

PROTEINS WEBINAR

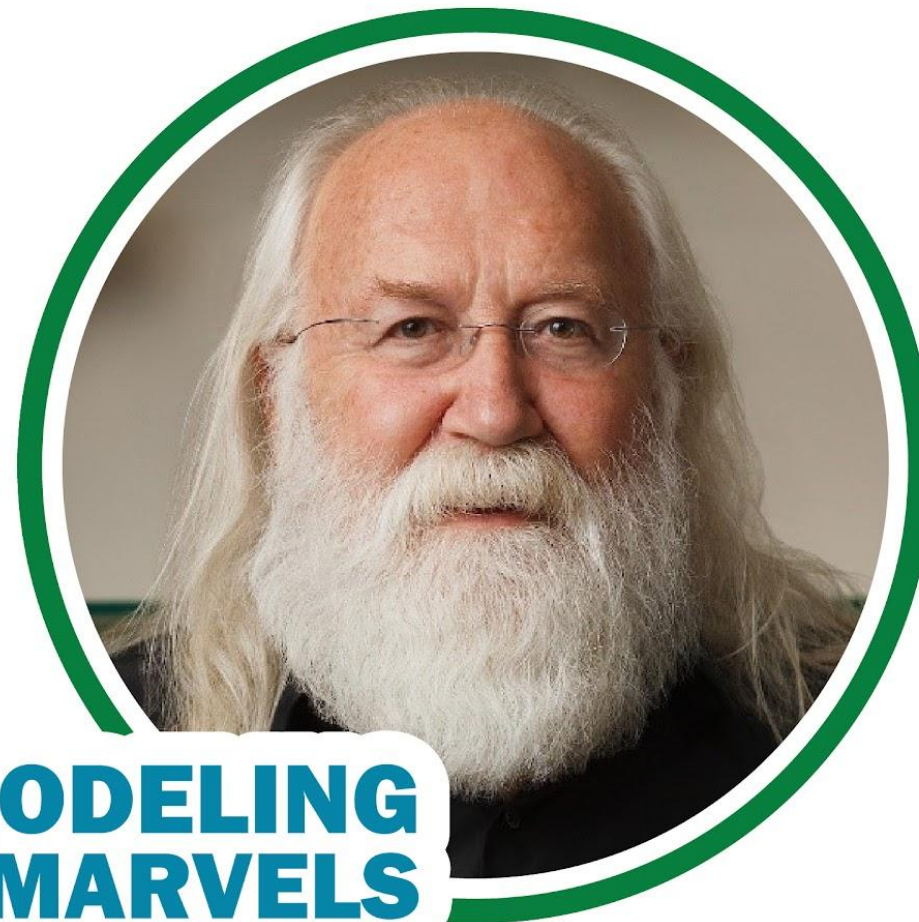
TUESDAY | MARCH 1 6:30 - 8 PM CST

PRESENTER:

TIM HERMAN, PhD

MSOE Center for BioMolecular Modeling &
3D Molecular Designs

Protein Folding Problem Nevermore



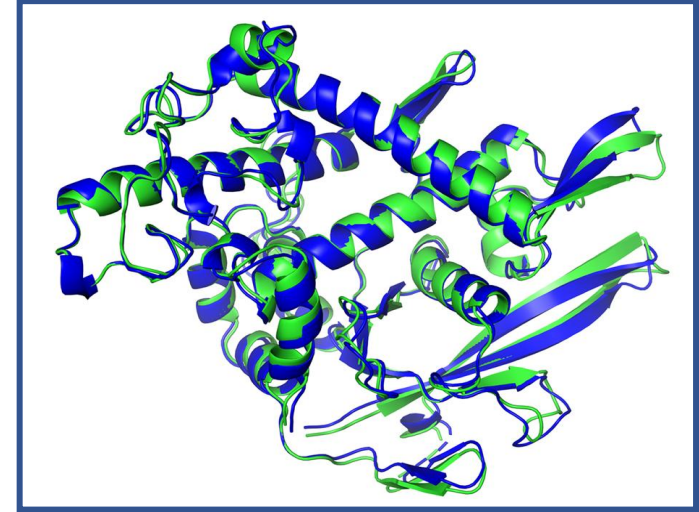
**MODELING
MARVELS**
2022 EDUCATORS WEBINARS

