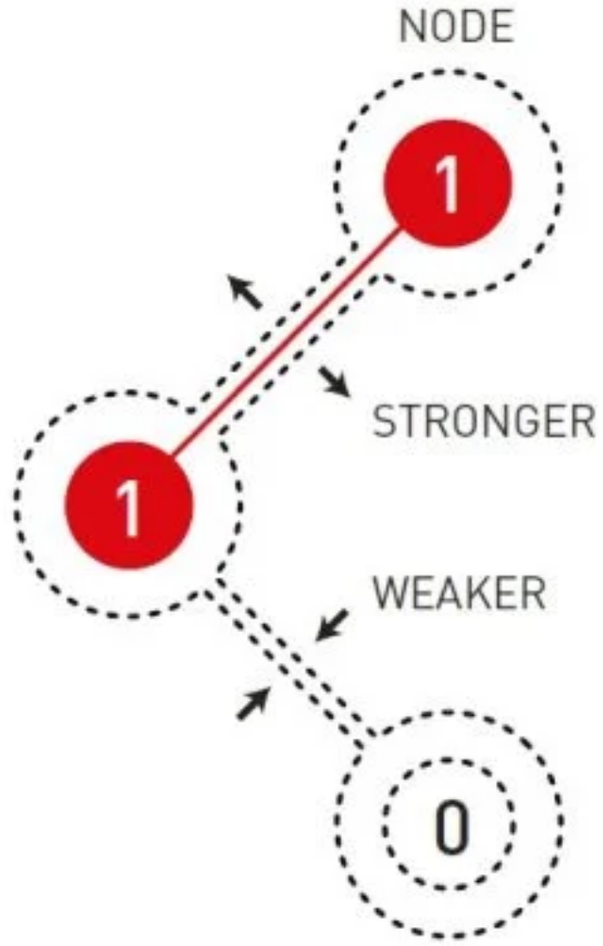
Physics

Natural and artificial neurons

The brain's neural network is built from living cells, neurons, with advanced internal machinery. They can send signals to each other through the synapses. When we learn things, the connections between some neurons get stronger, while others get weaker.



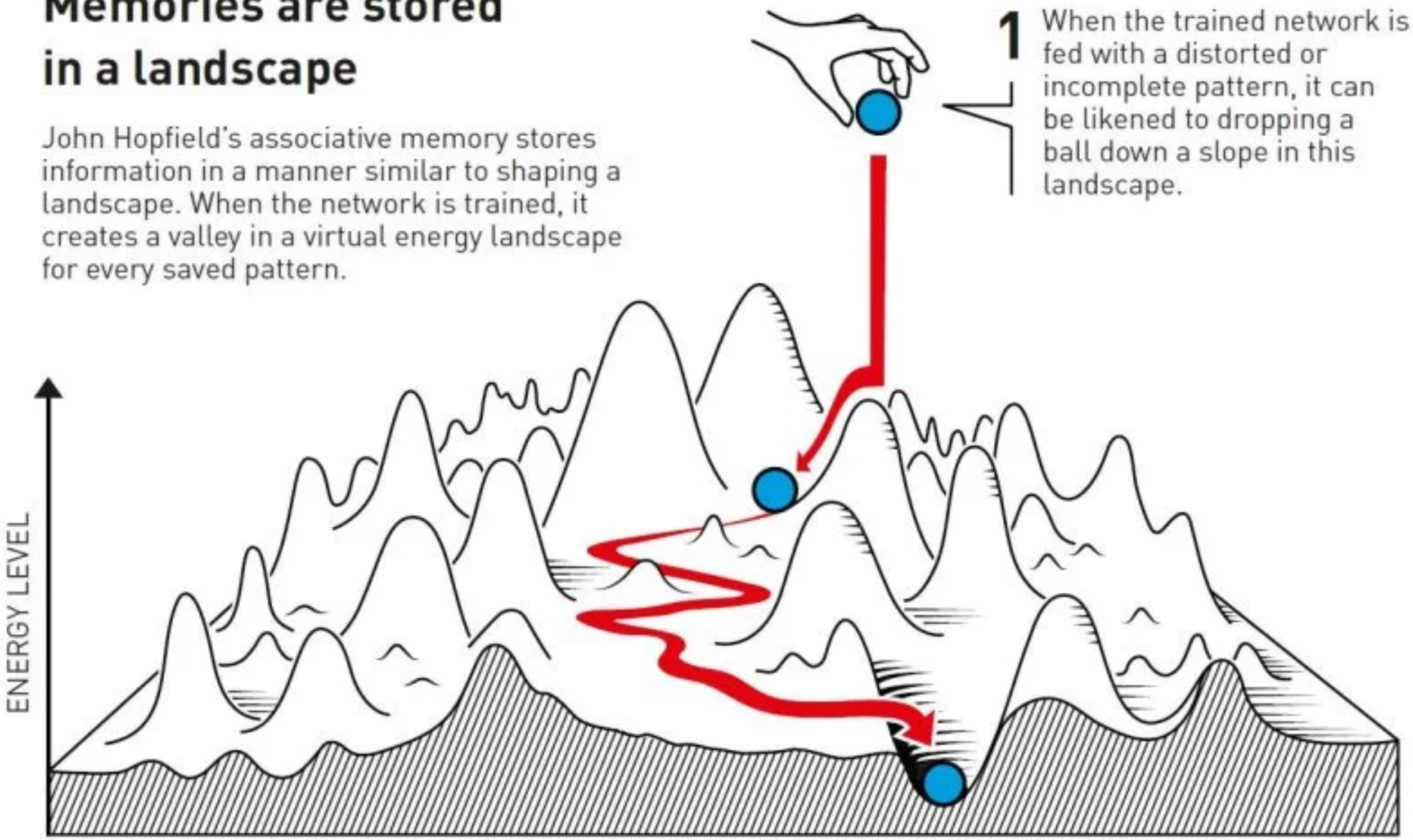
Artificial neural networks are built from nodes that are coded with a value. The nodes are connected to each other and, when the network is trained, the connections between nodes that are active at the same time get stronger, otherwise they get weaker.



