From Robots to Biomolecules: Computing Meets the Physical World

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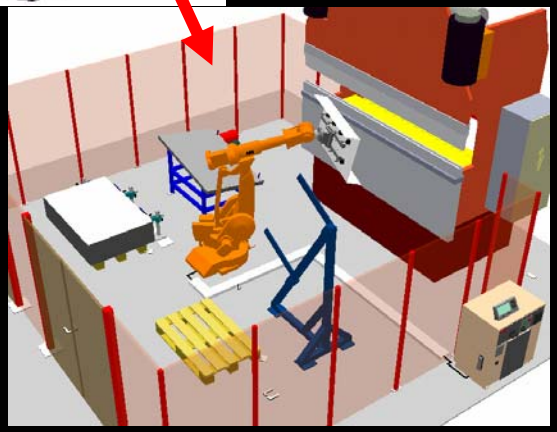
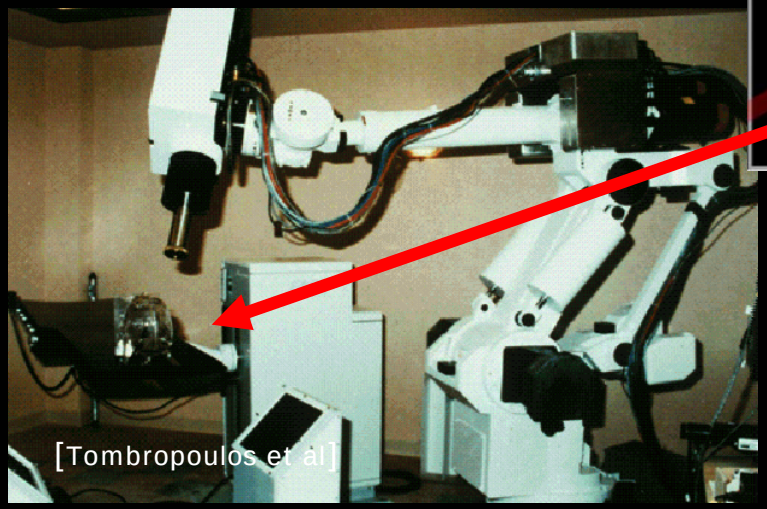
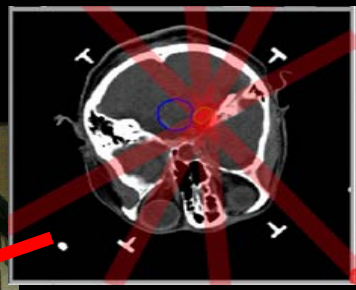
Robots Become Ubiquitous

[from ABB]





[Tombropoulos et al]



[from NASA]

[Sony ©]

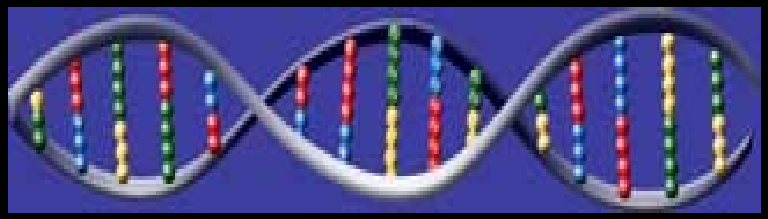
Applications:

- Industrial automation
- Robot-assisted surgery
- Service robots
- Virtual characters / Animation

[Koga, Latombe]

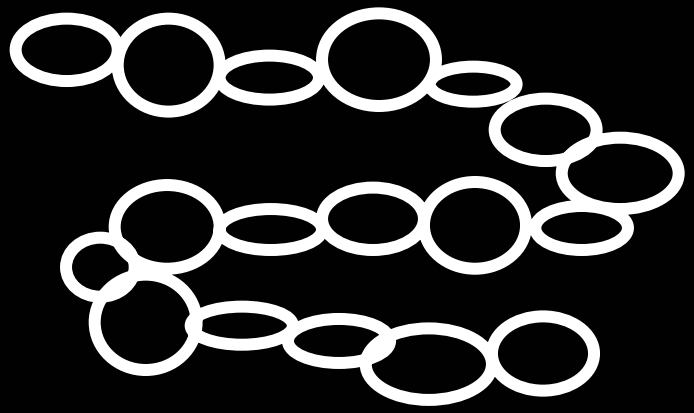
Biomolecules Govern Life

Central Dogma of Molecular Biology



Genetic Information

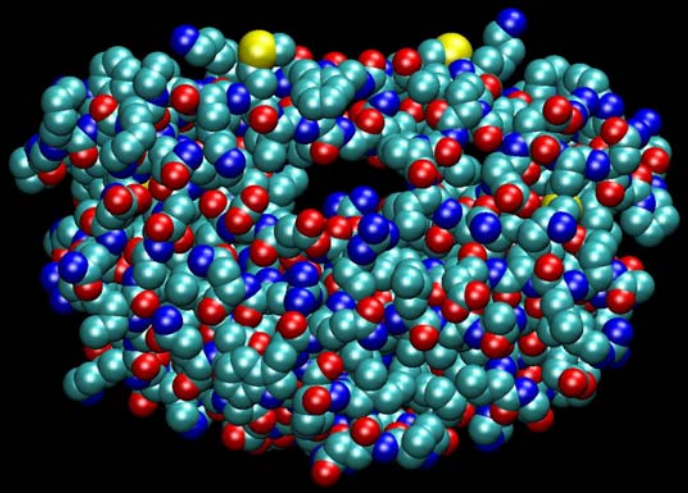
Transcription
Translation



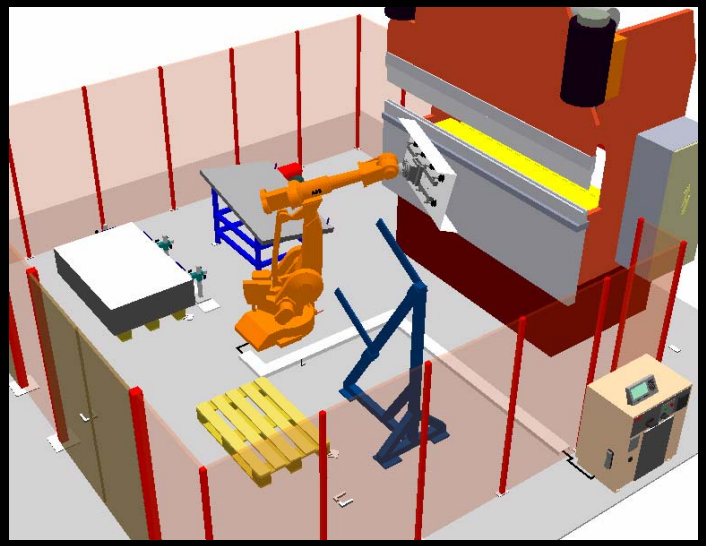
1-D Amino-acid Sequence

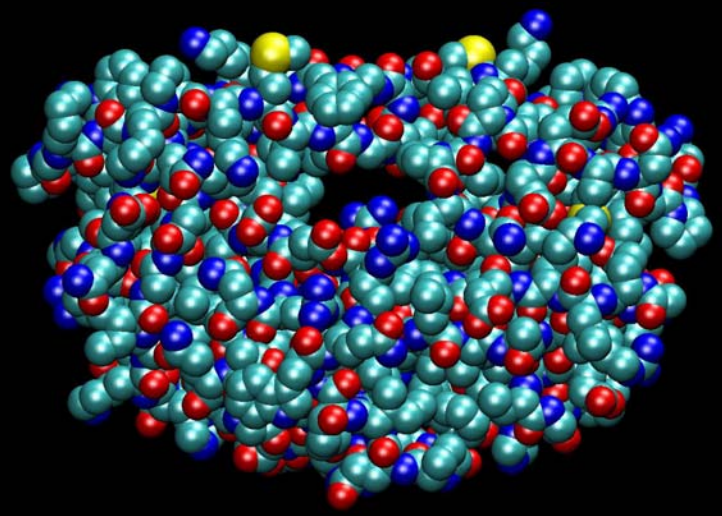
Folding

3-D Protein Structure



Robots and Biomolecules



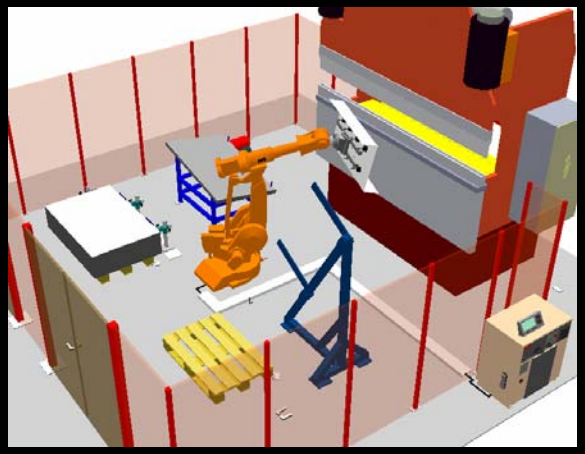


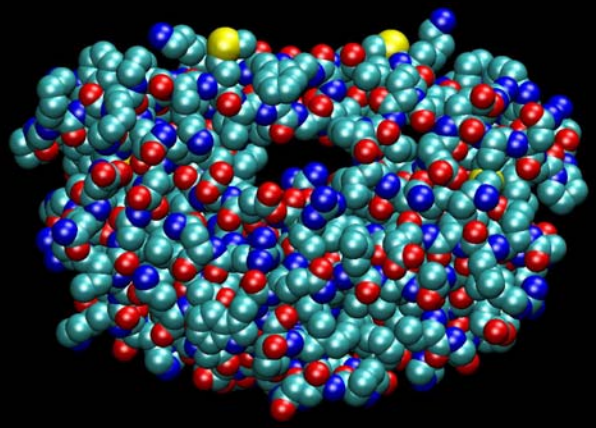
- How do these two problems relate?
- How do they relate to the advancement of Computer Science?

This Talk is about Computer Science

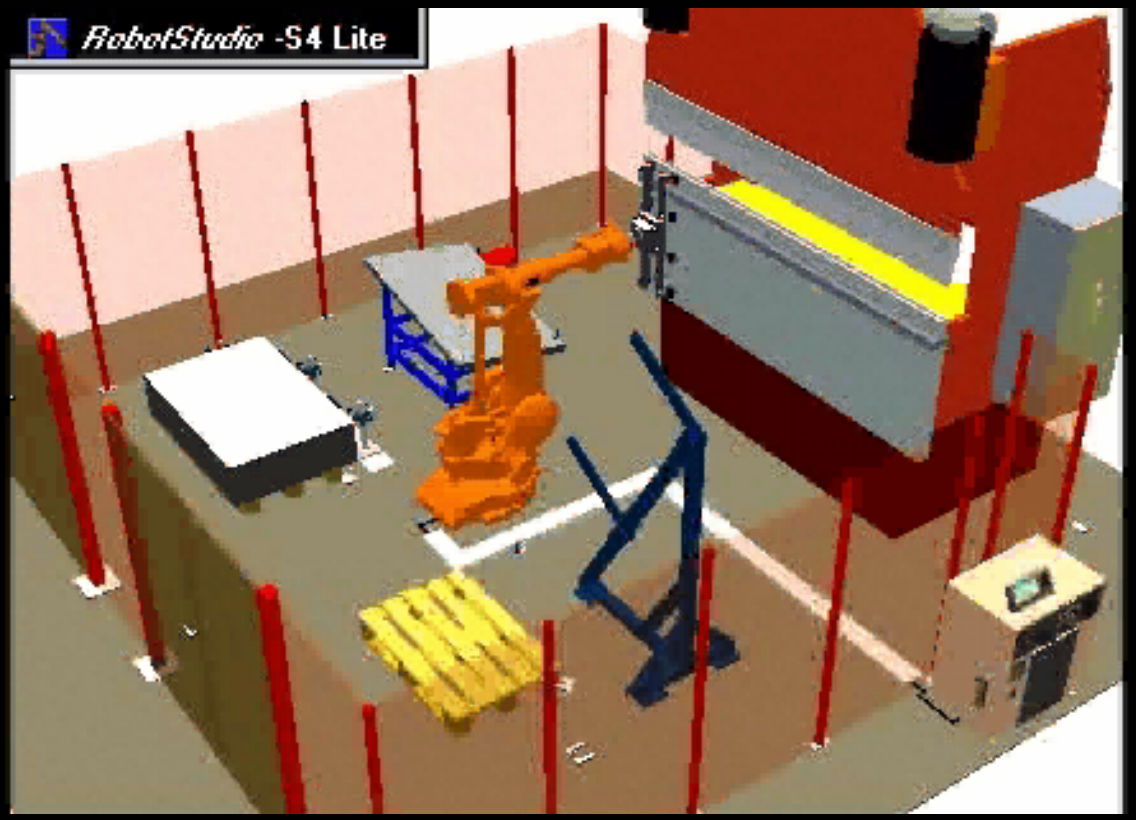
- Computer science has become an enabler for research that relates to the physical world

- To enable discovery at an unprecedented scale, basic research in computer science is needed





Automated Robotics Path Planning is a Research Topic



Probabilistic Roadmap Methods (PRMs)

PRM Planners are Adopted in Robotics

Universities:

- Rice University
- Texas A & M University
- Stanford University
- University of Pennsylvania
- University of Illinois, Urbana Champaign
- University of Washington
- Rensselaer Polytechnic Institute
- Washington University
- Simon Fraser, Canada
- Oxford, UK
- Göteborg University, Sweden
- Tel-Aviv University, Israel
- University of Utrecht, The Netherlands
- National University of Singapore
- Institut Polytechnique de Toulouse, France

and others

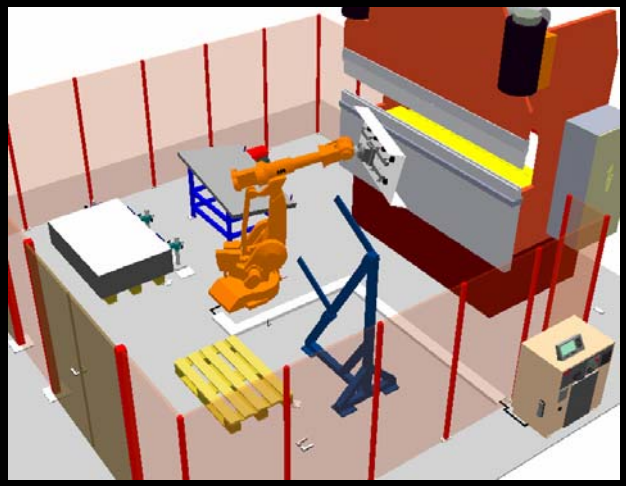
Companies:

- General Electric
- General Motors
- ABB Robotics
- Prosolvia
- Amrose Automation
- Electricité de France
- Honda
- Volvo
- Draper Laboratories