Teaching Proteins... *now that everything has changed.*

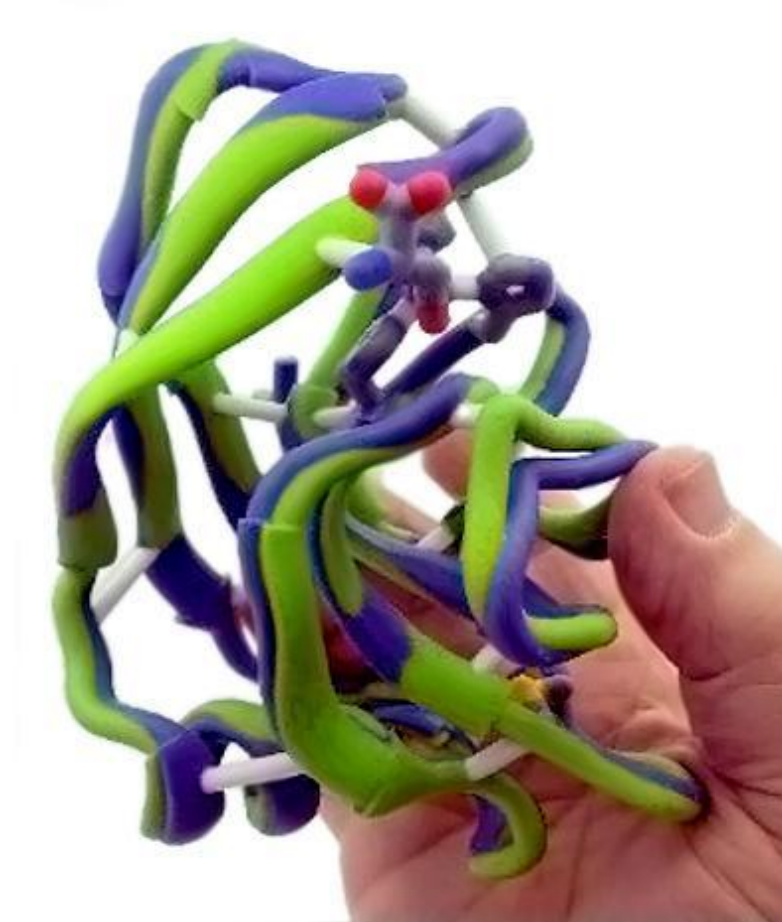
On December 30, 2020, the results of the CASP competition were announced.

With this announcement came the declaration that a grand challenge in science... a solution to the *protein folding problem*... had been solved.

“This is a big deal,” says John Moult, a computational biologist at the University of Maryland in College Park, who co-founded CASP in 1994 to improve computational methods for accurately predicting protein structures. “In some sense the problem is solved.”



Two physical models of the same protein,....one structure solved by x-ray diffraction, and the other predicted by AlphaFold.



Now that the **Protein Folding Problem** has been solved,
should we change how we “teach proteins”?

Yes...

- * we must acknowledge this milestone achievement in the molecular biosciences.
- * we must talk about Artificial Intelligence, Machine Learning and the value of Large Datasets of nucleotide sequences.

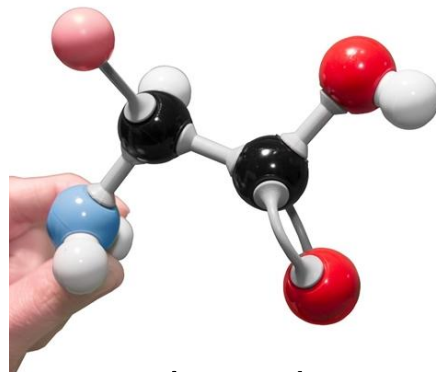
and **NO....**

- * we don't have to know/teach how AlphaFold works
- * but we should show students how yesterday's science and today's *data science* has led to the solution of the protein folding problem.

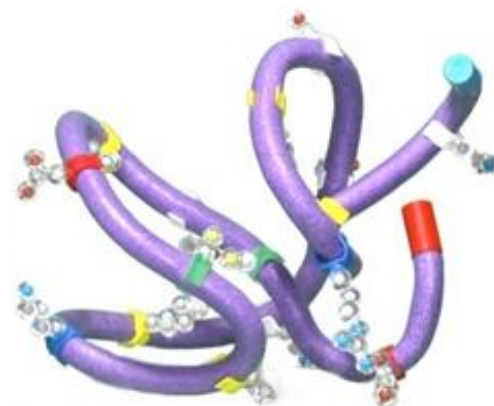
Tactile Teaching Tools....