Physics

Memories are stored in a landscape

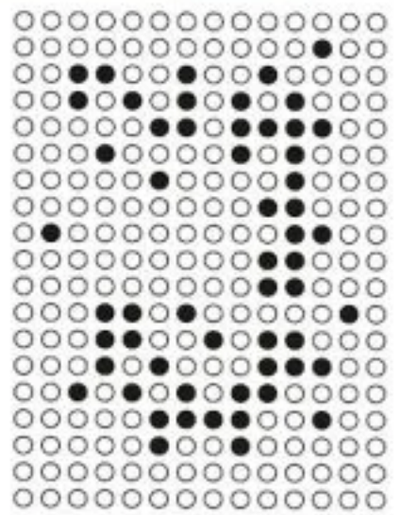
John Hopfield's associative memory stores information in a manner similar to shaping a landscape. When the network is trained, it creates a valley in a virtual energy landscape for every saved pattern.



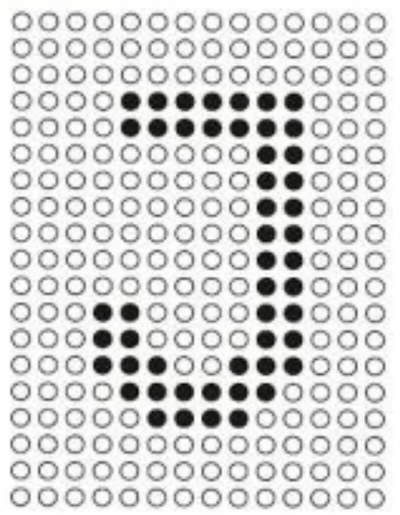
1 When the trained network is fed with a distorted or incomplete pattern, it can be likened to dropping a ball down a slope in this landscape.

2 The ball rolls until it reaches a place where it is surrounded by uphills. In the same way, the network makes its way towards lower energy and finds the closest saved pattern.