Research Laboratories

- Parc
- Compaq
- CNRS, France
- INRIA, France
- NASA

Path Planning is all about Algorithms



Solving the problem on a current desktop:

- 1987 methods — 100 years?
- 1995 methods — 12 hours
- PRM methods — 0.01 sec

A new algorithm not just a faster machine

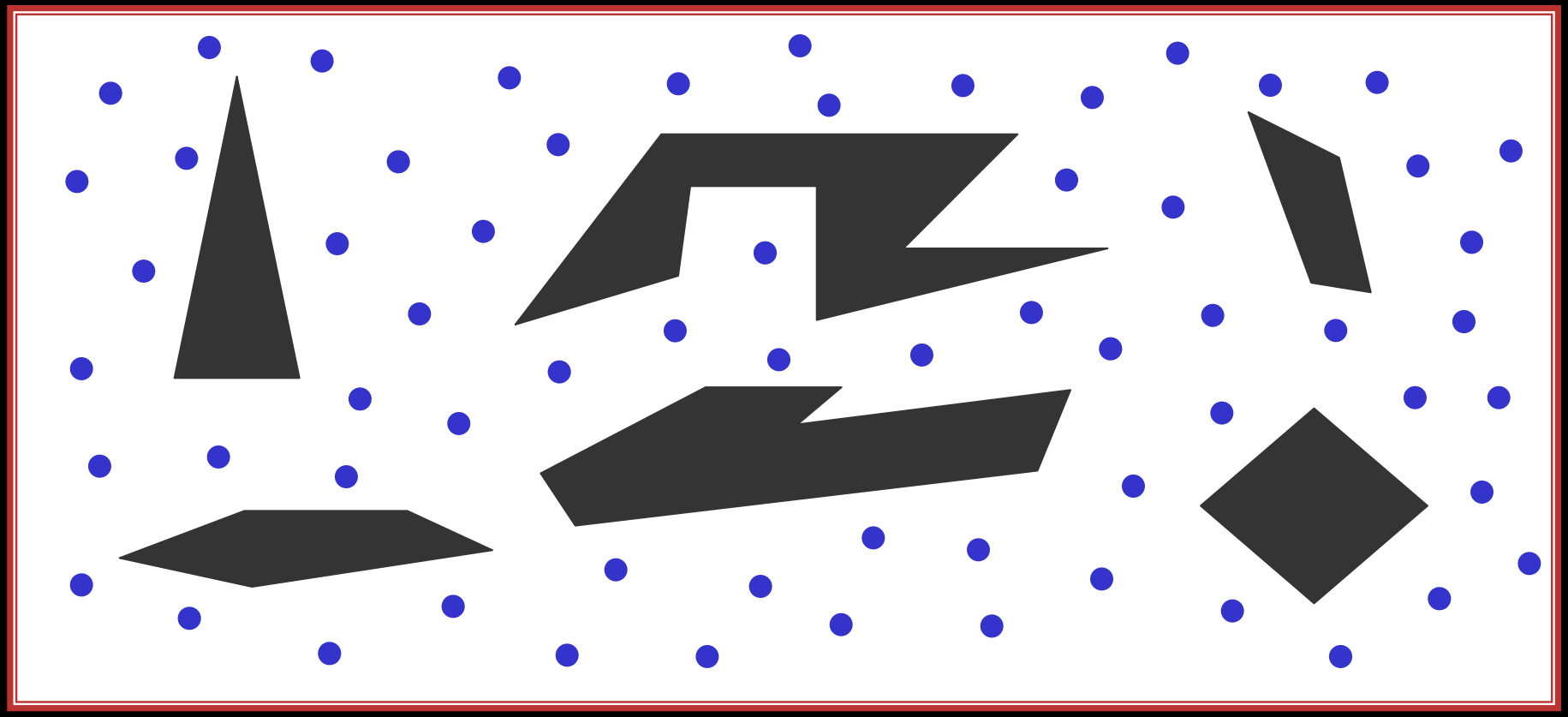
Probabilistic Roadmap Method (PRM)

- A robot configuration

Robot is a point

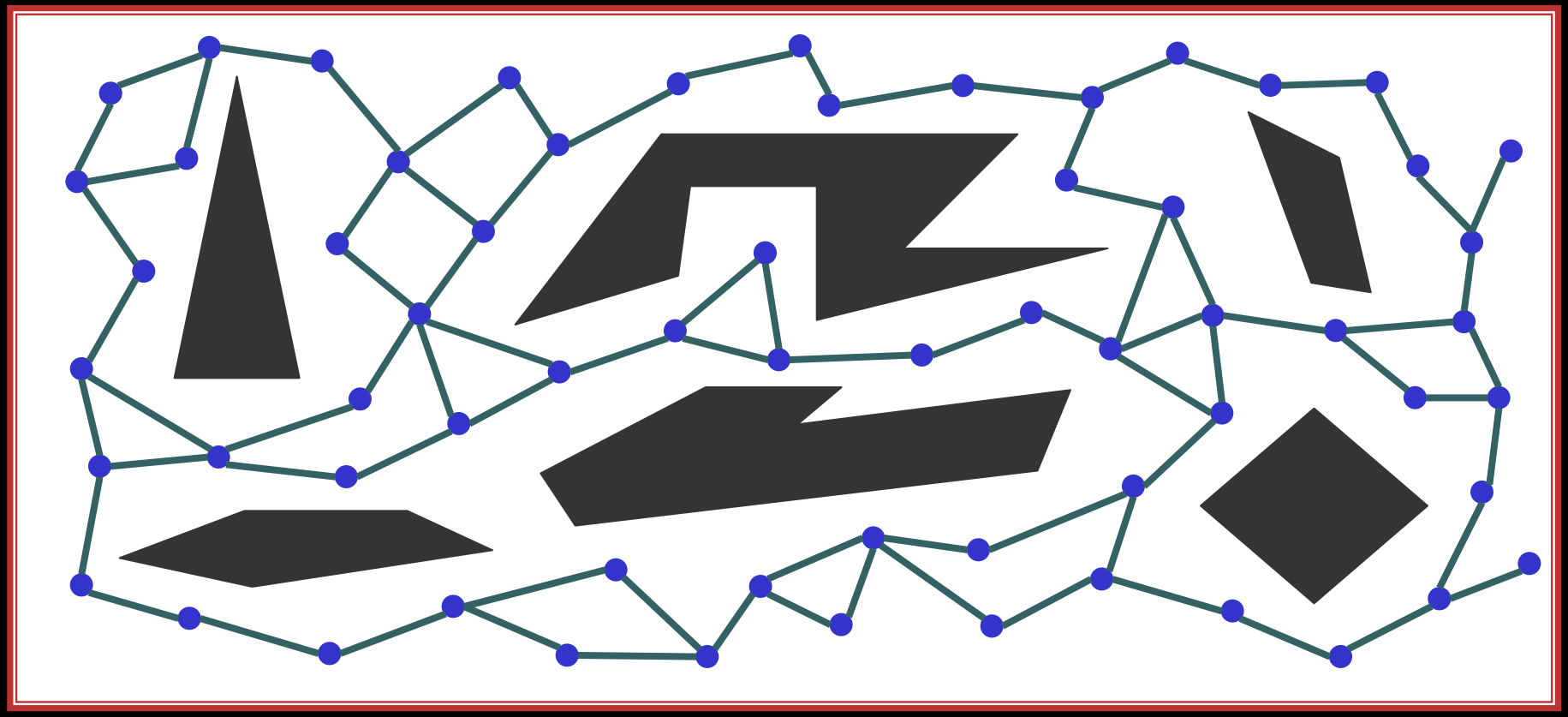
Probabilistic Roadmap Method (PRM)

Probabilistic Roadmap Method (PRM)



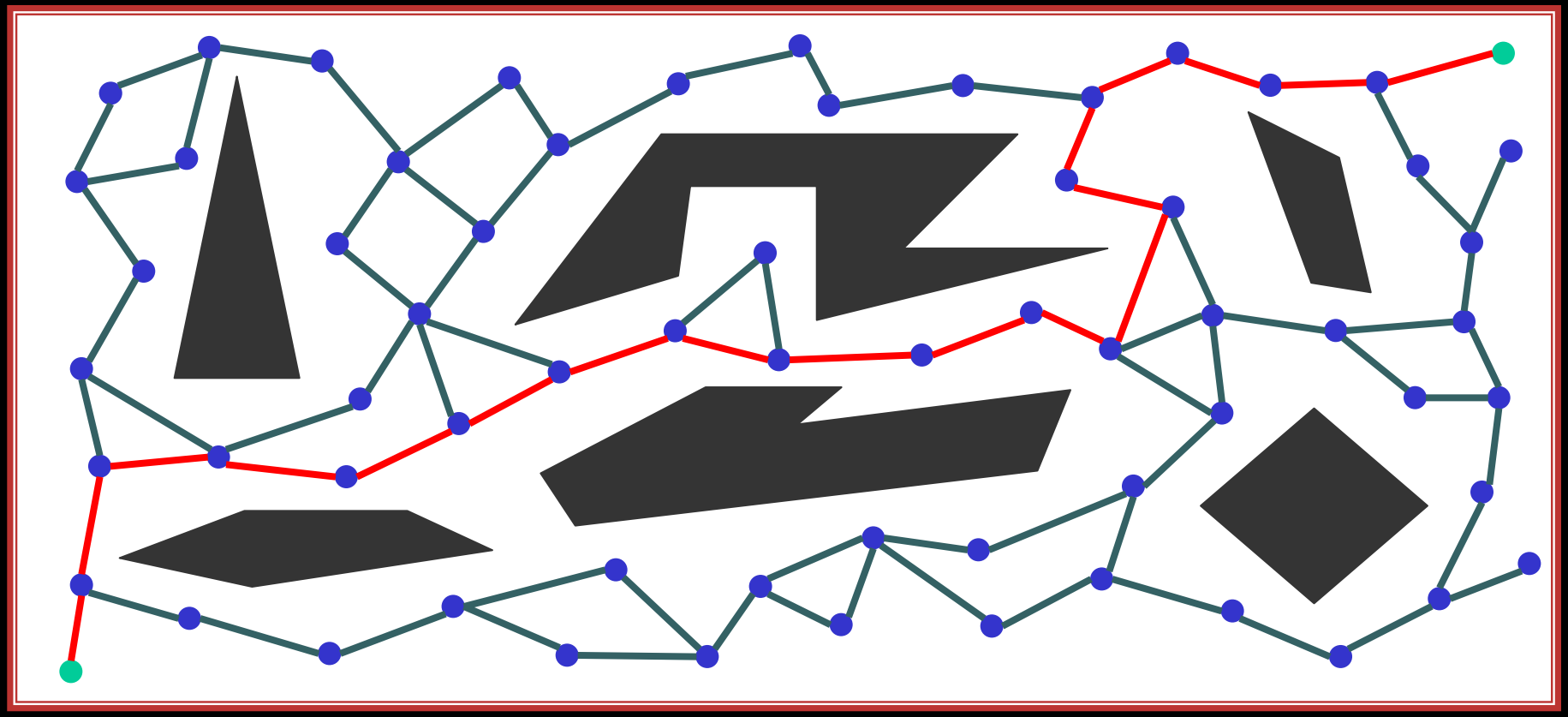
- **Nodes:** random configurations

Probabilistic Roadmap Method (PRM)



—**Edges:** computed by some local planner

Probabilistic Roadmap Method (PRM)