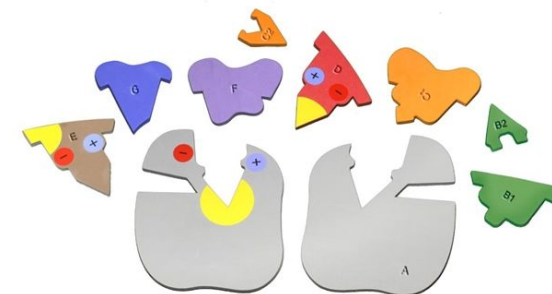
Water Kit



MolyMod
Amino Acids



Amino Acid
Starter Kit



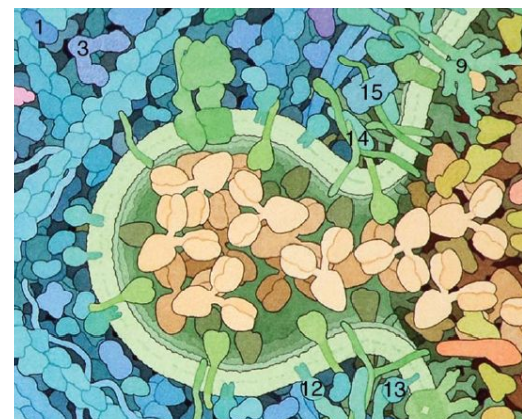
Enzymes in Action
Kit



Substrate Specificity Kit



Molecular Explorations



Molecular Landscapes

How can you help your students appreciate the protein folding problem?

- **Amino Acid Starter Kit...**

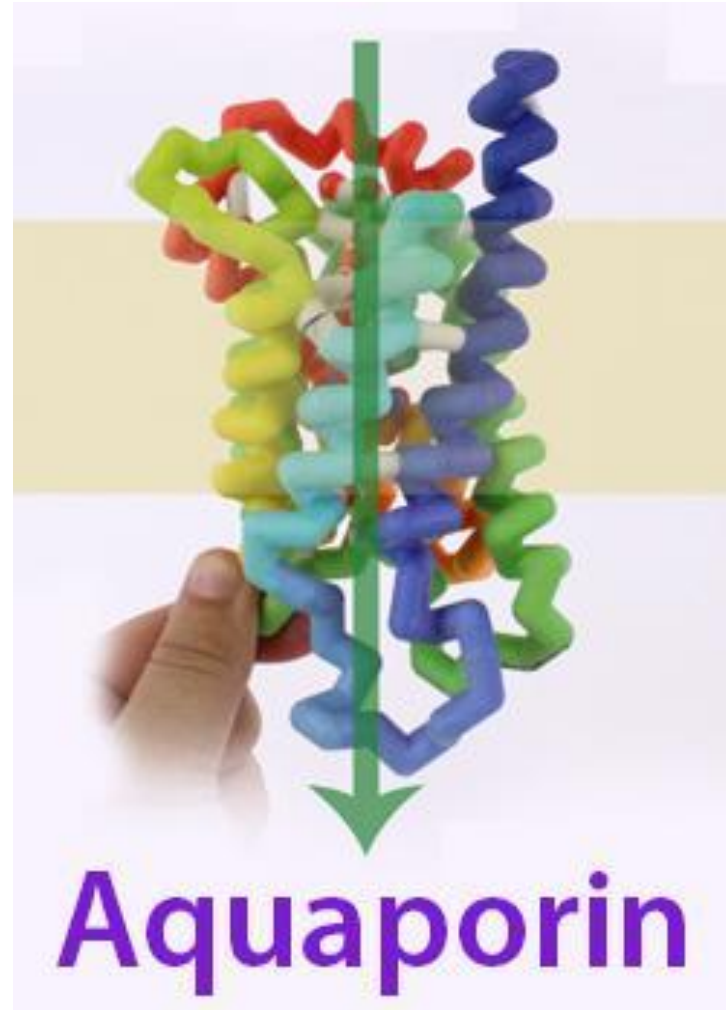
Following principles of chemistry

- **MolyMod Amino Acids...**

Protein folding is all about bond rotation.