INPUT PATTERN

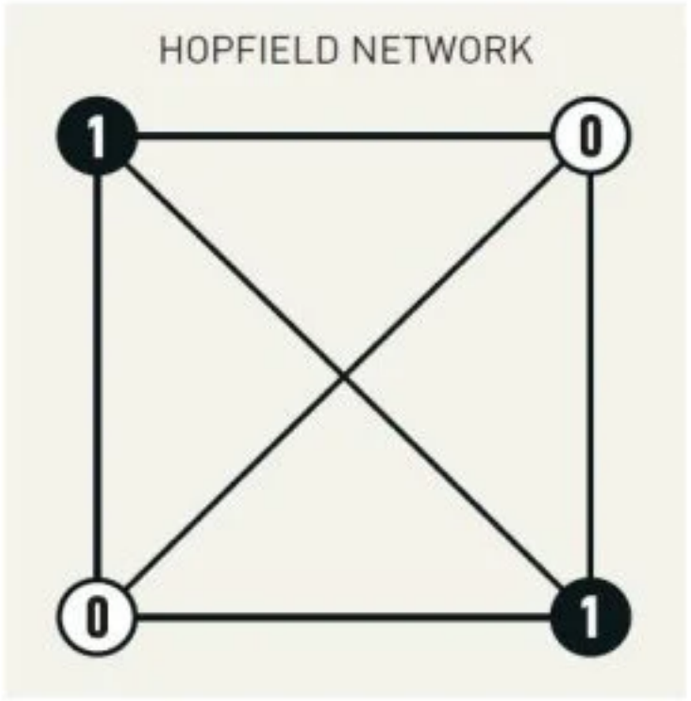


SAVED PATTERN

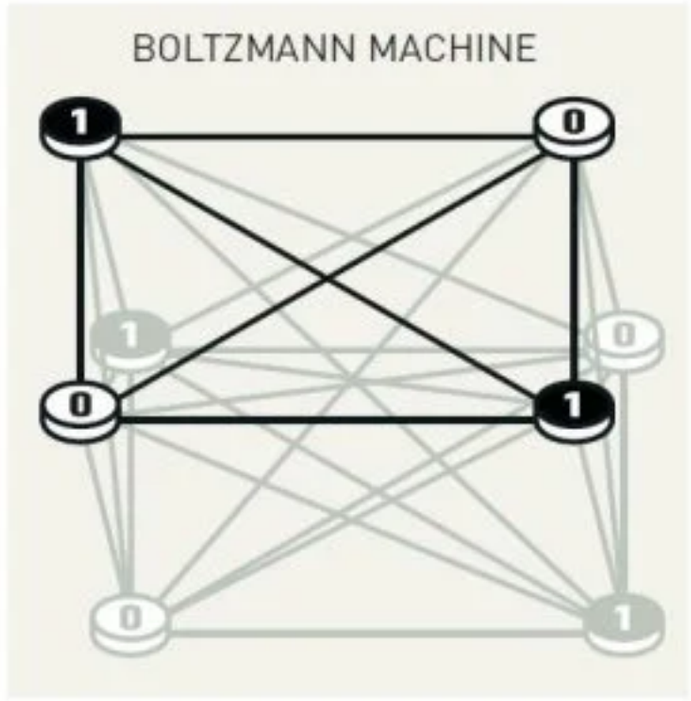


Physics

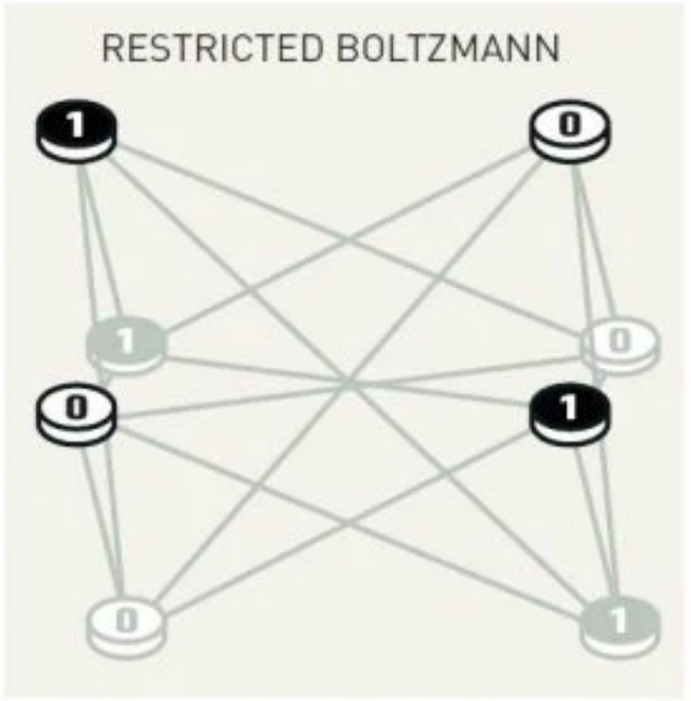
Different types of network



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.

Physics

Implications

- Understanding of data processing
- Powerful tool for pattern matching for use in a variety of fields (because “deep learning” is enabled — Bayesian)
- Higgs boson detection was an ANN highlight
- Mammary tumor detection or other diagnostic uses
- AI
- [transitional topic] AlphaFold for predicting protein structure based on a deep learning of previously solved structures

Chemistry

David Baker Demis Hassabis & John Jumper

David Baker. Ill. Niklas Elmehed © Nobel Prize Outreach

Demis Hassabis. Ill. Niklas Elmehed © Nobel Prize Outreach

John Jumper. Ill. Niklas Elmehed © Nobel Prize Outreach

for the discovery of for computational protein design and for protein structure prediction