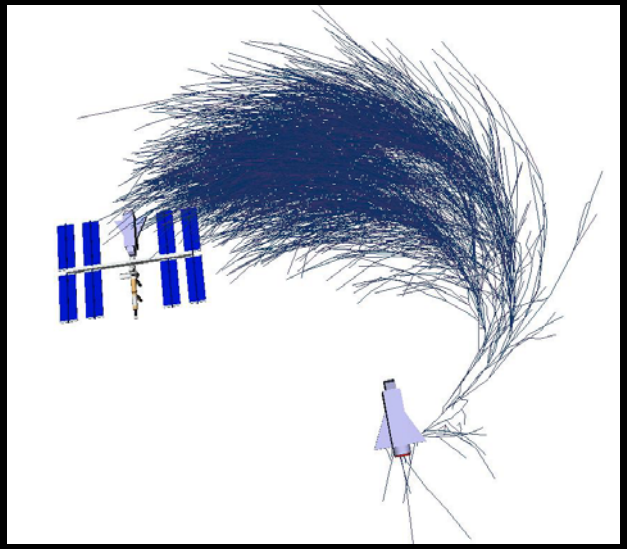
Plan a path

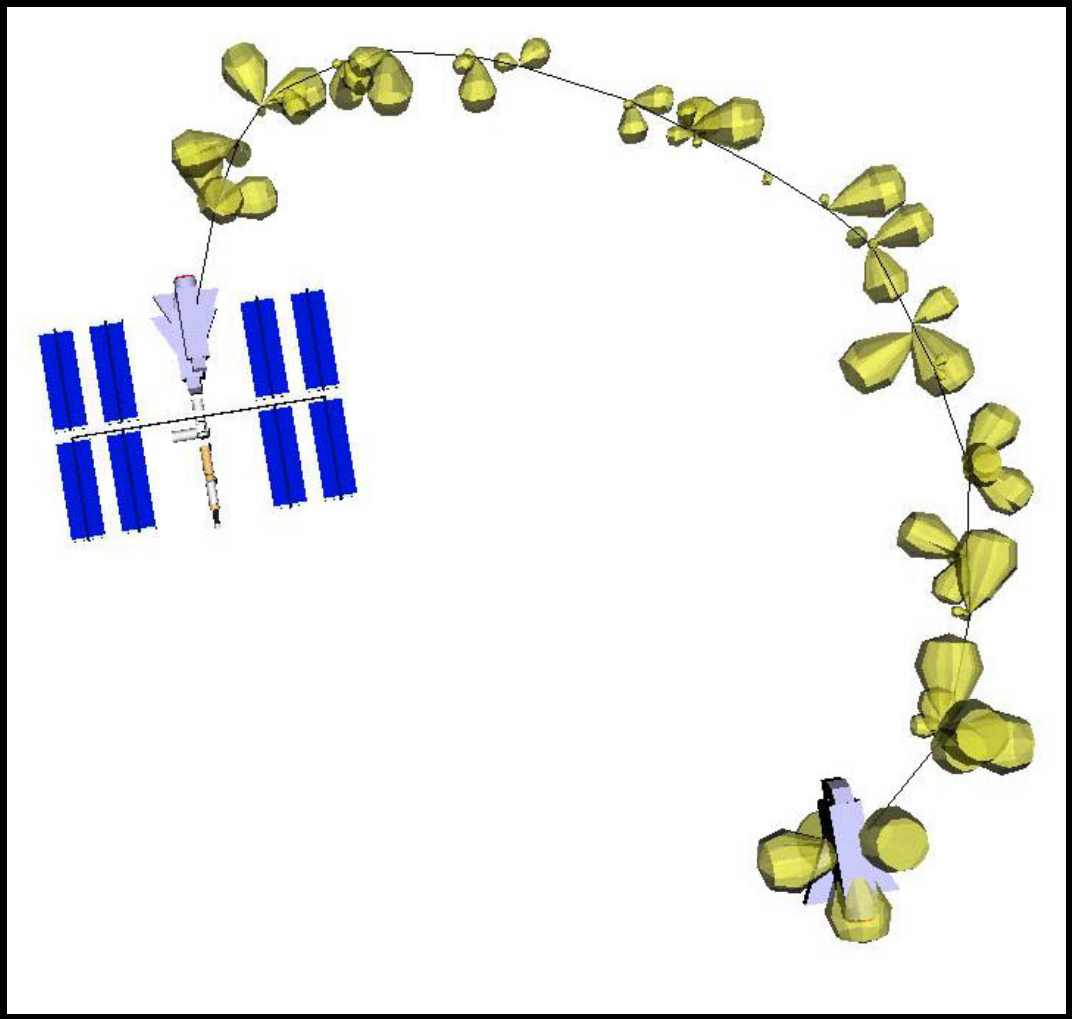
Connect start & goal to roadmap

Perform graph search

The Truth:
Search is Performed in High-dimensional Spaces

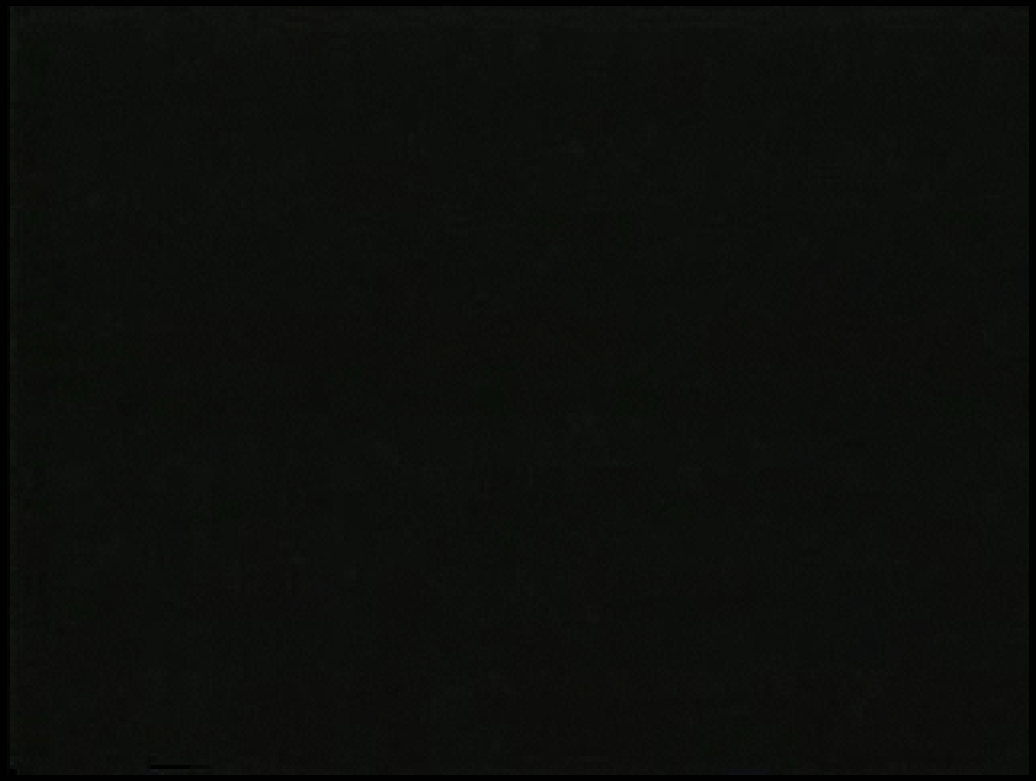
The Space Shuttle is a Robot





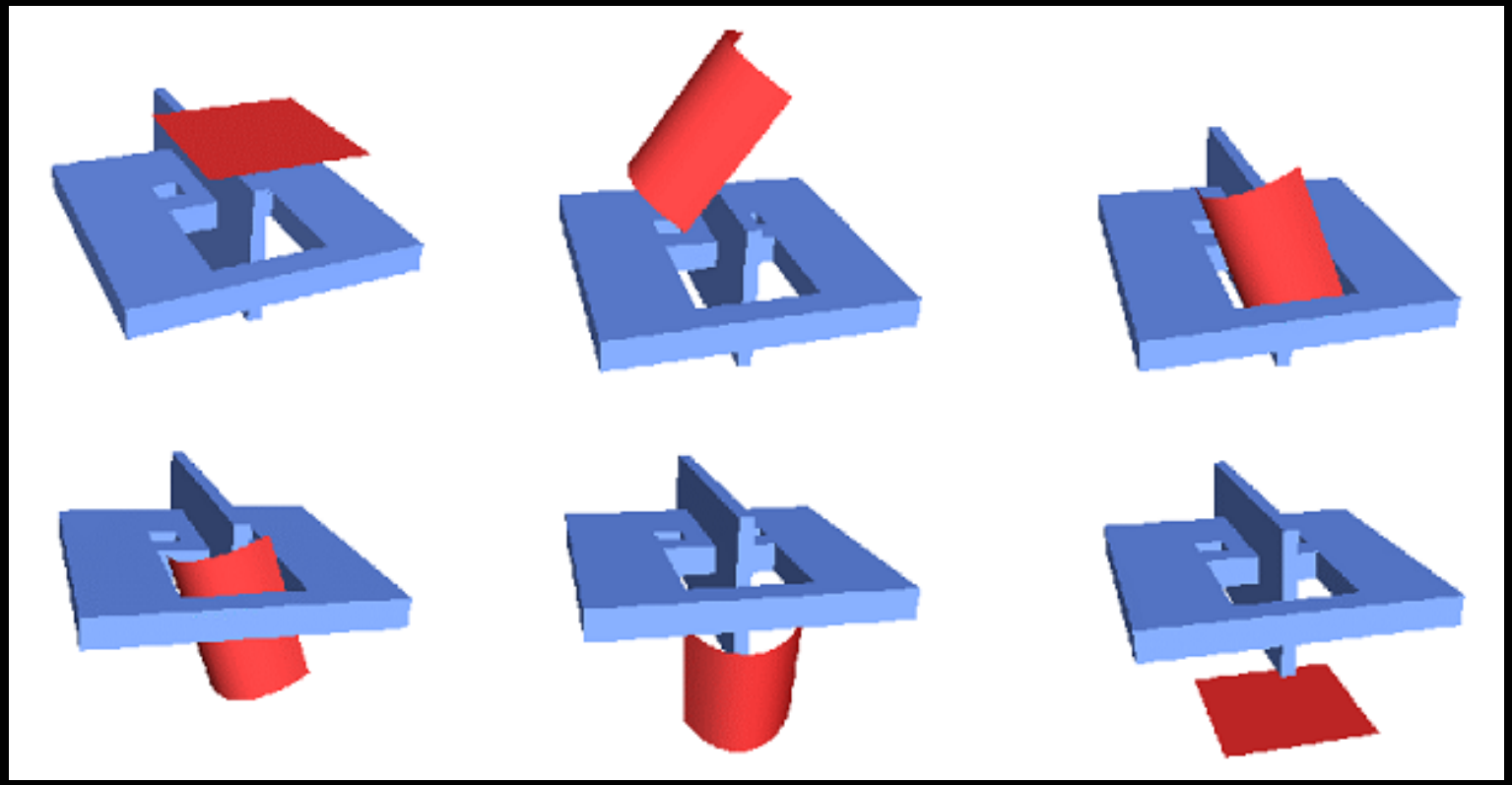
Docking the shuttle to the space station [Phillips, Kavraki, Bedrossian]

Parts are Robots!



[Li and Chen]

Flexible Parts are Robots

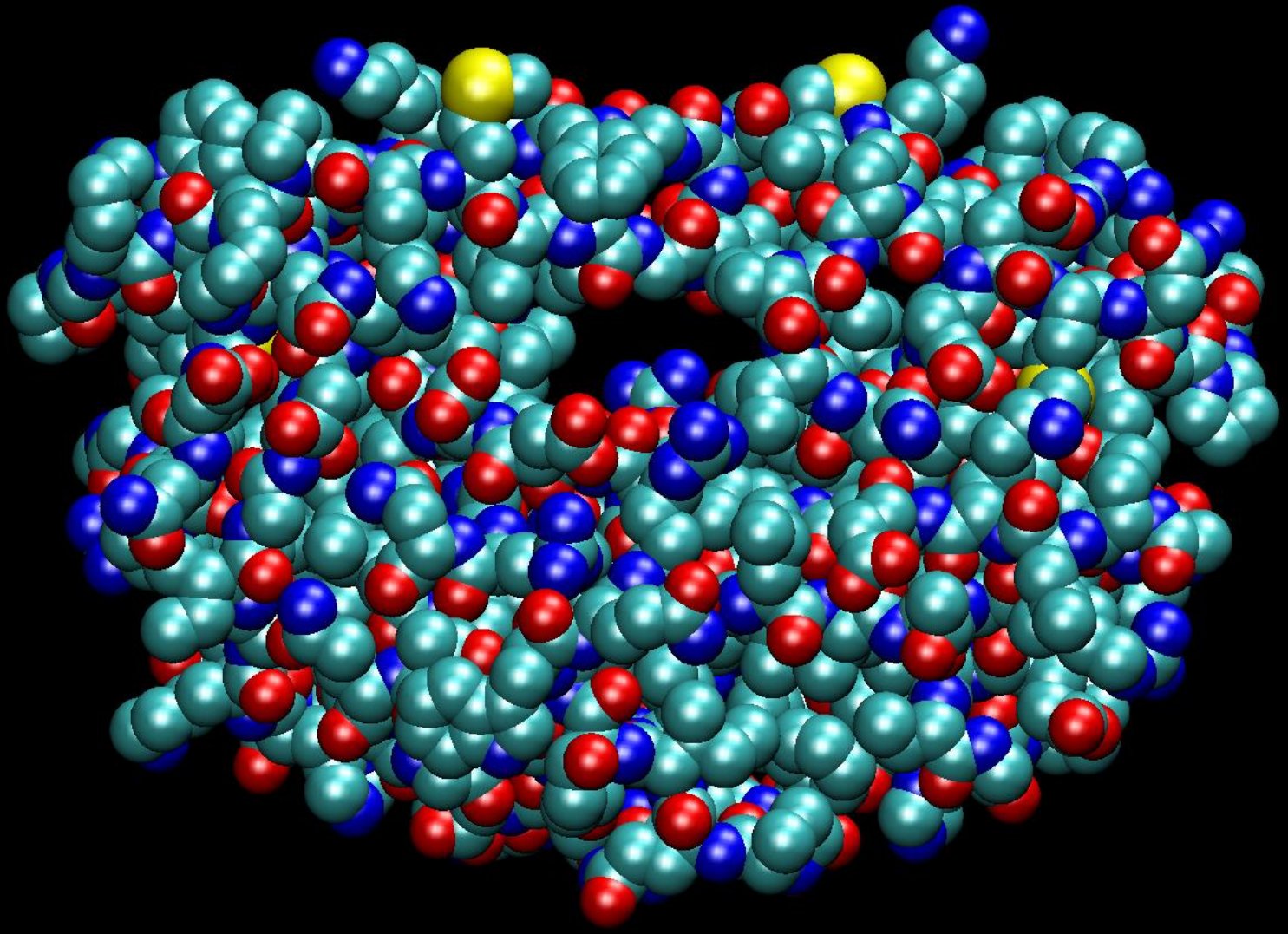


[Lamiraux and Kavraki]

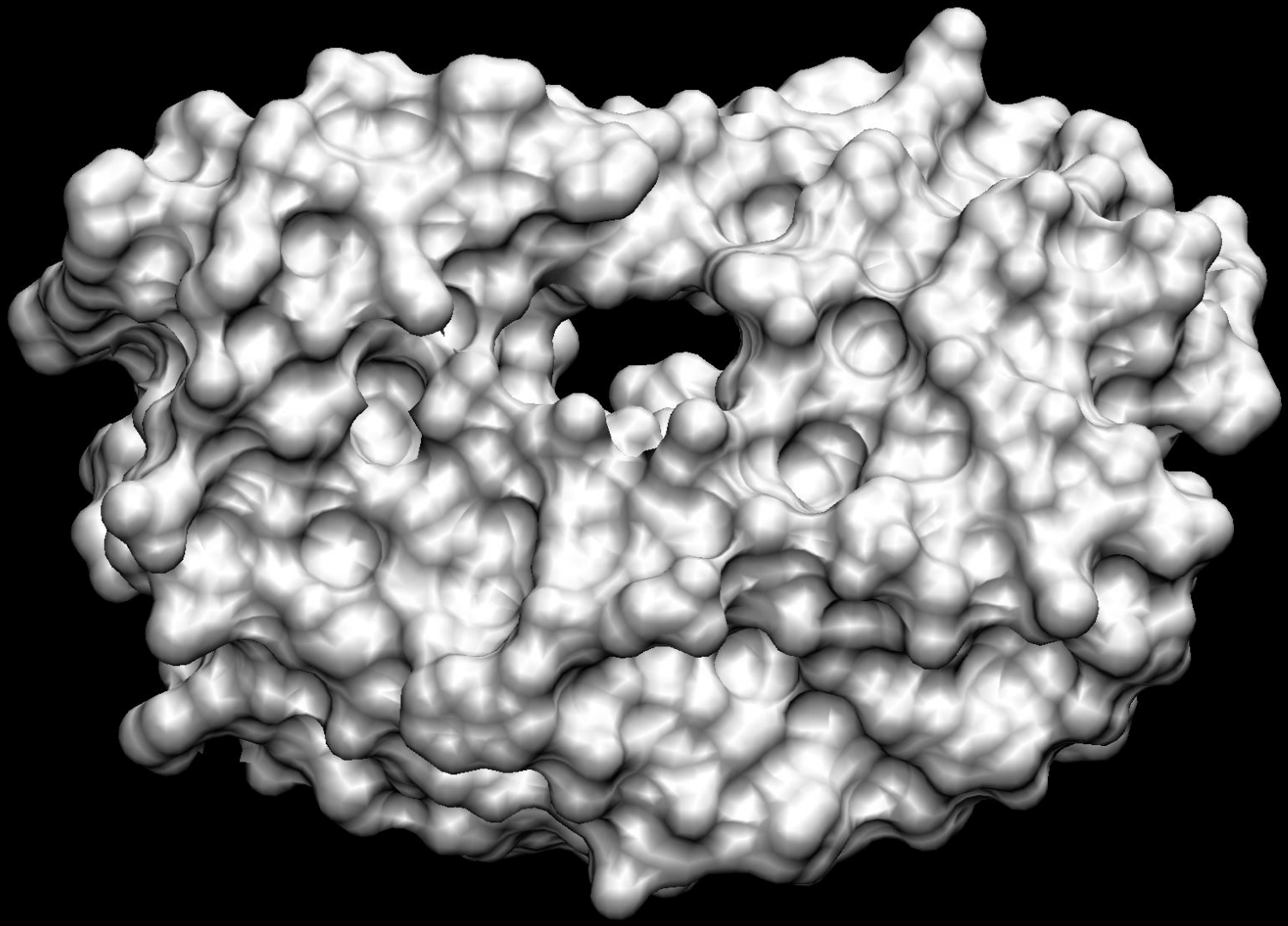
[Moll and Kavraki]

