BMC WorkShop

Protein Structure Prediction

Introduction

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Objective

TO LEARN HOW-TO MODEL A 3D-STRUCTURE FROM SEQUENCE

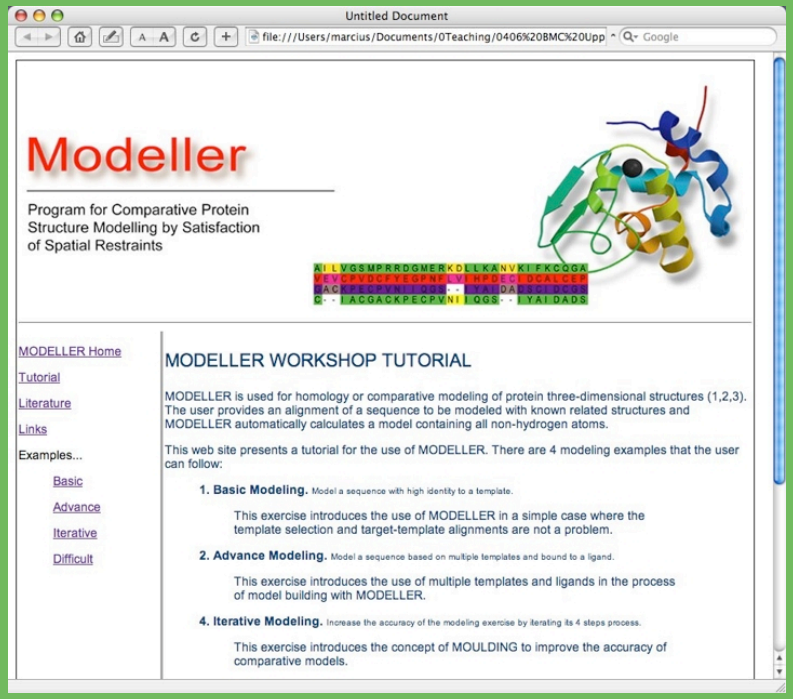
Program

Template Search

Target – Template Alignment

Model Building

Model Evaluation



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What are we going to do?

- Ask!
- Each day…
  - Basic introduction
  - Theory (representation-scoring-optimization)
  - Available programs
  - Application

Nomenclature

Homology: Sharing a common ancestor, may have similar or dissimilar functions

Similarity: Score that quantifies the degree of relationship between two sequences.

Identity: Fraction of identical aminoacids between two aligned sequences (case of similarity).

Target: Sequence corresponding to the protein to be modeled.

Template: 3D structure/s to be used during protein structure prediction.

Model: Predicted 3D structure of the target sequence.

protein prediction .vs. protein determination

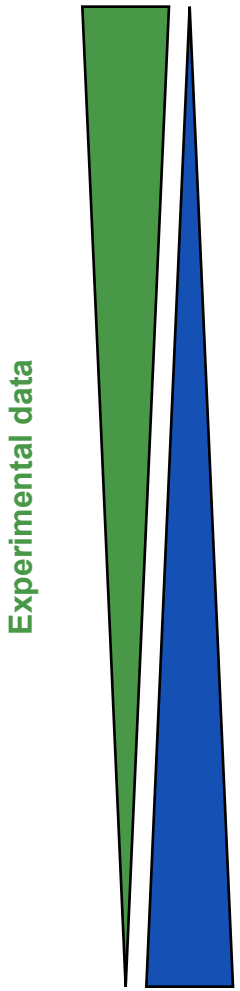
X-Ray

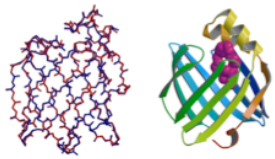
NMR

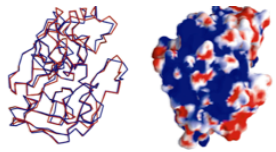
Comparative Modeling

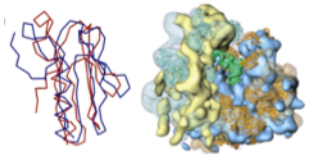
Threading

Ab-initio









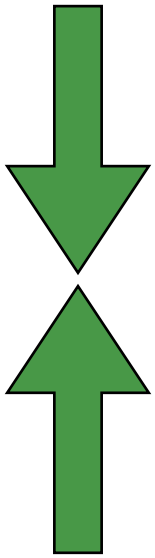
Why protein structure prediction?

	Y 2004	Y 2006
Sequences	1,500,000	millions
Structures	28,000	50,000

Why protein structure prediction?