- **Predicting structure from amino acid sequence...**

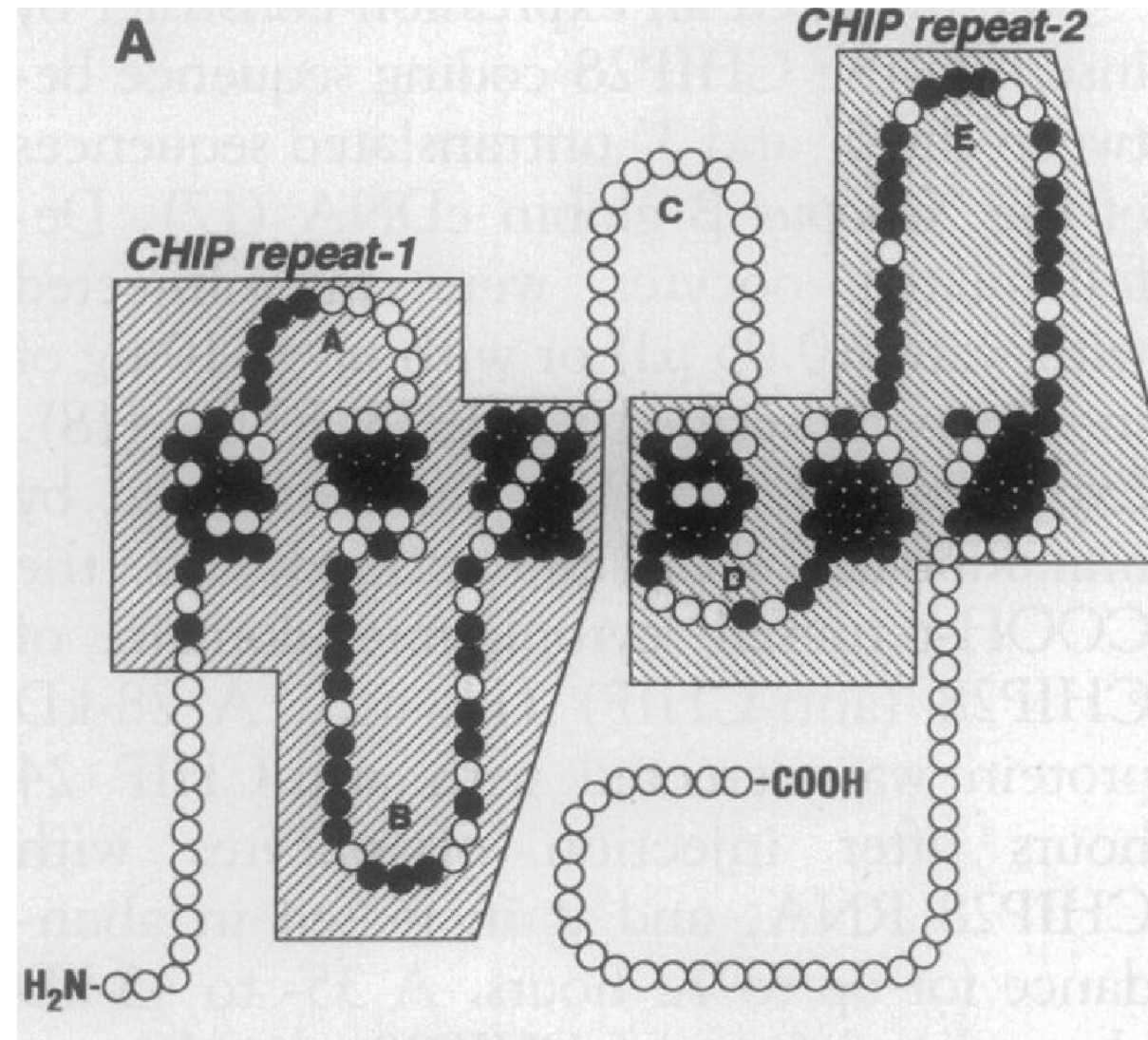
Recognizing patterns is a cross-cutting concept



Model of Aquaporin

....in 1992.....