Biomolecules

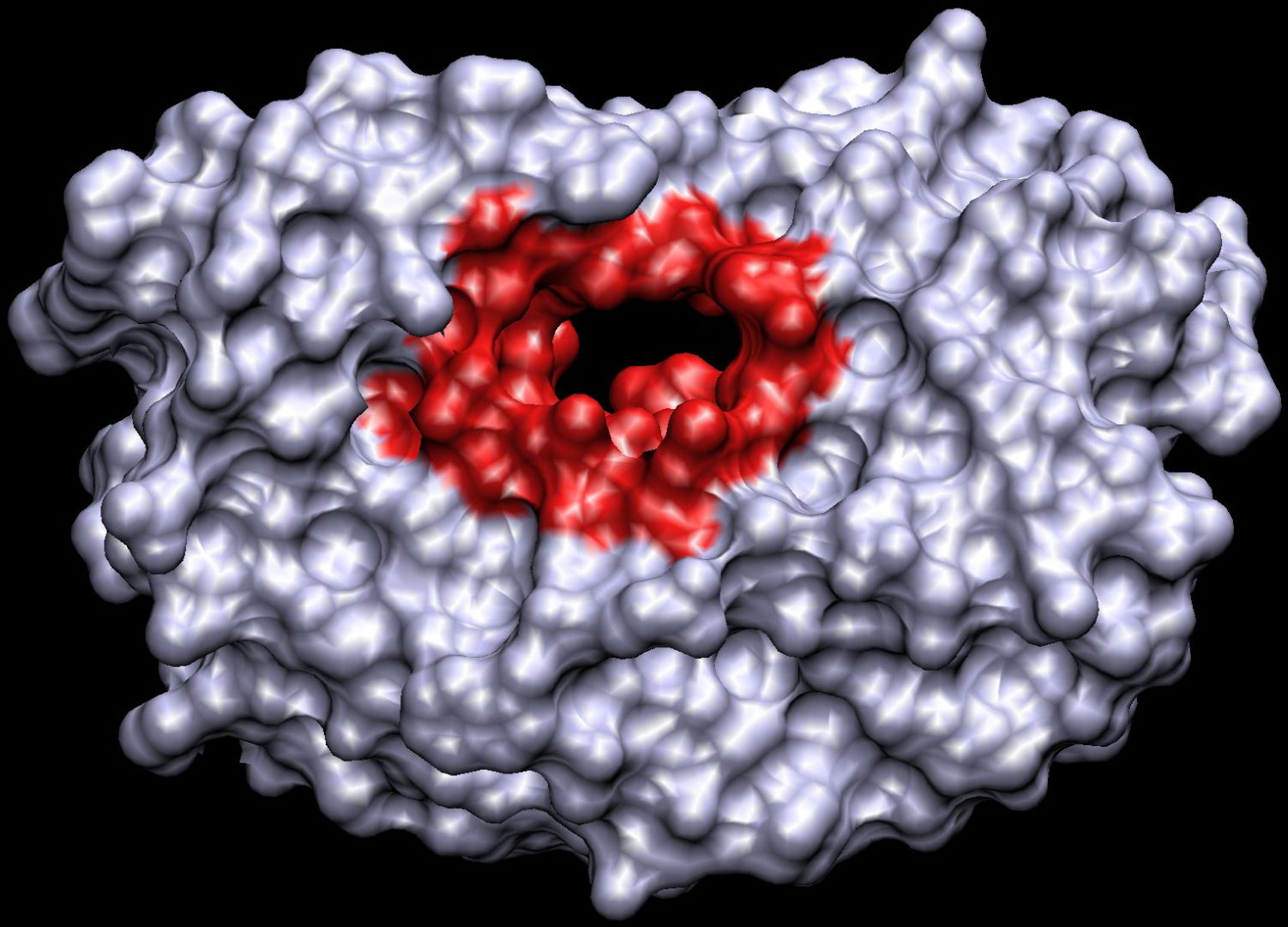
Proteins are Studied for Drug Discovery



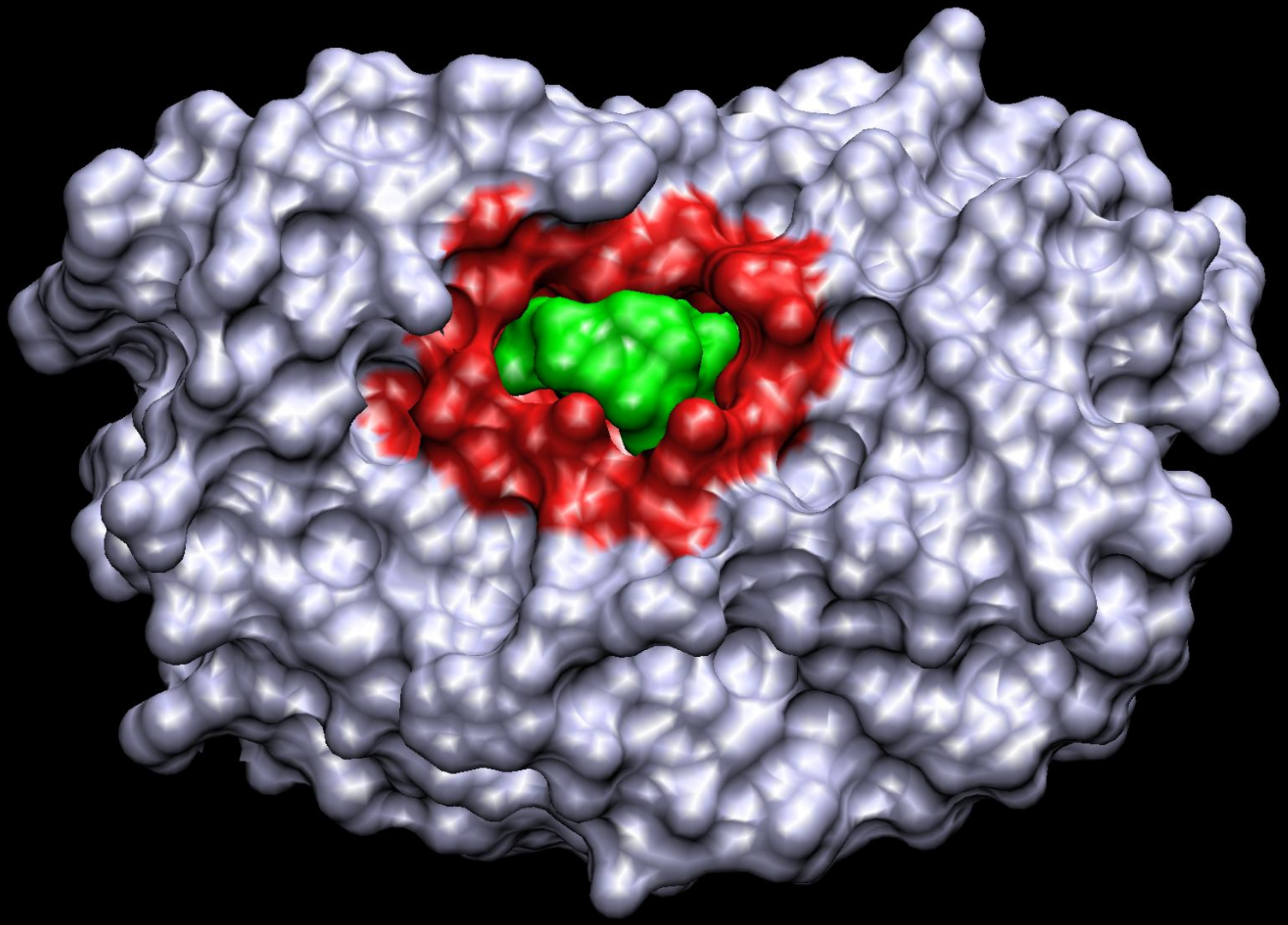
Proteins are Studied for Drug Discovery



Proteins are Studied for Drug Discovery

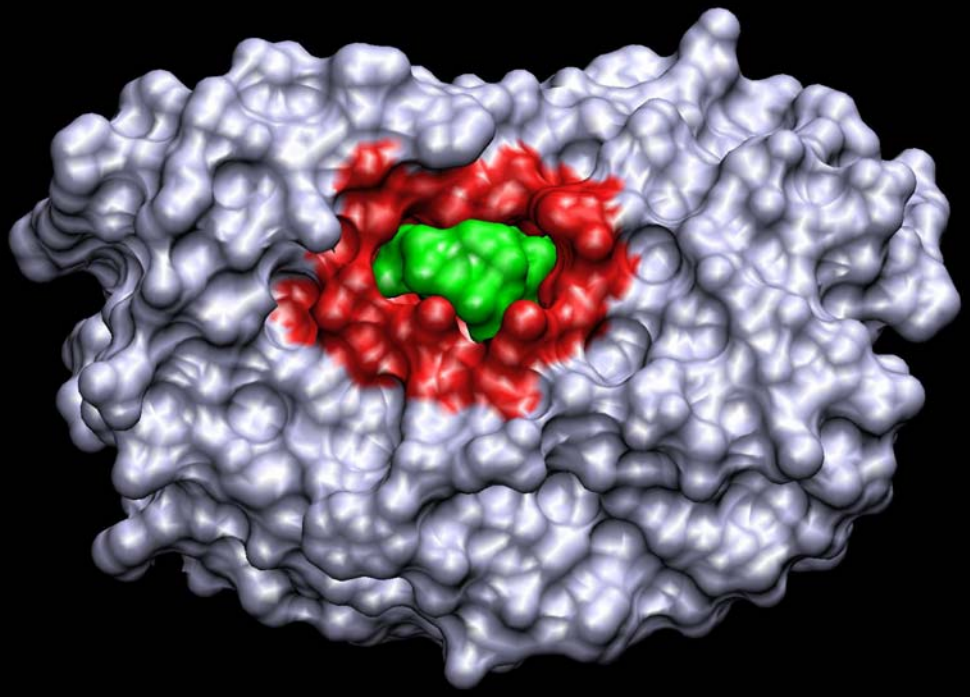


Proteins are Studied for Drug Discovery

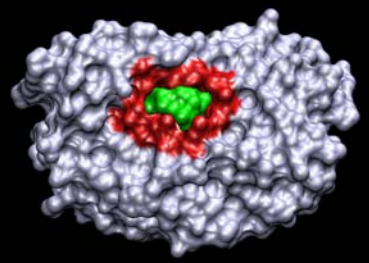


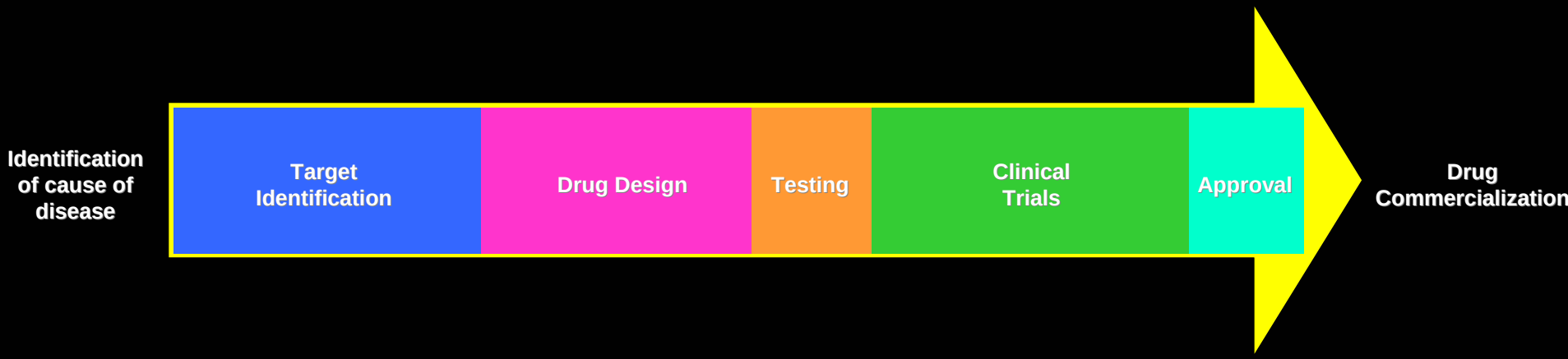
Computer-Aided Drug Discovery is a Reality

- Automated systems for screening *in silica* potential drugs
- Fast selection of good leads from a large database