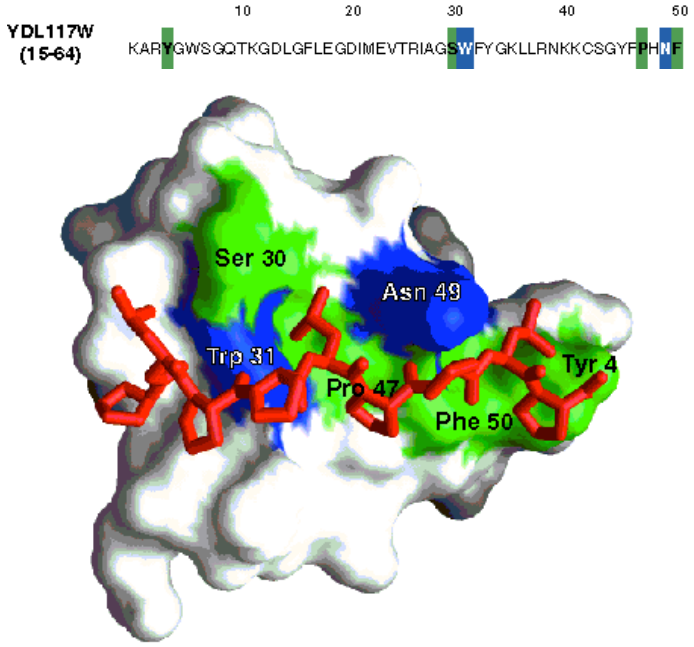
	Y 2004
Sequences	1,500,000
Structures	400,000

http://salilab.org/modbase/



Why is it useful to know the structure of a protein, not only its sequence?

- The biochemical function (activity) of a protein is defined by its interactions with other molecules.
-
- The biological function is in large part a consequence of these interactions.
-
- The 3D structure is more informative than sequence because interactions are determined by residues that are close in space but are frequently distant in sequence.

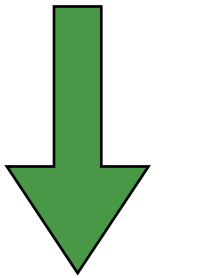


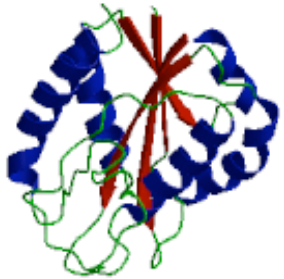
In addition, since evolution tends to conserve function and function depends more directly on structure than on sequence, structure is more conserved in evolution than sequence.

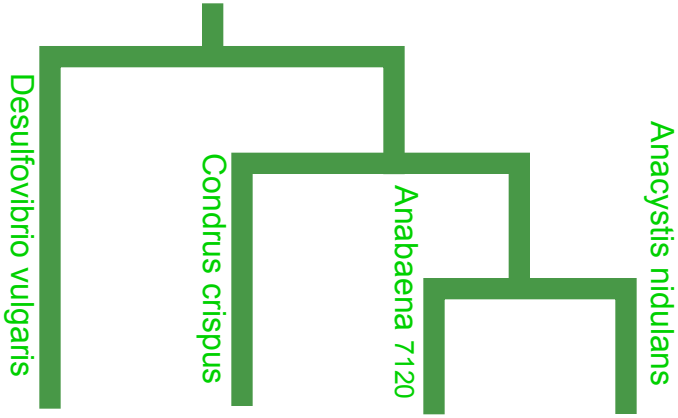
The net result is that patterns in space are frequently more recognizable than patterns in sequence.