based on its
amino acid sequence

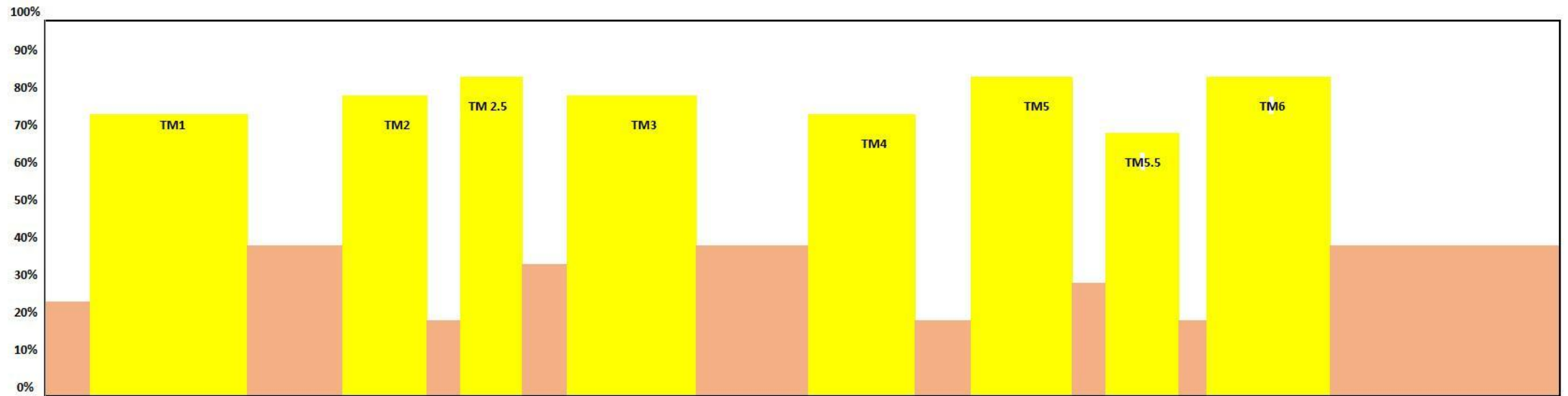


Aquaporin TransMembrane helix prediction.

<https://cbm.msoe.edu/markMyweb/aquaporinBioinformatic/student.html>

<https://cbm.msoe.edu/markMyweb/aquaporinBioinformatic/teacher.html>

The six hydrophobic Transmembrane Alpha Helices of aquaporin can be predicted



Aquaporin Amino Acid Sequence (1-269)

The recent solution to the protein folding problem was made possible by decades of work by researchers around the world who...

- **sequenced genes**...and deposited these sequences in freely accessible databases....(revealing coevolving amino acids)
- **determined protein structures**... by x-ray diffraction methods, nuclear magnetic resonance and most recently, by cryo-electron microscopy. As of 2020, there were 187,423 experimentally determined protein structures in the Protein Data Bank.
- **and developed Artificial Intelligence systems**

Protein 3D Structure Computed from Evolutionary Sequence Variation

Debora S. Marks¹ *, Lucy J. Colwell², Robert Sheridan³, Thomas A. Hopf¹, Andrea Pagnani⁴, Riccardo Zecchina^{4,5}, Chris Sander³