The Drug Discovery Process





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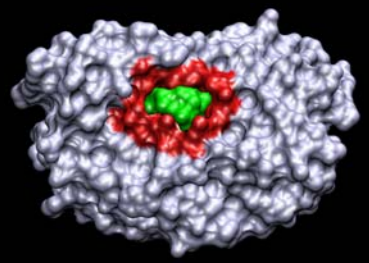
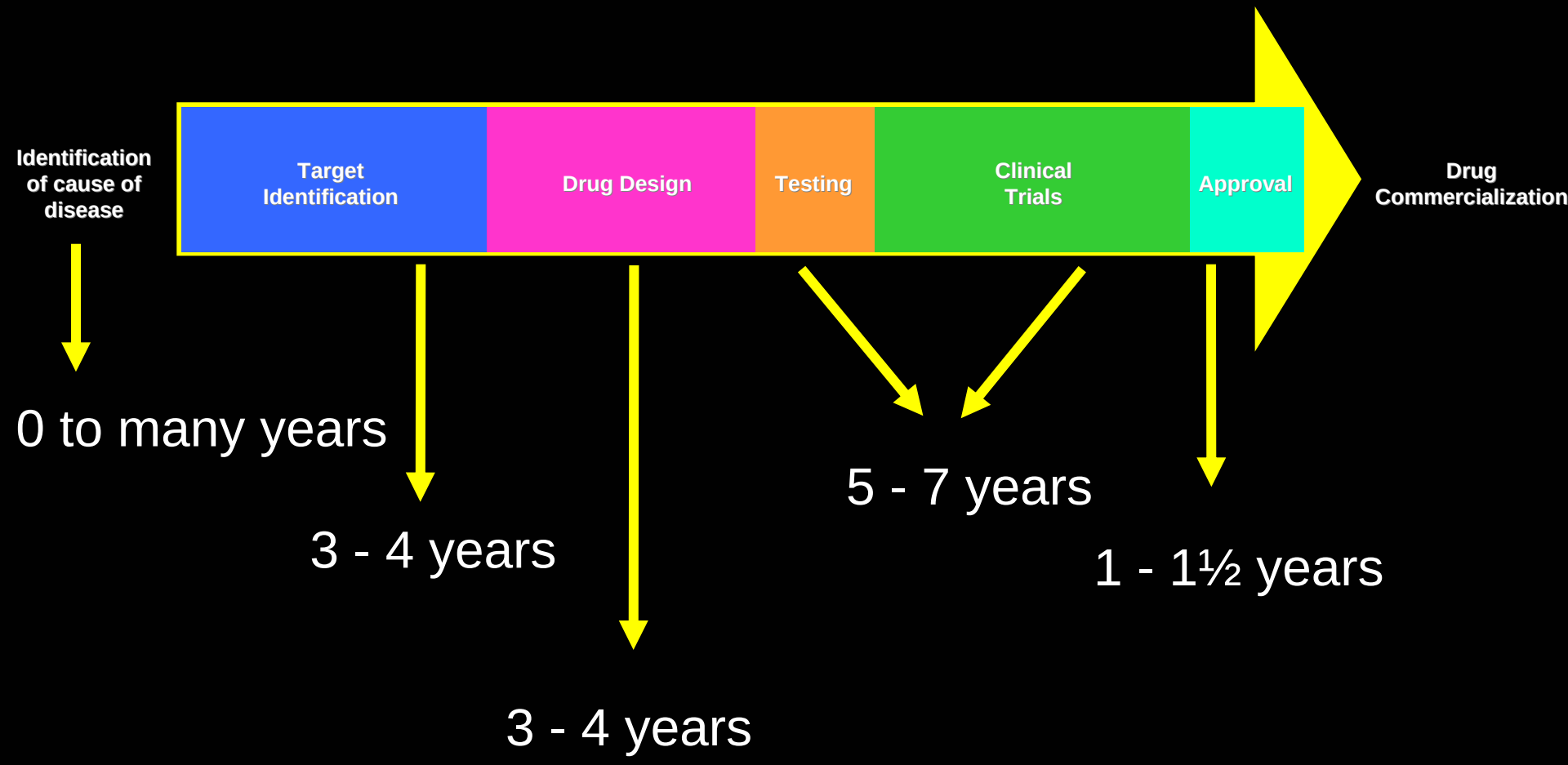
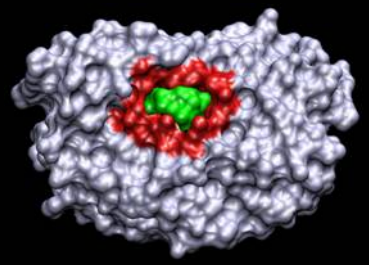
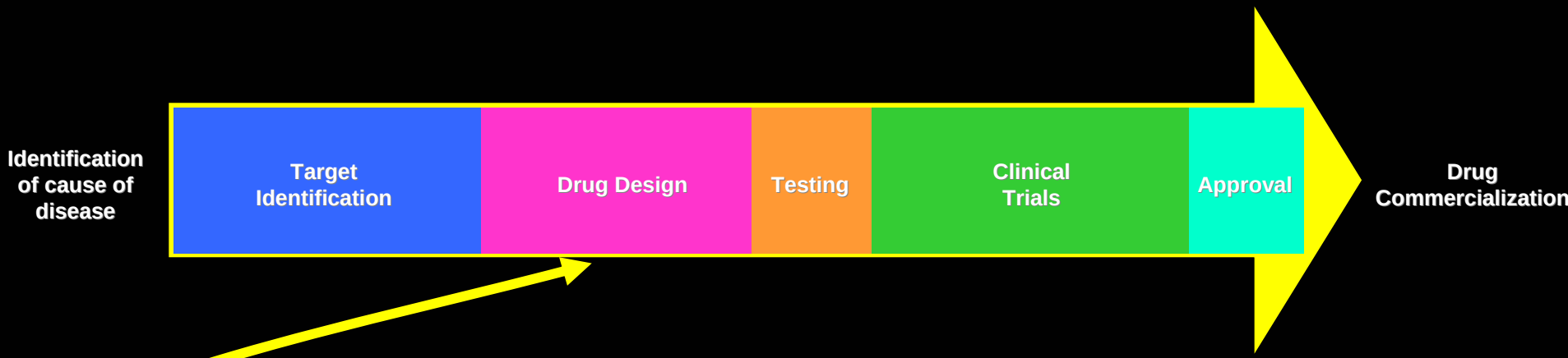




The Drug Discovery Process (Or Why Drugs Are Expensive)



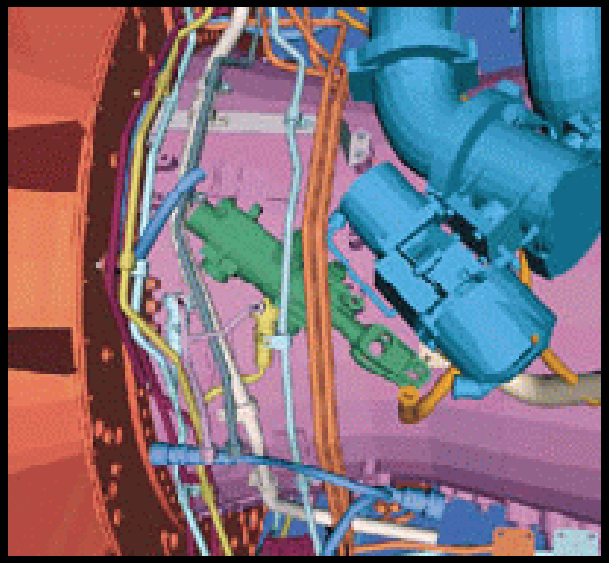


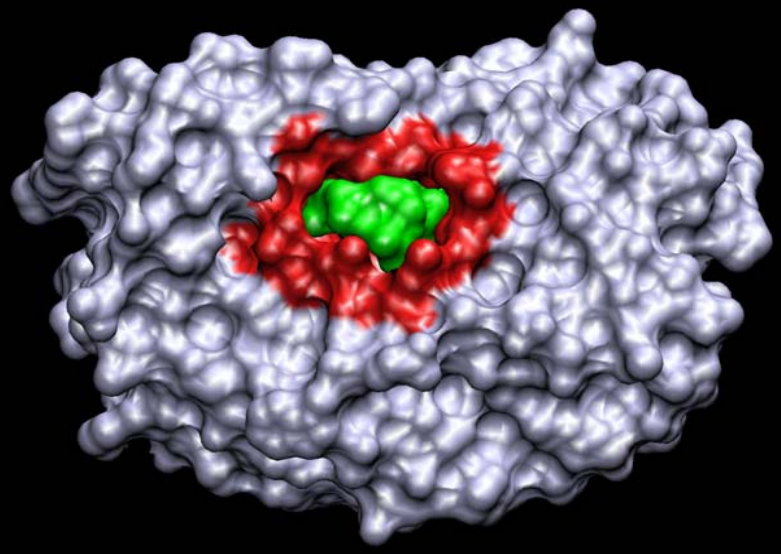
Total cost = 600 to 800 million dollars

Total time = 10 to 16 years

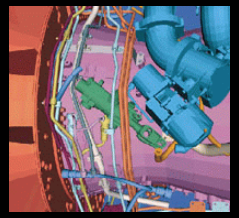
Fast selection of good leads is extremely important

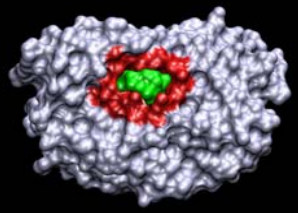
Drug Discovery: A Robotics-Inspired Solution