Chemistry

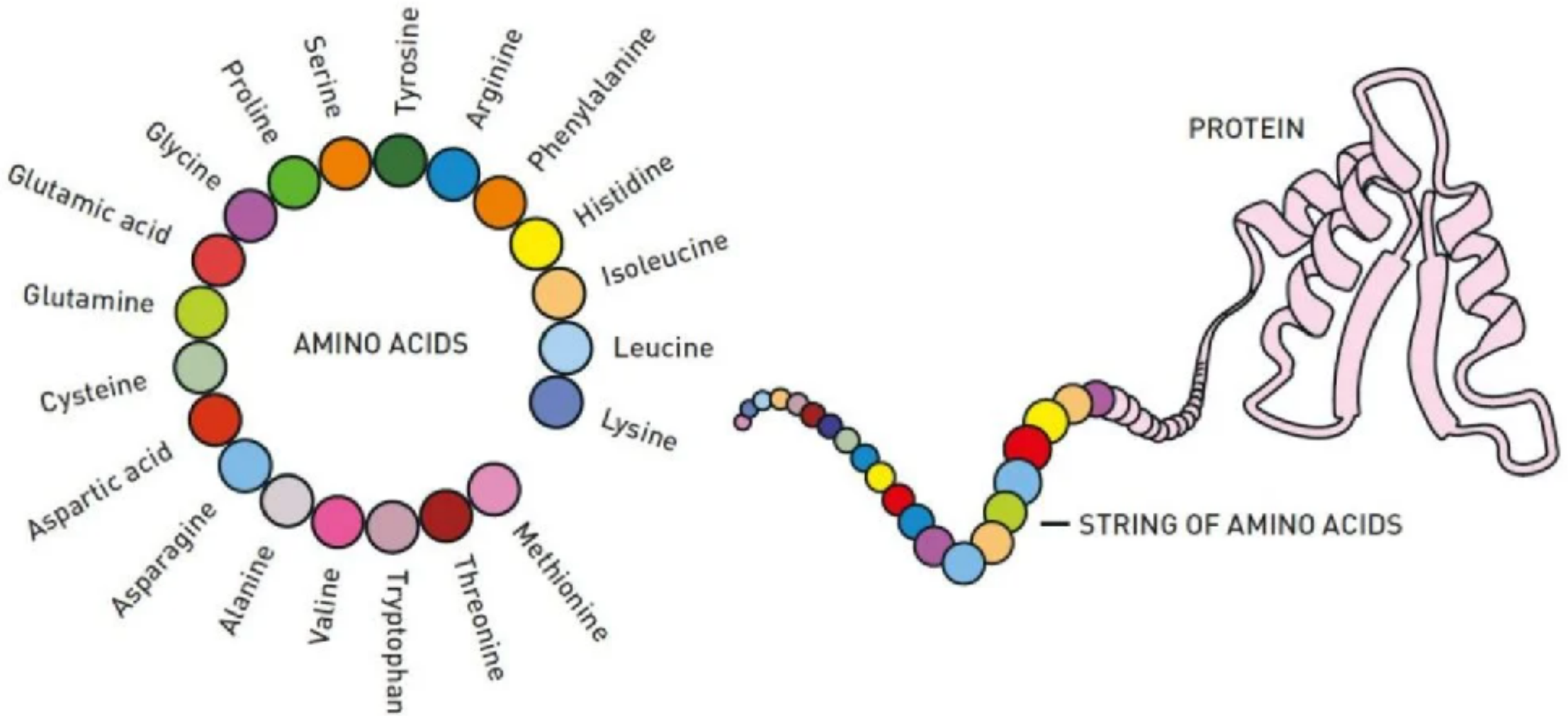


Figure 1. A protein can consist of everything from tens of amino acids to several thousand. The string of amino acids folds into a three-dimensional structure that is decisive for the protein's function. ©Johan Jarnestad/The Royal Swedish Academy of Sciences © Johan Jarnestad/The Royal Swedish Academy of Sciences

