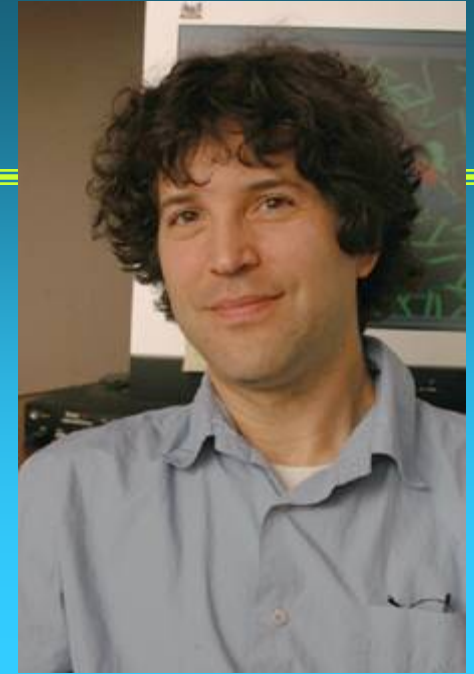

The Family Business

Computational Biologist David Baker:
Modeling Protein Structures

David Baker Shapes Proteins

Computational biologist Baker is fighting disease with a better picture of proteins.



Proteins

- Consist of amino acids
- Attach to other molecules
- Trigger chemical reactions in the body

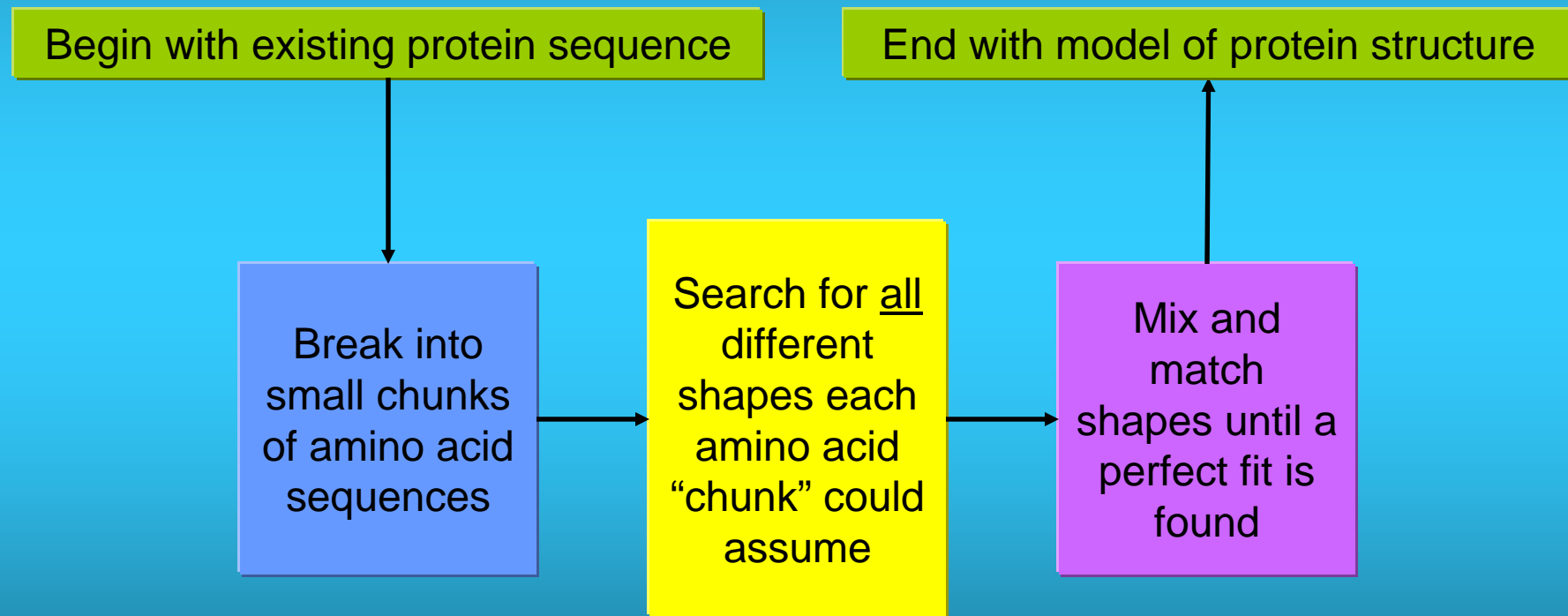
Question:

How do scientists
predict protein
shapes?