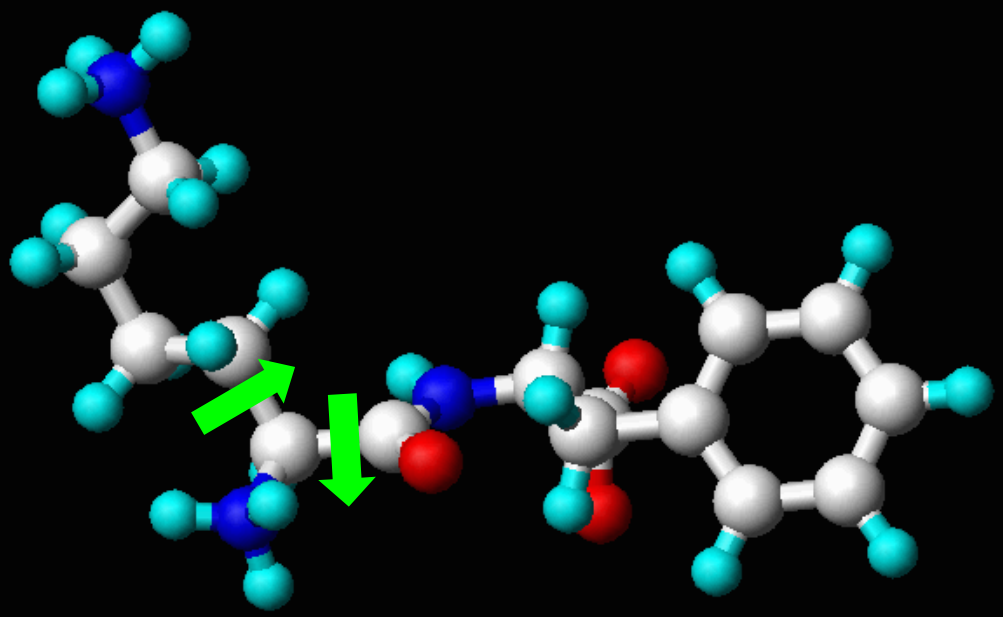




Small Molecule is Challenging

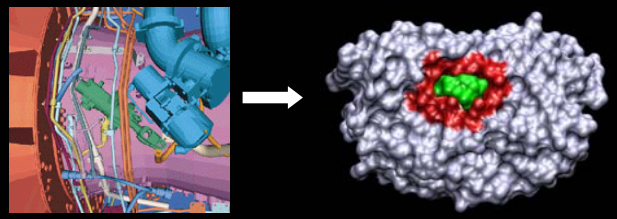


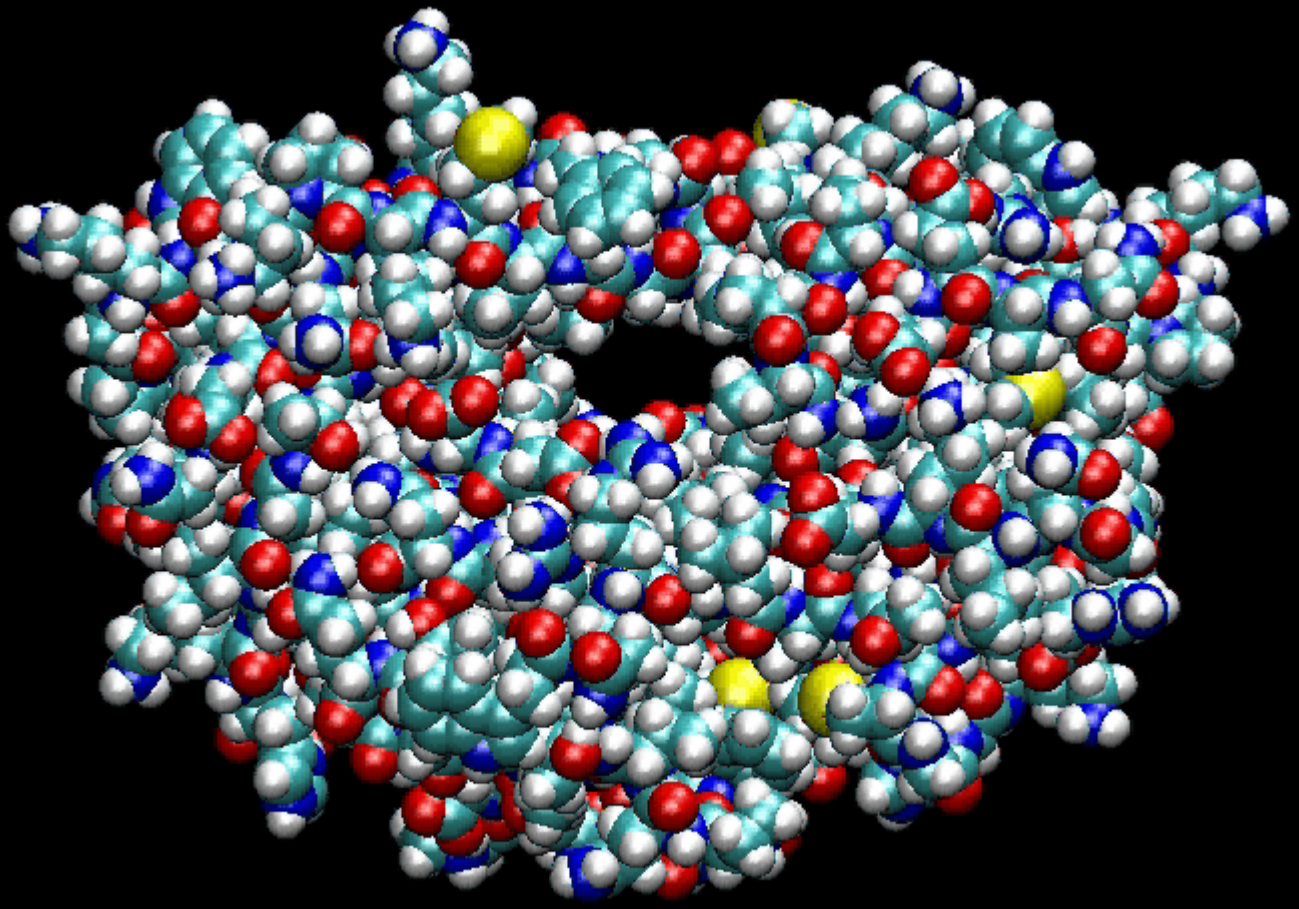




Parameters = Flexibility

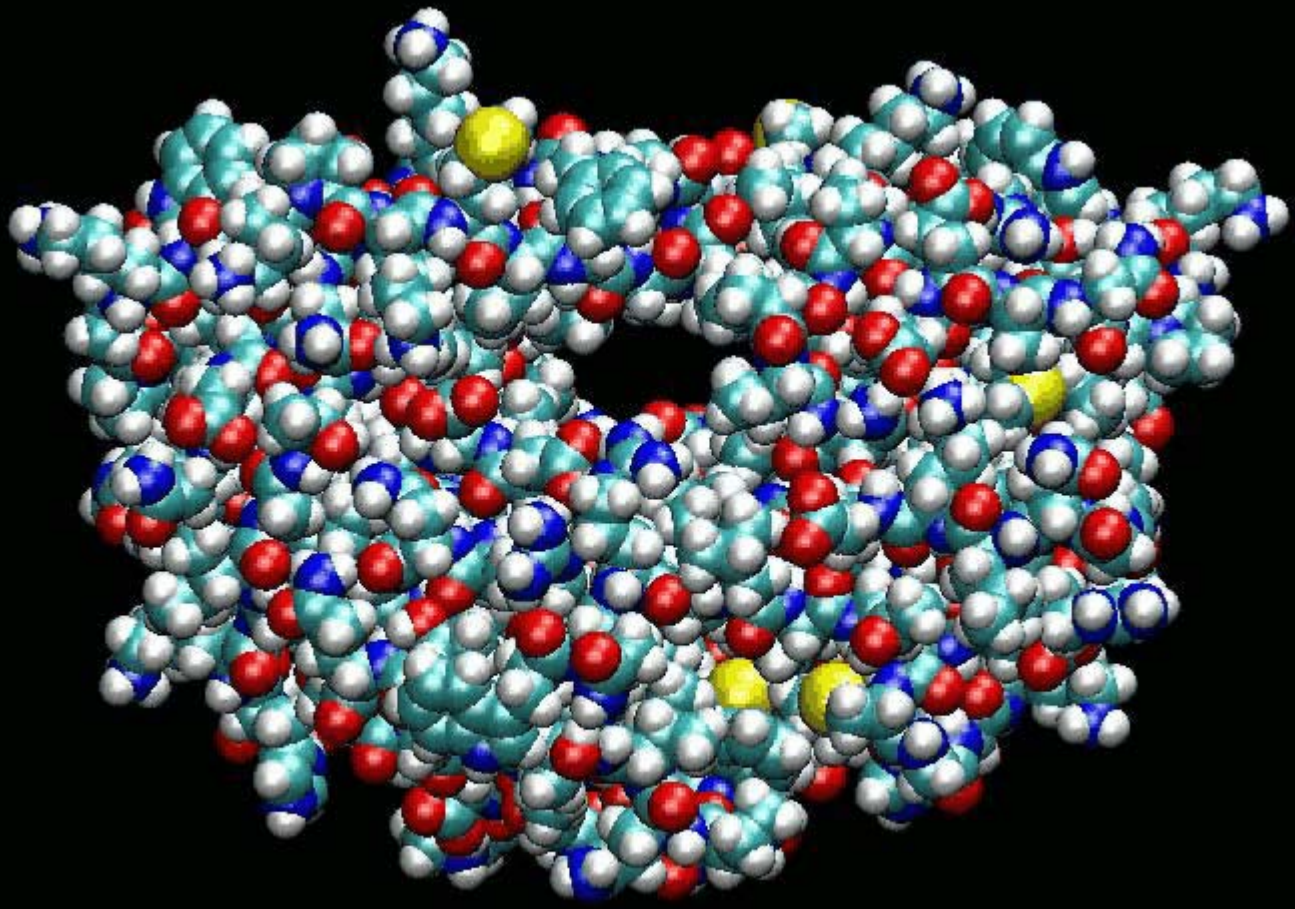
The Target Molecule is BIG



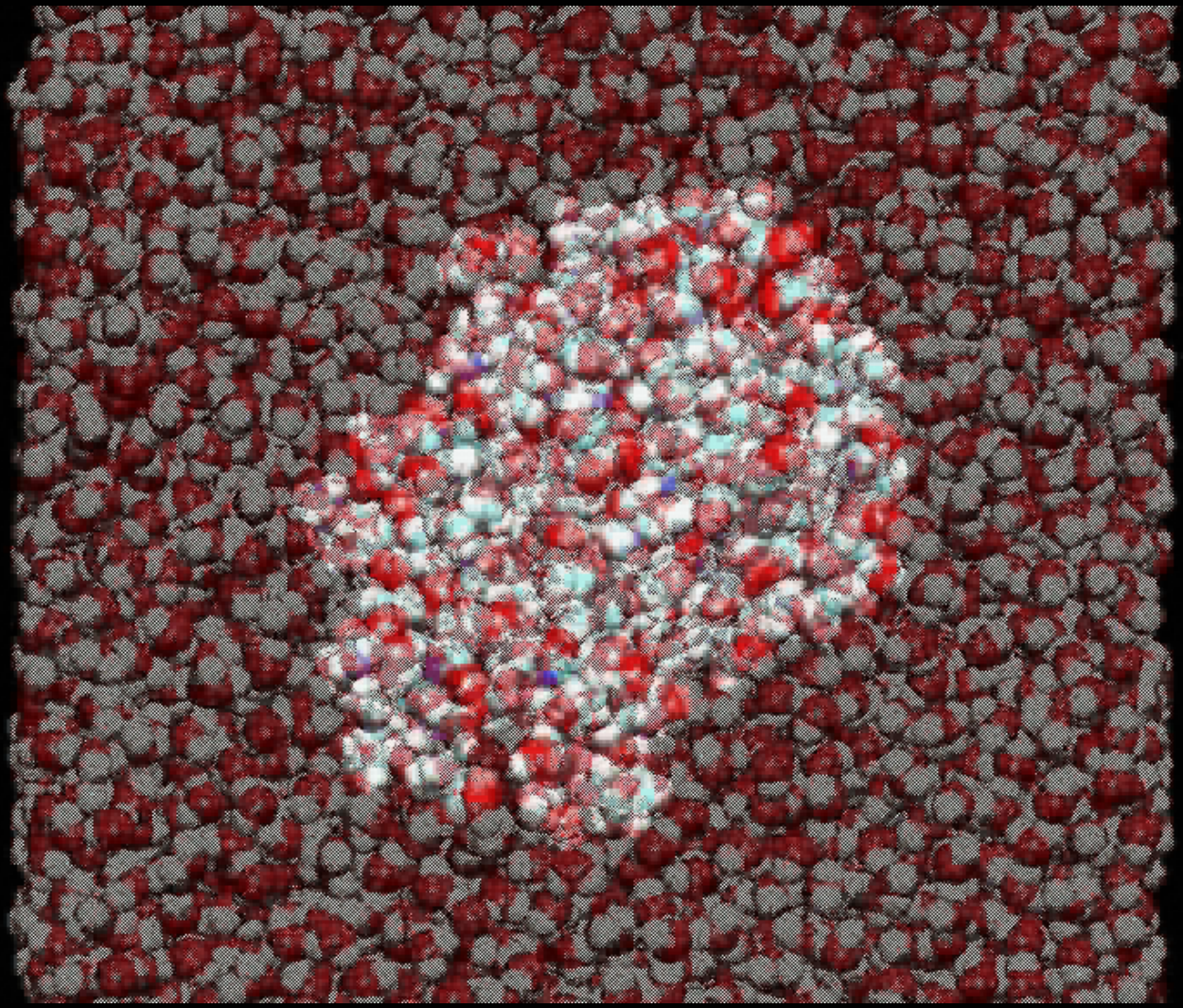


Do not think the molecule looks like this….

… it probably looks like this…

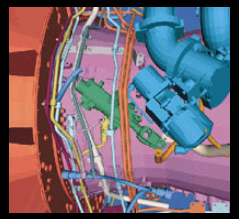


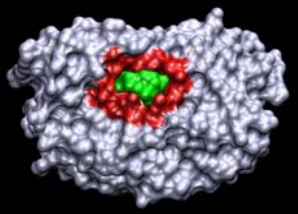
… or better like this…



[Cates, Teodoro, Phillips]

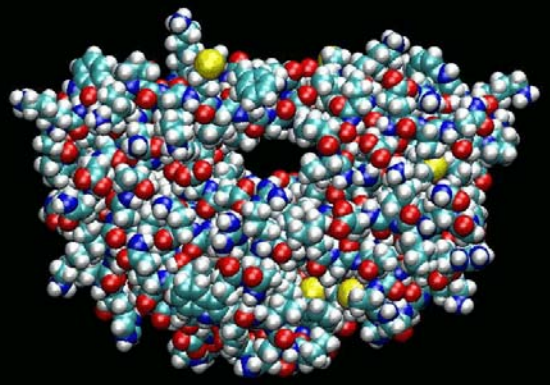
A Robotics-Inspired Solution

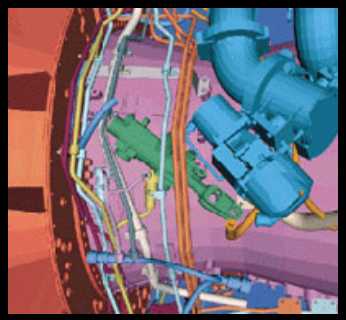


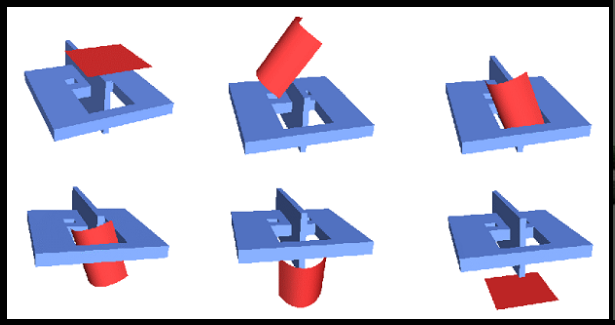


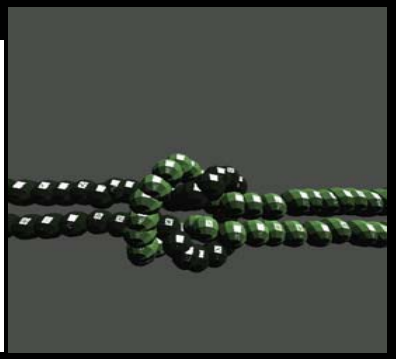
- Fit a flexible drug in a moving target
- Problem: too many parameters and too many constraints