Chemistry

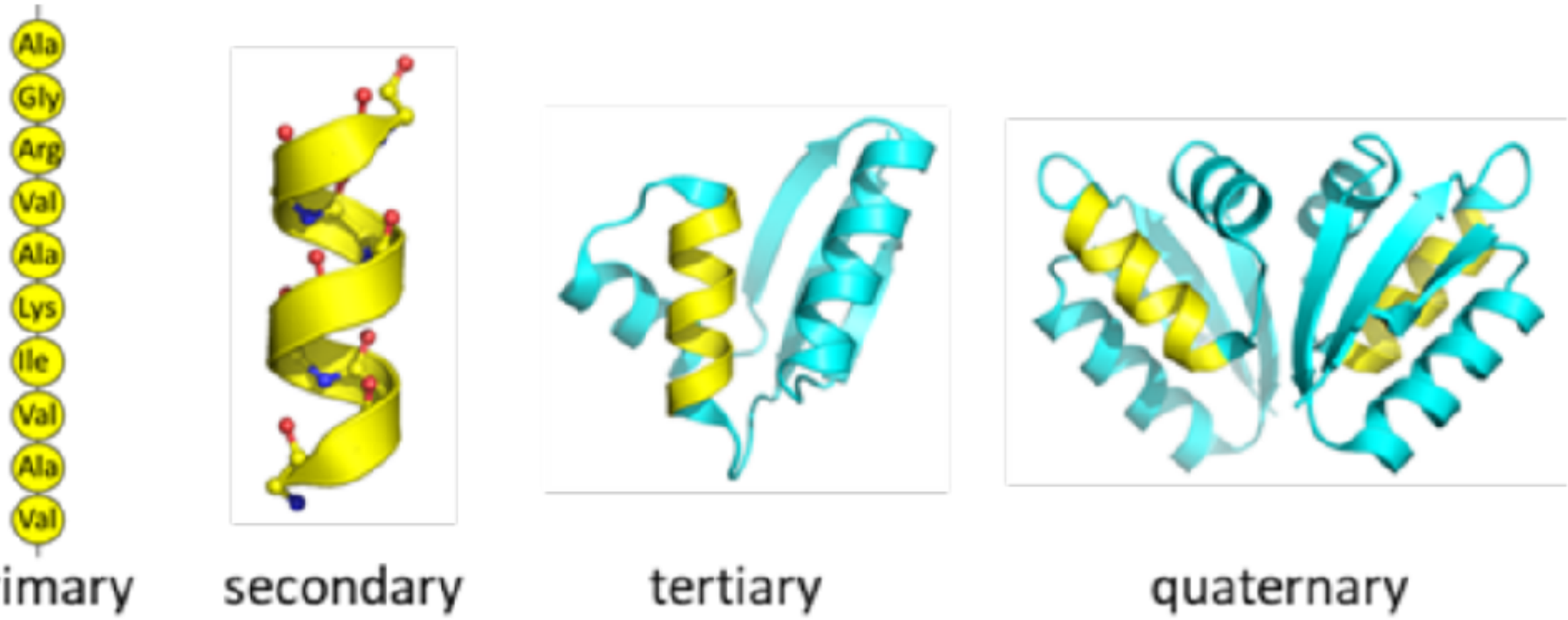


Figure 1. Hierarchy of protein structure. Primary: the amino acid sequence that is determined by the corresponding sequence of DNA base triplets. Secondary: formation of regular geometric patterns of α-helices and β-sheets. Tertiary: the detailed 3D shape of the polypeptide chain. Quaternary: the association of several polypeptide chains or subunits.

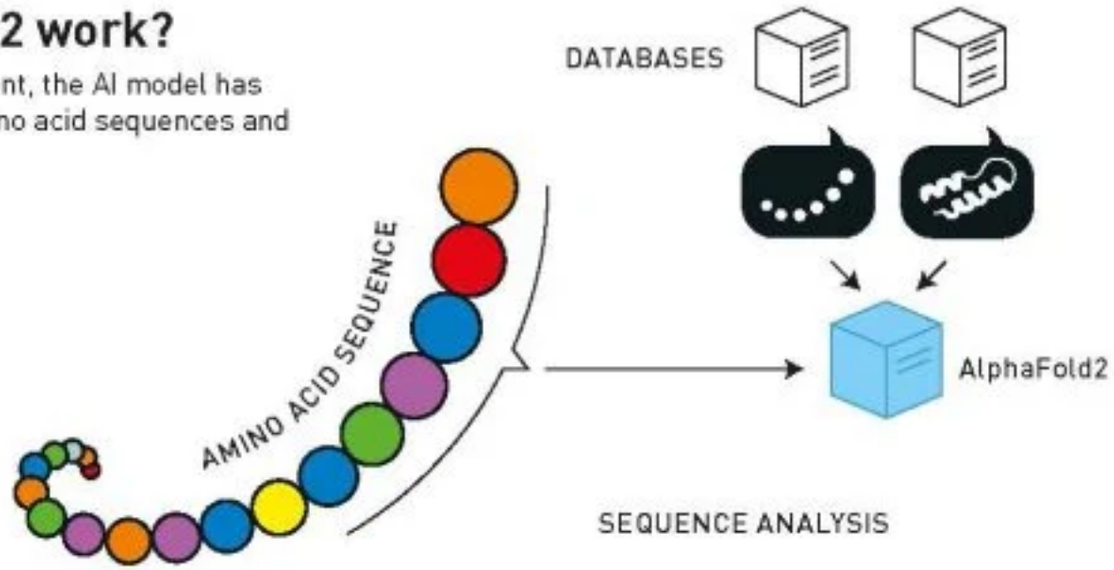
Chemistry

How does AlphaFold2 work?