Answer: Using approaches from physics and computer sciences

	Approach	Drawbacks
Physics	X-ray crystallography	Labor intensive and sometimes expensive
	Nuclear Magnetic Resonance (NMR) spectroscopy	
Computer	Computers analyze possibilities and make models	Can be inaccurate and unreliable

Rosetta Software Models Protein Structure



Making a Protein from Scratch

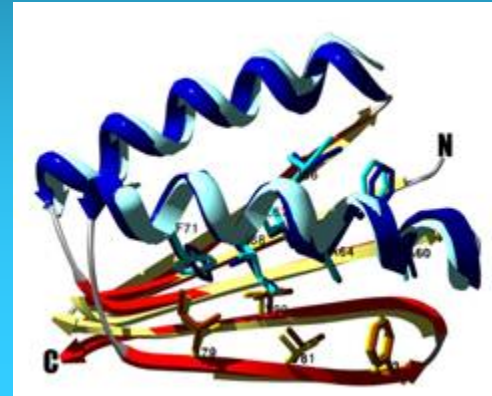
Begin with a sketch of made-up protein structure



Piece together string of amino acids most likely to link up to create the new protein

Make the protein, using identified amino acids

Compare new protein with sketch



End with real protein matching made-up structure

Many Rosetta Flavors

Different versions of Rosetta

- Predict how a protein interacts with another protein or with DNA
- Add in experimental data
- Use structural information of other, similar proteins



How might scientists use this knowledge?



What's experimental data?



Why study similar proteins?

Goals of Computational Biology

Computational biologists have more than one goal

Identify atoms, bonds, and places where chemical reactions occur

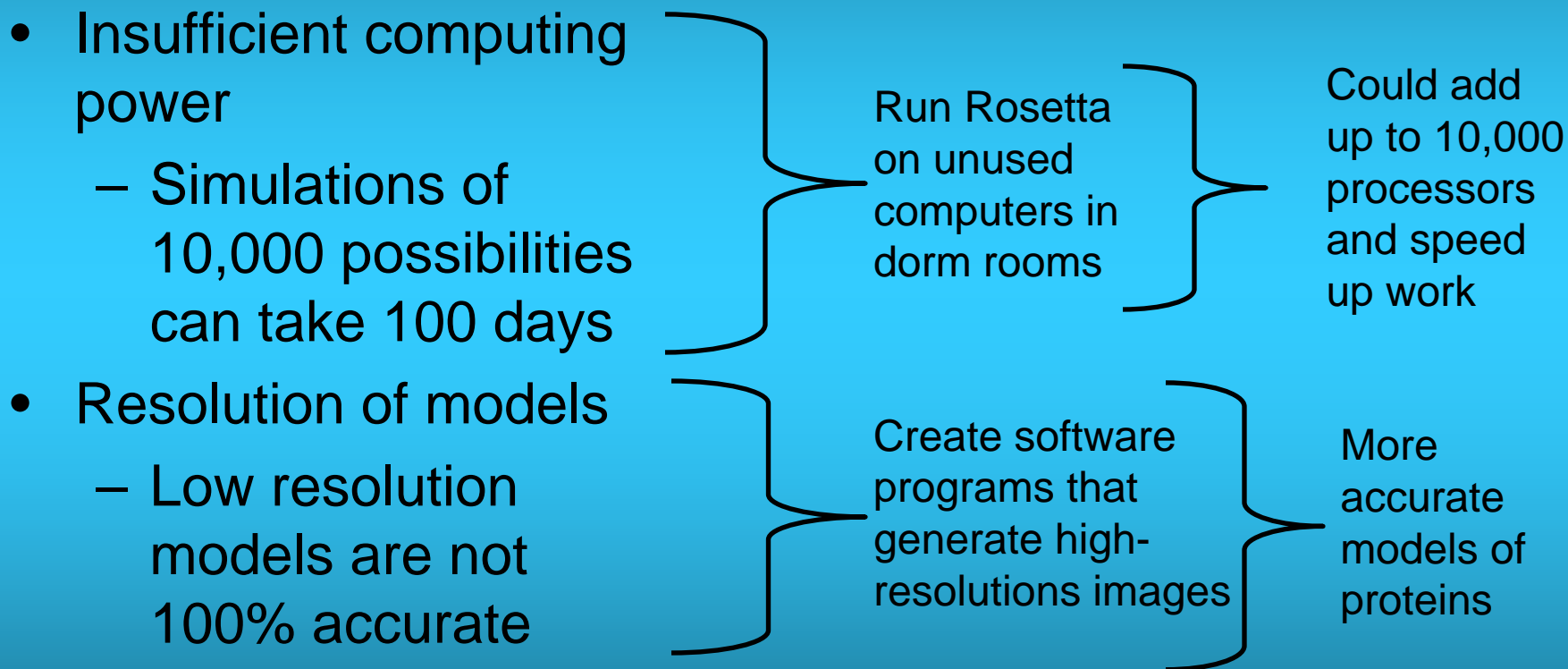
Develop accurate models of protein structures