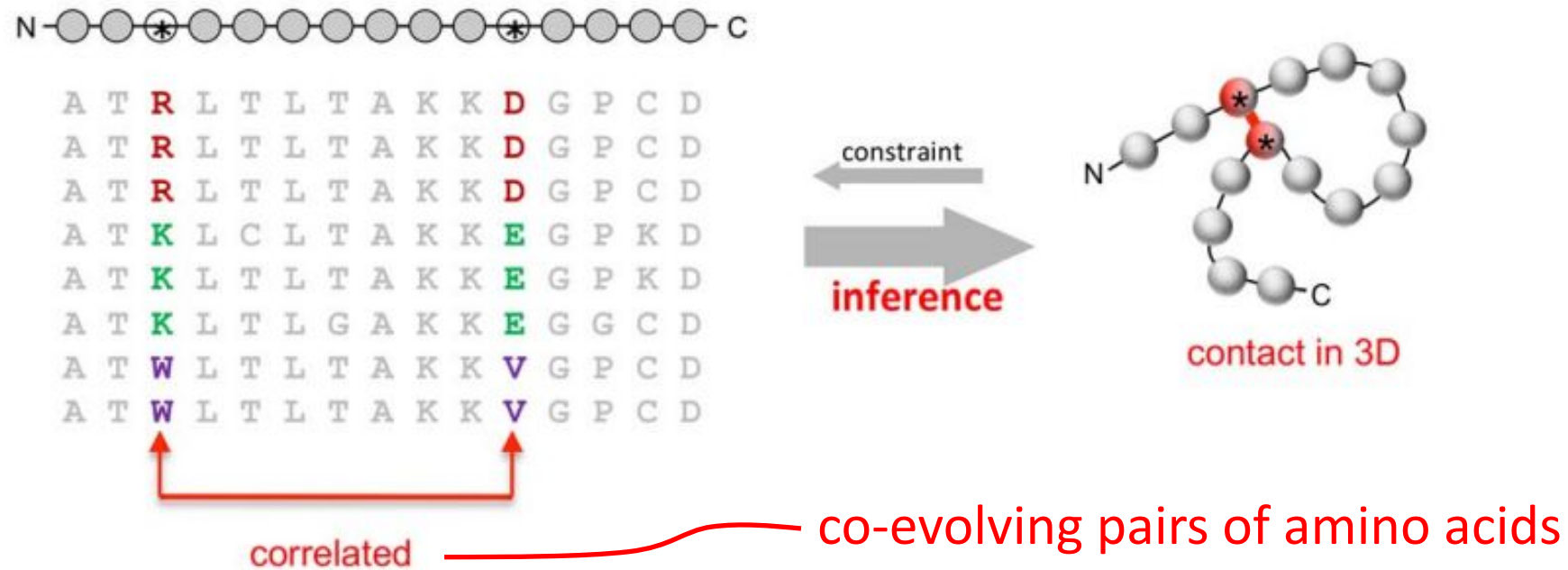


Figure 1. Correlated mutations carry information about distance relationships in protein structure. The sequence of the protein for

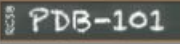
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PROTEIN DATA BANK

174507 Biological Macromolecular Structures
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Celebrating  **YEARS OF Protein Data Bank**    

**PROTEIN
DATA BANK**



Celebrating 50 Years of the Protein Data Bank Archive

PROTEINS,... *now that everything has changed.....*



AlphaFold: a solution to a 50-year-old grand challenge in biology | DeepMind

<https://deepmind.com/research/open-source/alphafold-protein-structure-database>

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AlphaFold Protein Structure Database

AlphaFold is our AI system that predicts a protein's 3D structure from its amino acid sequence. In [CASP14](#), AlphaFold was the top-ranked protein structure prediction method by a large margin, producing predictions with high accuracy, many of which are competitive with experimentally-determined measurements.

We've partnered with Europe's flagship laboratory for life sciences – EMBL's European Bioinformatics Institute ([EMBL-EBI](#)) – to create the AlphaFold Protein Structure Database to make these predictions freely available to the scientific community.

The initial release of the database covers all of the 20,000 proteins in the human proteome, along with the proteomes of several other biologically significant organisms, from E.coli to yeast, and from the fruit fly to the mouse. In the coming months we plan to

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Why should we teach *proteins*?

1. Proteins are part of the Central Dogma of molecular biology....

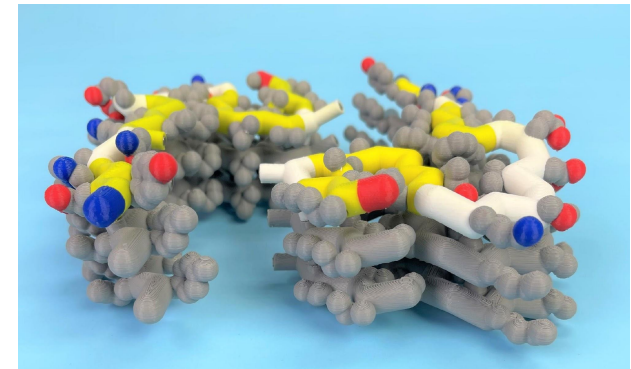
DNA □ RNA □ Protein

the only reason we have DNA is to encode ... in a sequence of nucleotides...the sequence of amino acids in proteins

2. Many neurocognitive disorders are protein misfolding diseases.

Alzheimer's / Mad-Cow Disease / Chronic Wasting Disease

3. Proteins are drug targets
structure - function relationship



THANK YOU FOR ATTENDING!

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