As part of AlphaFold2's development, the AI model has been trained on all the known amino acid sequences and determined protein structures.

1. DATA ENTRY AND DATABASE SEARCHES

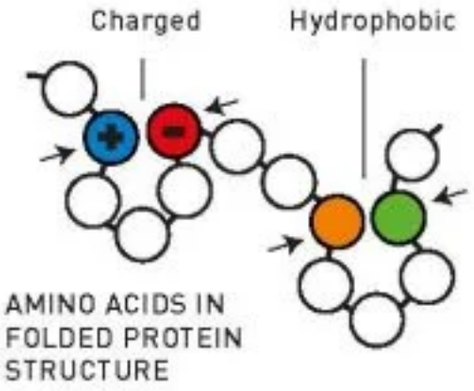
An amino acid sequence with unknown structure is fed into AlphaFold2, which searches databases for similar amino acid sequences and protein structures.

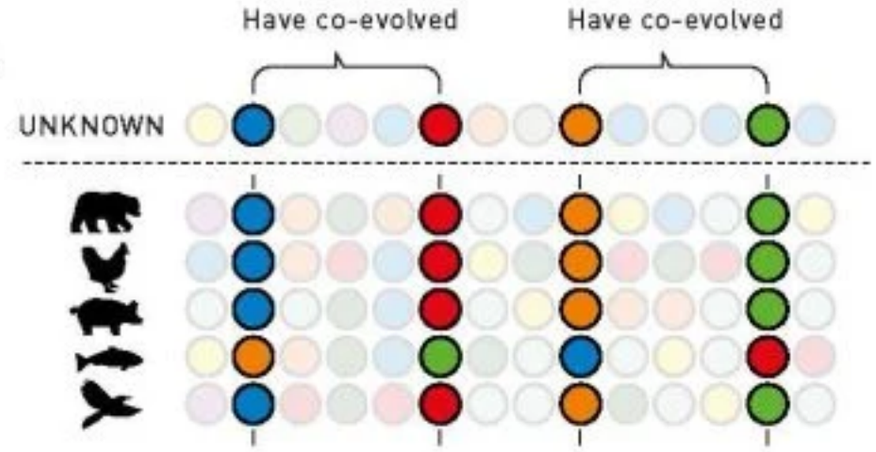


2. SEQUENCE ANALYSIS

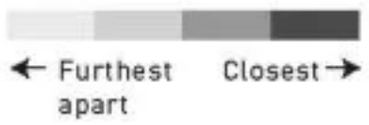
The AI model aligns all the similar amino acid sequences – often from different species – and investigates which parts have been preserved during evolution.

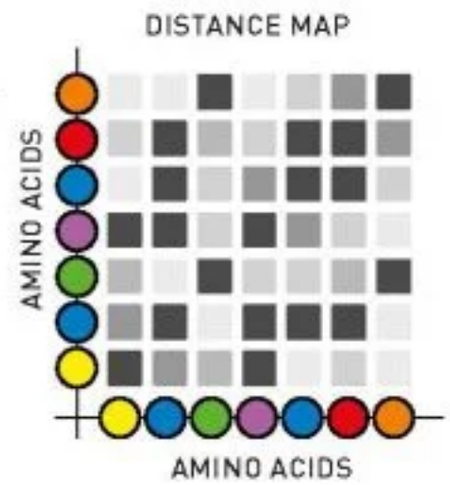
In the next step, AlphaFold2 explores which amino acids could interact with each other in the three-dimensional protein structure. Interacting amino acids co-evolve. If one is charged, the other has the opposite charge, so they are attracted to each other. If one is replaced by a water-repellent (hydrophobic) amino acid, the other also becomes hydrophobic.





Using this analysis, AlphaFold2 produces a distance map that estimates how close amino acids are to each other in the structure.