Track interactions of single proteins with other molecules

Create custom proteins to interrupt or enhance reactions inside a cell

Develop new drugs and vaccines based on interactions

Challenges & Solutions



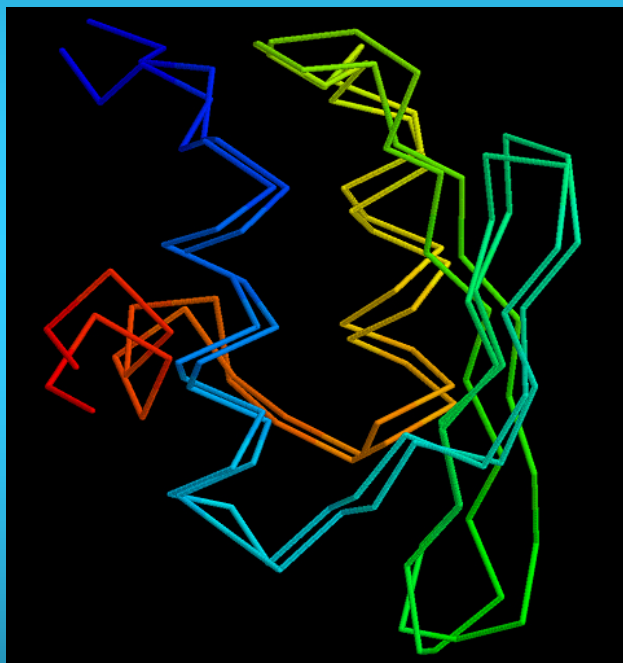
Community-wide Experiment

Critical Assessment of Techniques for Protein Structure Prediction (CASP)

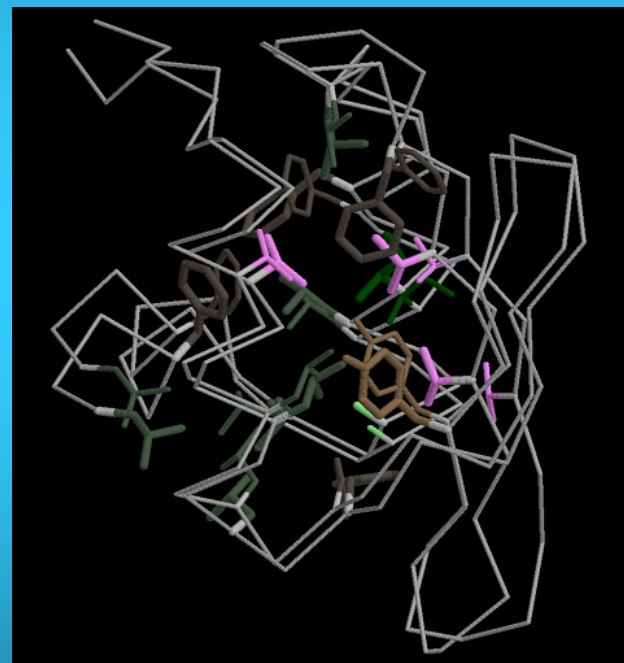
- Scientific competition
- Entrants from >200 labs worldwide
 - Work together
 - Learn about current challenges
 - Set future goals
 - Assess methods and technology for predicting protein structures

Team Baker's CASP Rainbow

Rosetta highlighted even more detail than X-ray method



Protein's actual X-ray
crystallographic structure



Team's computer model

FINDINGS

National Institutes of Health
National Institute of General Medical Sciences

Research Applications

How might custom proteins keep people healthy?