1000s of parameters



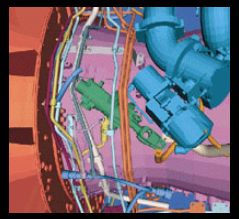


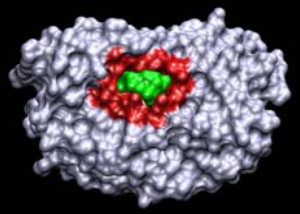




< 50 parameters

A Robotics-Inspired Solution

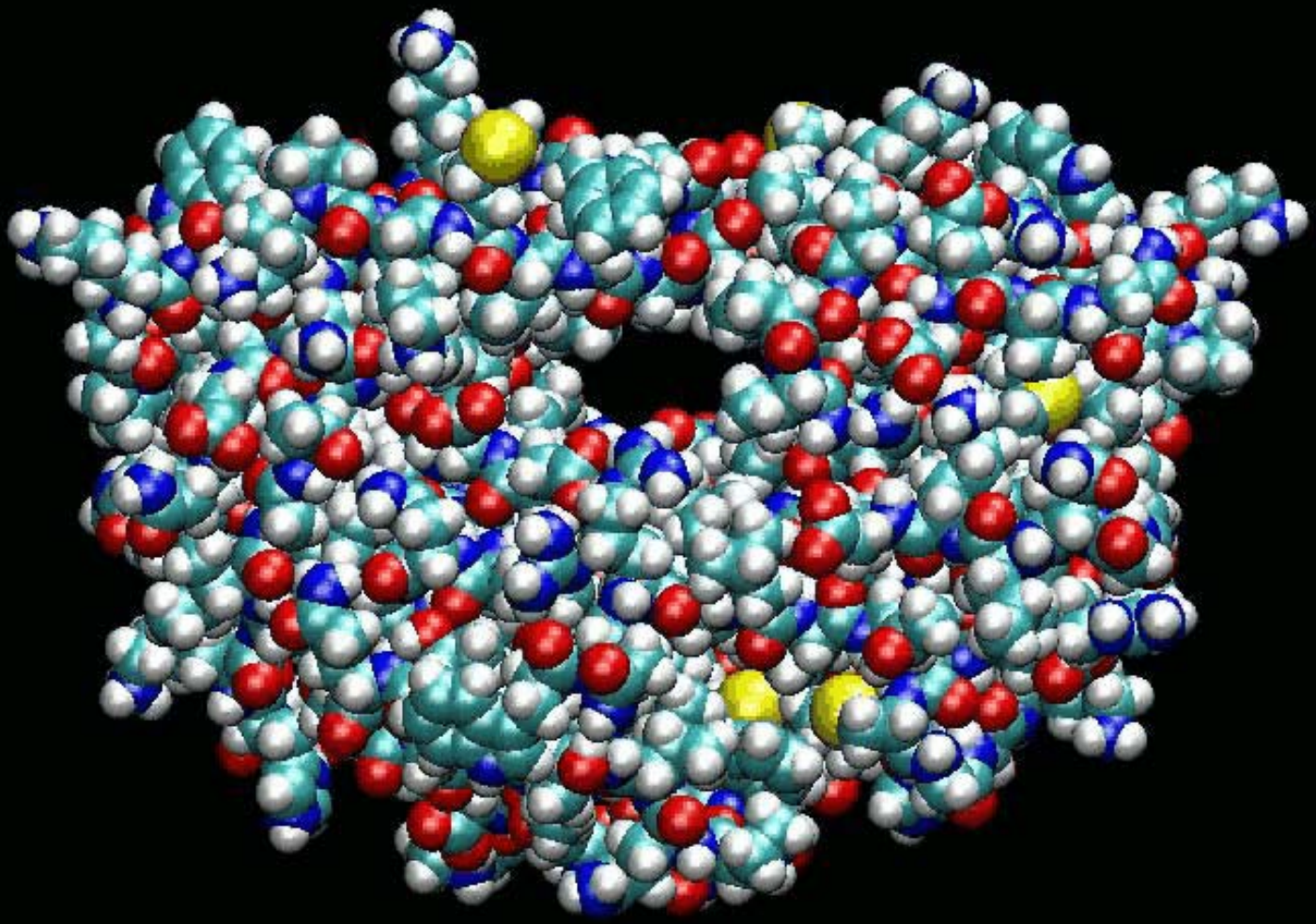




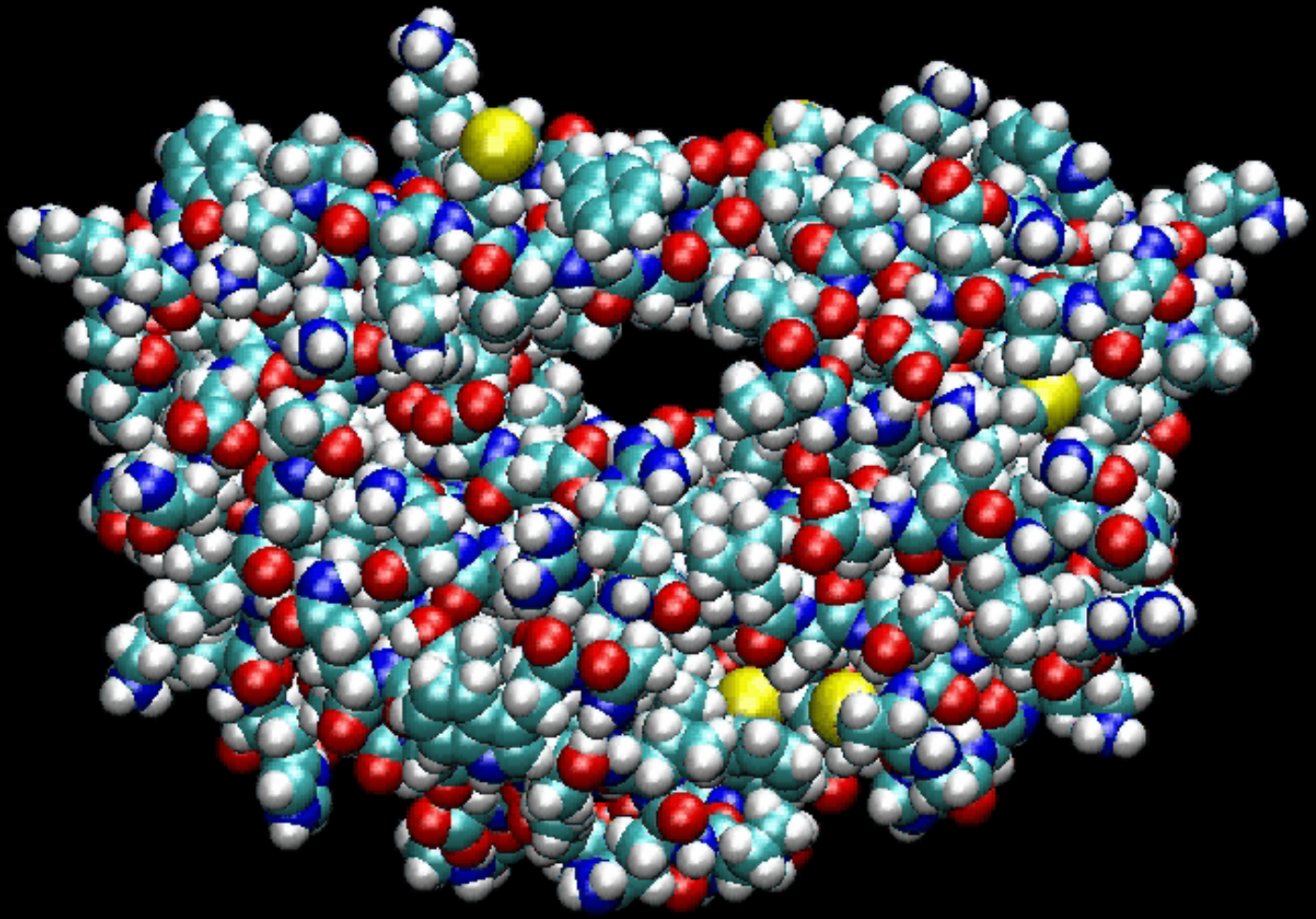
Fit a flexible drug in a moving target

- **STEP 1:** Reduce the parameters of the target
  (Model only essential flexibility)
- **STEP 2:** Simulate molecules with robots
- **STEP 3:** Use robotics methods

STEP 1: Model Essential Flexibility of the Target



STEP 1: Model Essential Flexibility of the Target



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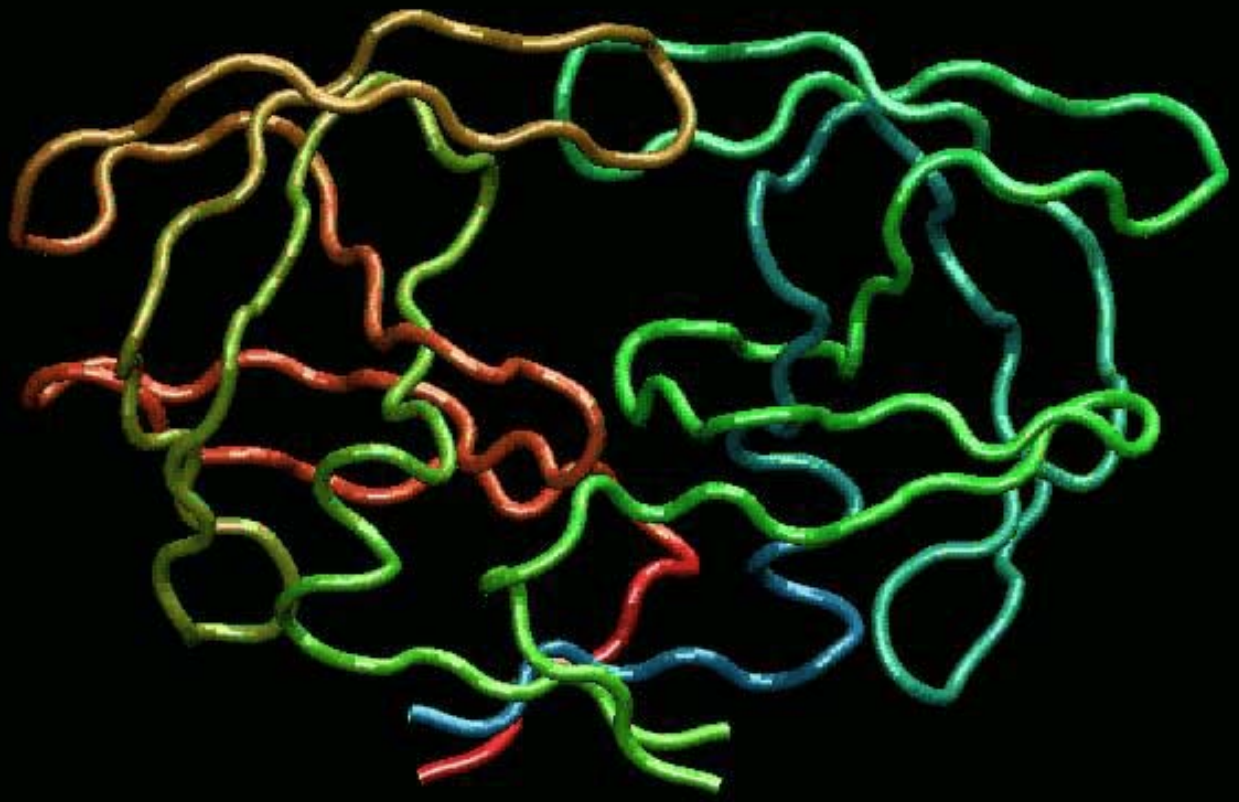
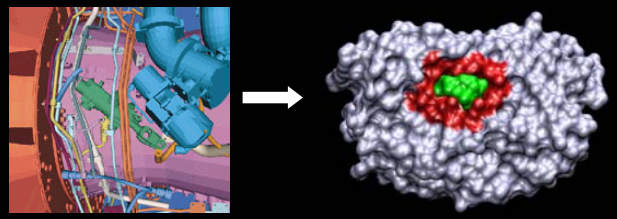


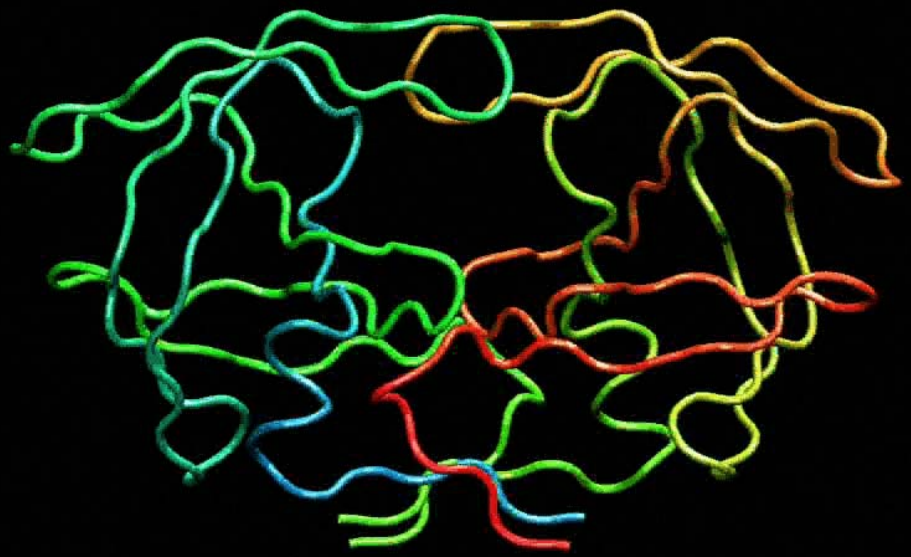
A Robotics-Inspired Solution



STEP 1:

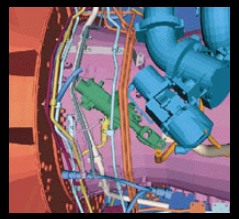
- Dimension-reduction methods isolate essential motion
- Meaningful new reduced parameterization

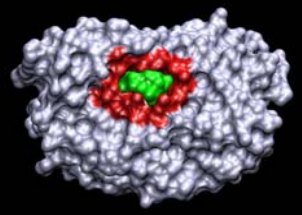
1st parameter:

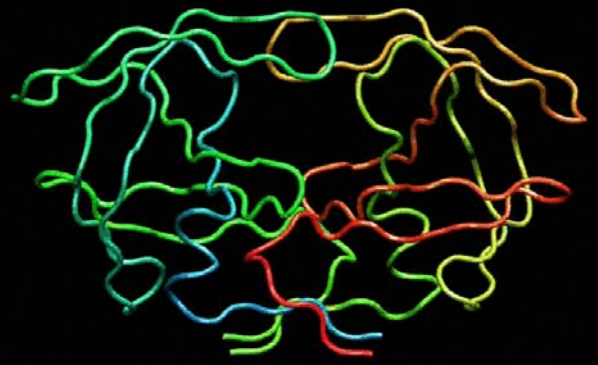


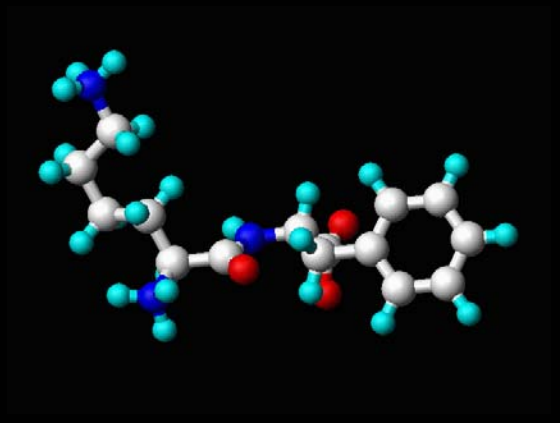
40 parameters capture 90% of motion

A Robotics-Inspired Solution









Reduced parameter set (~40)

Full parameter set (~10)

+ Energy

(statistical mechanics and biophysics)

Use PRMs

OK, but new approaches are needed

Things Have to Change

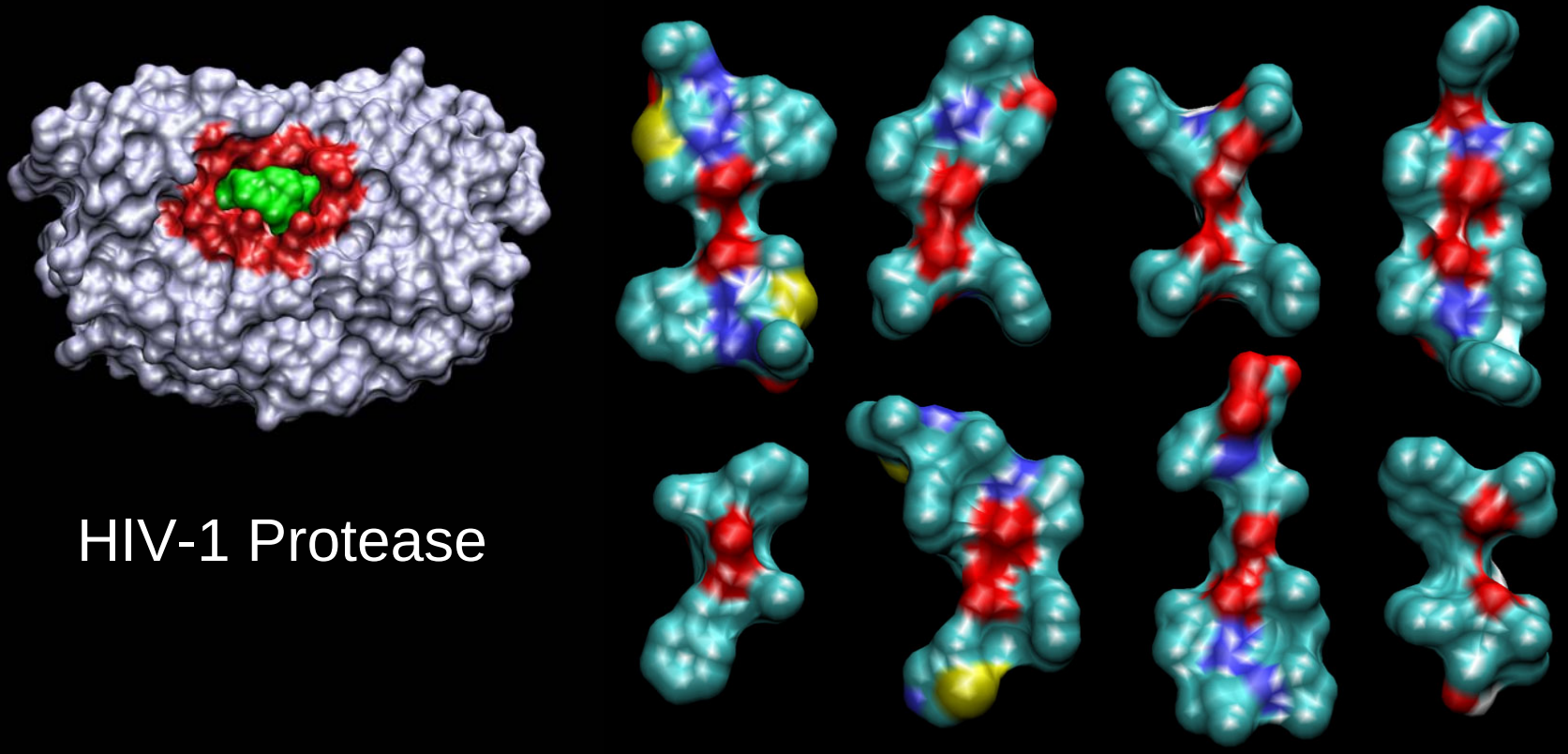
- New algorithms
- High Performance Computing

- New ways of mining the data

Guess What?