NEURAL NETWORK

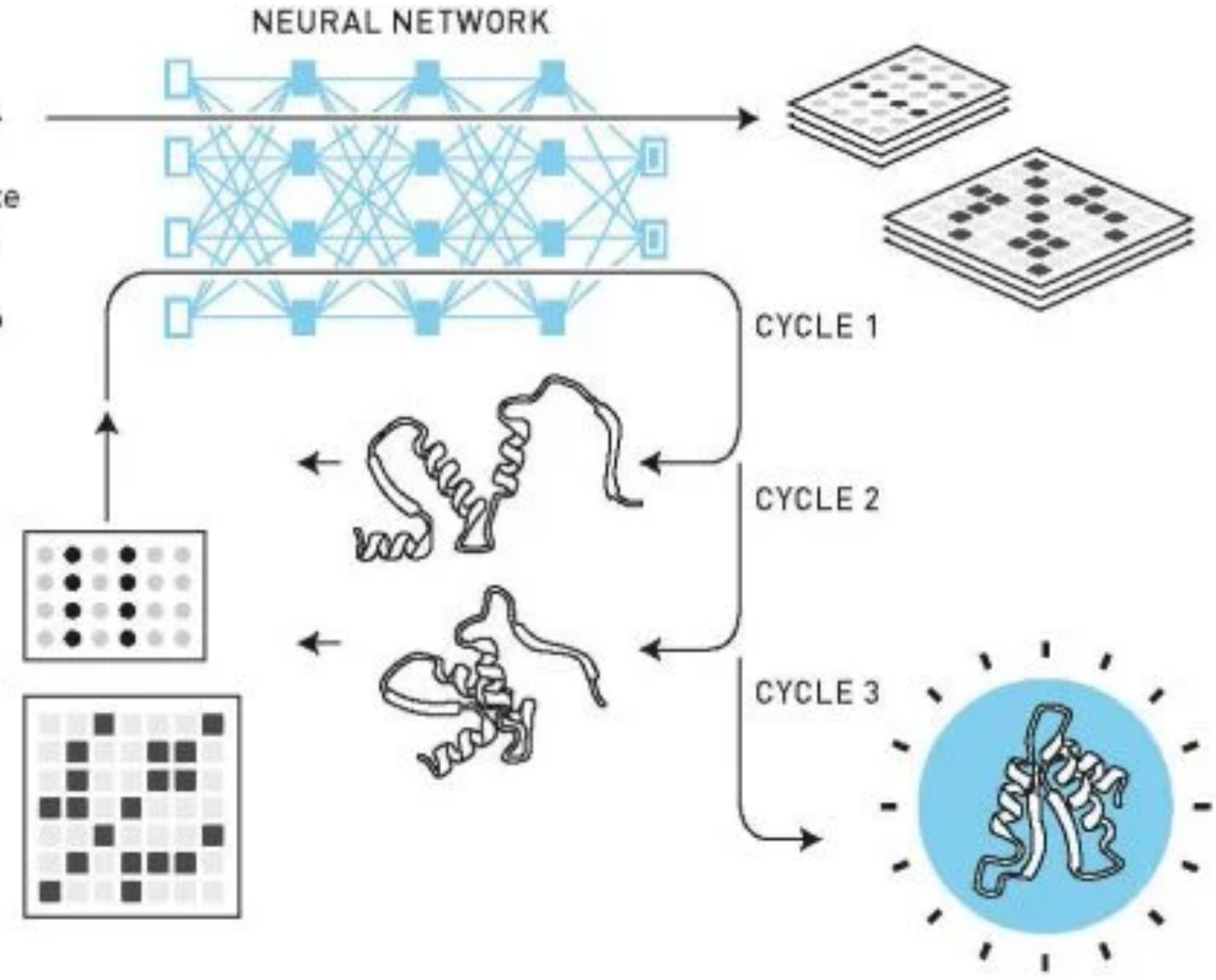
Chemistry

3. AI ANALYSIS

Using an iterative process, AlphaFold2 refines the sequence analysis and distance map. The AI model uses neural networks called transformers, which have a great capacity to identify important elements to focus on. Data about other protein structures – if they were found in step 1 – is also utilised.

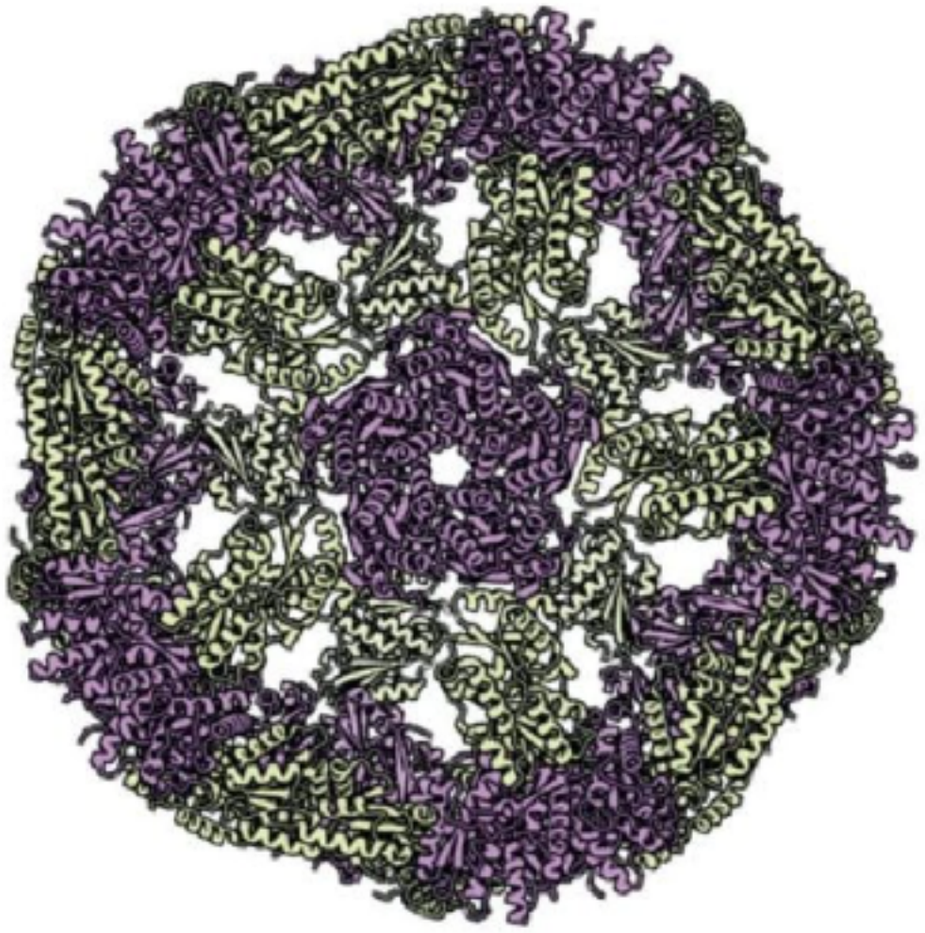
4. HYPOTHETICAL STRUCTURE

AlphaFold2 puts together a puzzle of all the amino acids and tests pathways to produce a hypothetical protein structure. This is re-run through step 3. After three cycles, AlphaFold2 arrives at a particular structure. The AI model calculates the probability that different parts of this structure correspond to reality.

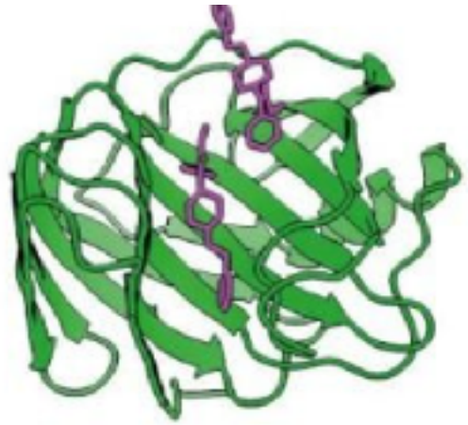


Chemistry

Examples of Rosetta created proteins

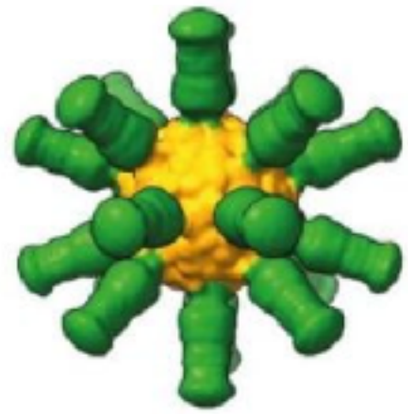


2016: New nanomaterials where up to 120 proteins spontaneously link together.



2017: Proteins that bind to an opioid called fentanyl (purple). These could be used to detect fentanyl in the environment.

2022: Proteins that function as a type of molecular rotor.



2021: Nanoparticles (yellow) with proteins imitating influenza virus on the surface (green) that can be used as a vaccine for influenza. Successful in animal models.

2024: Geometrically shaped proteins that can change their shape due to external influences. Could be used for producing tiny sensors.

Figure 4. Proteins developed using Baker's program Rosetta.

Chemistry

Implications

- Vastly hastening the understanding of protein structure at much lower cost
- Within research this enables scientists/engineers to more quickly modify or adapt to some purpose
- *de novo* proteins also accelerate that type of purpose driven invention process
- Understanding insect control toxins to protect crops
- Drug delivery or detection
- Novel chemistry like degrading plastics