Along the way, we developed a more powerful robotics planner too

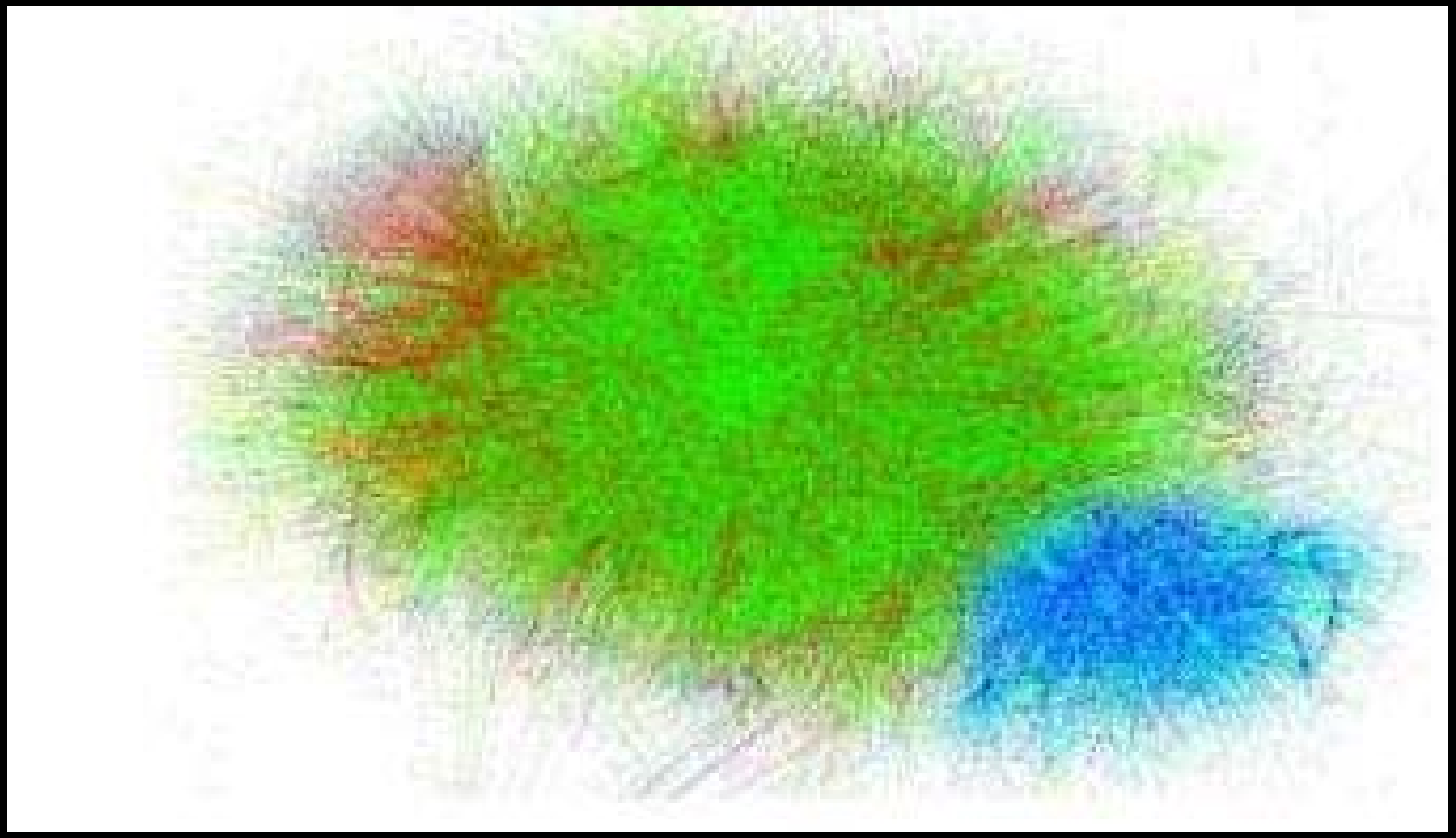
Have we Solved the Problem?



HIV-1 Protease

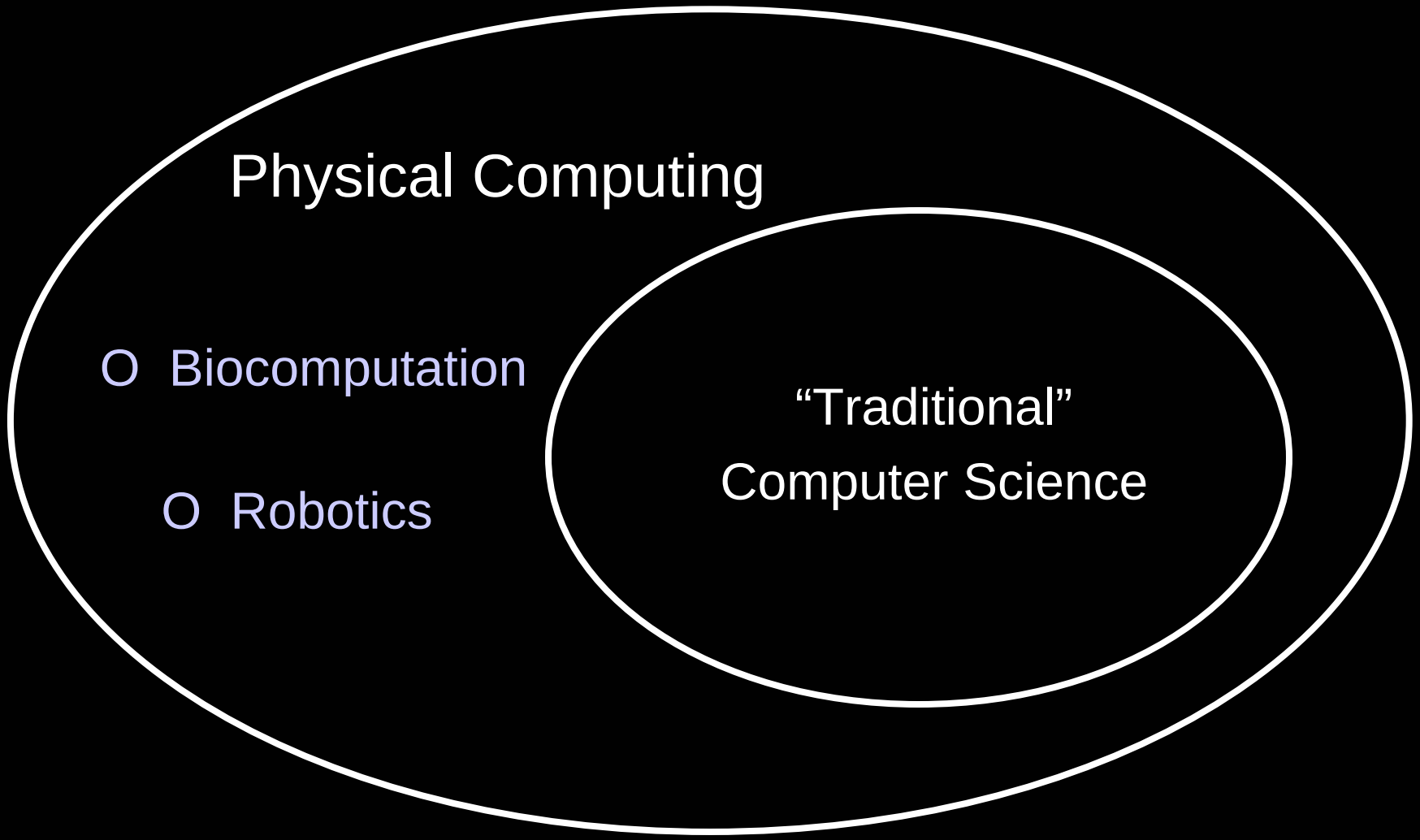
A challenge for Computer Science

Systems Biology: Making Connections



From C&EN, 2005

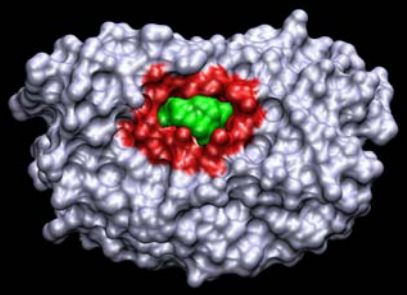
What's in this for Computer Science?

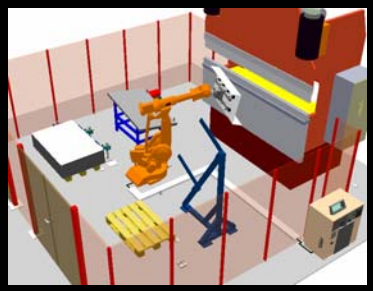


What's in This for Computer Science?

Characteristics of physical problems:

- Very high-dimensional problems
- Geometric complexity
- Physical constraints
- Imperfect models and uncertainty





Needed:

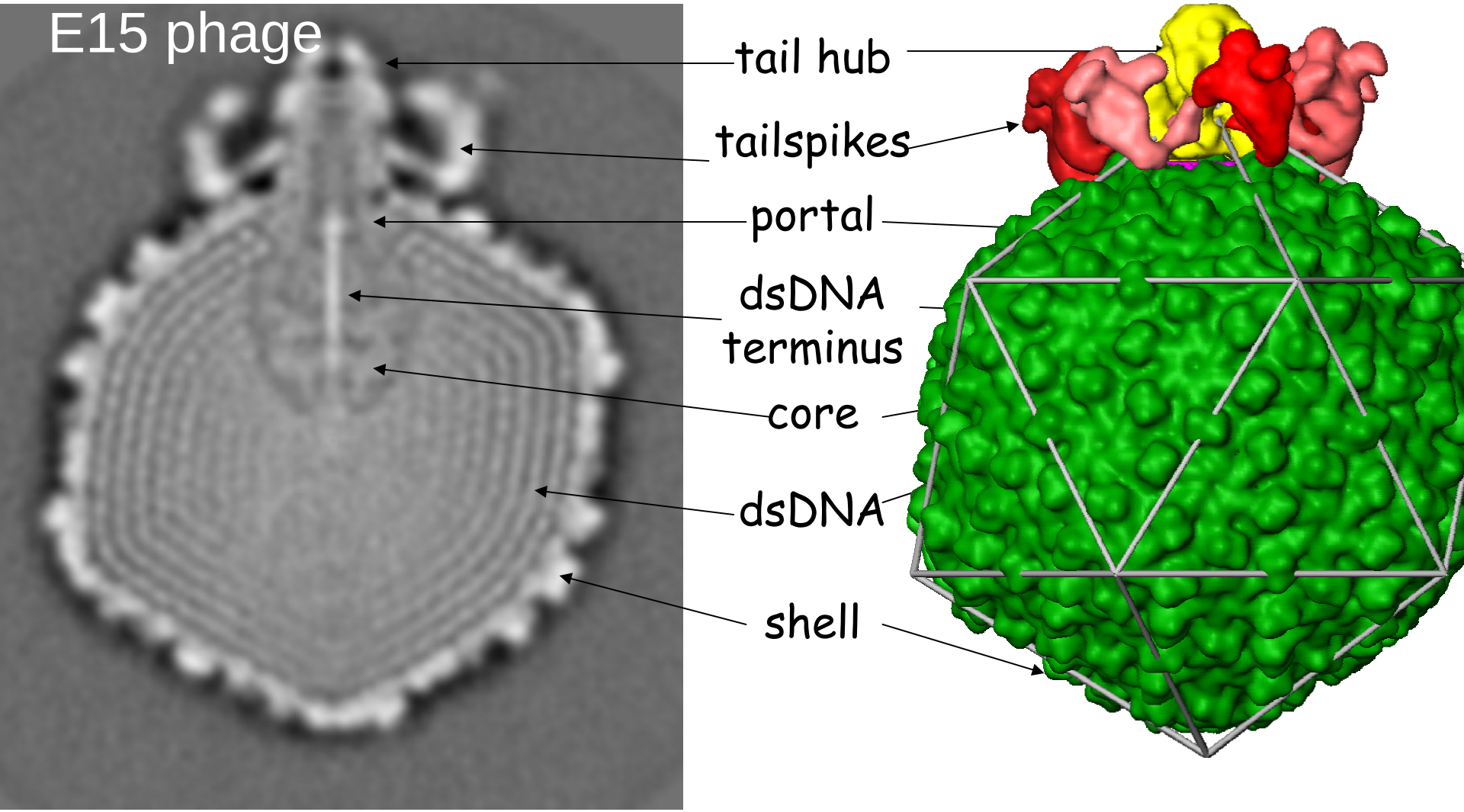
- New kinds of algorithms and analysis methods
- Representations for mobile data
- Meaningful approximations
- Critical discretizations and adaptive parameterizations

What's in This for Computer Science?

Needed:

- Representation and visualization techniques
- Storage, transfer and coordination of huge amounts of data
- New programming paradigms, languages and compilers
- New computer architectures, high performance systems, and software support

Biocomputations are Growing in Complexity

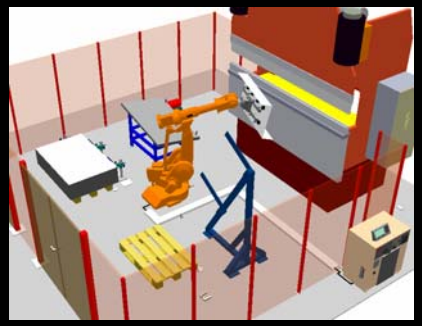
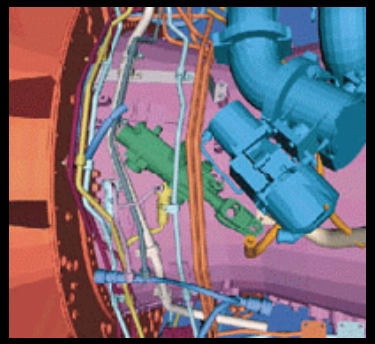
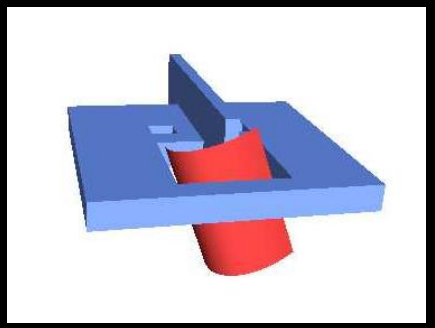
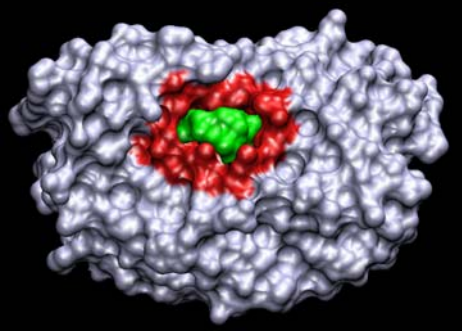


W. Jiang, J.Chang, J. Jakana, P. Weigele, J. King, W. Chiu, Nature 2006

Computer Science for Science
will not work in the long run
without fundamental advances in Computer Science

Physical Computing

- Robotics: Development of human-centered devices
- Drug Discovery: In silica design of new therapeutics

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Thank you