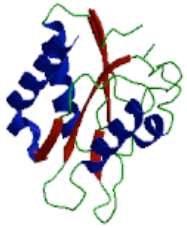
Principles of Protein Structure

GFCHIKAYTRLIMVG…

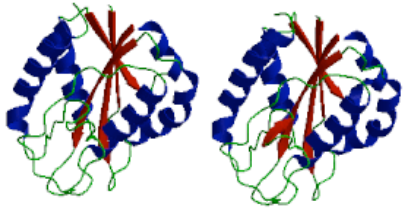








GFCHIK
AYTRLI
MVG…



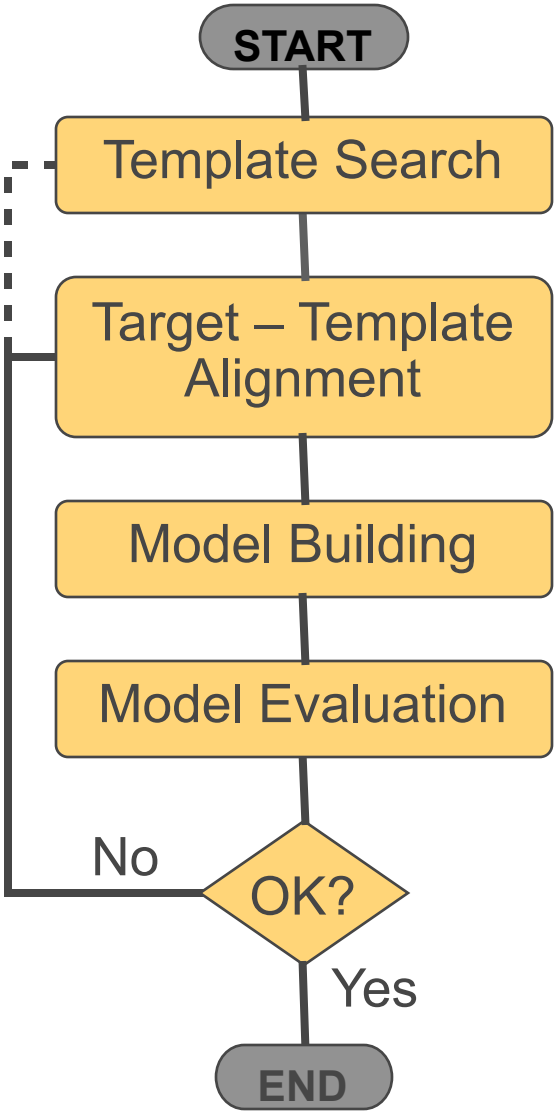
Folding

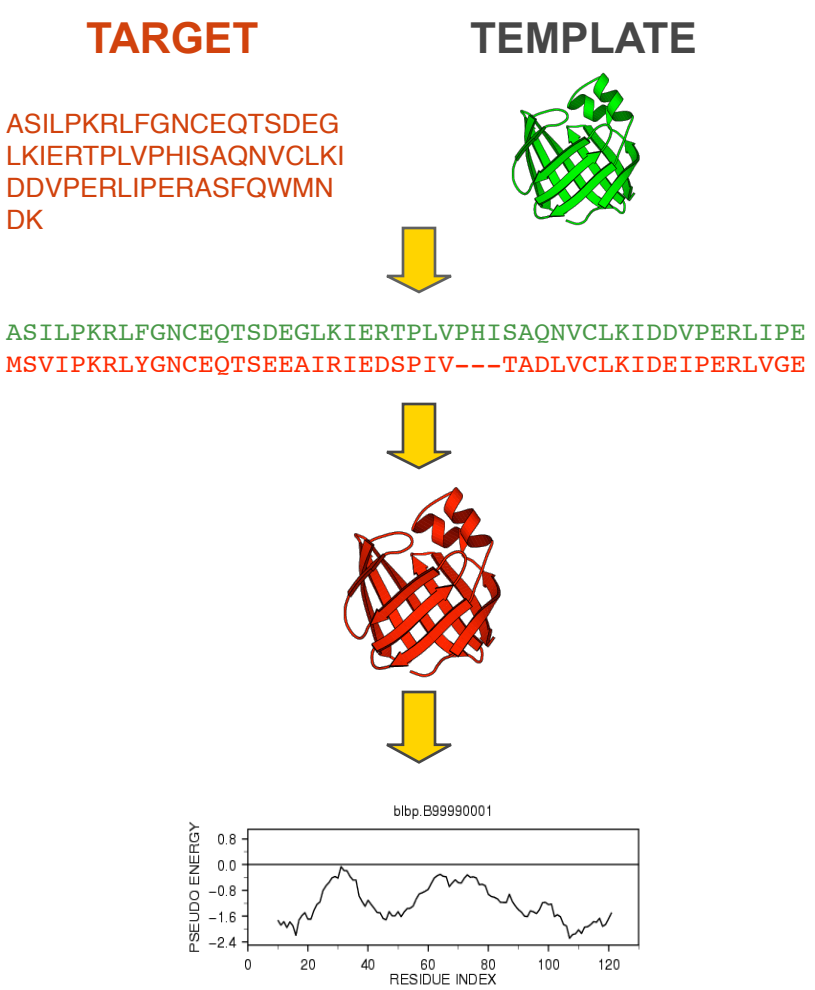
Ab initio prediction

Evolution

Threading
Comparative Modeling

Steps in Comparative Protein Structure Modeling





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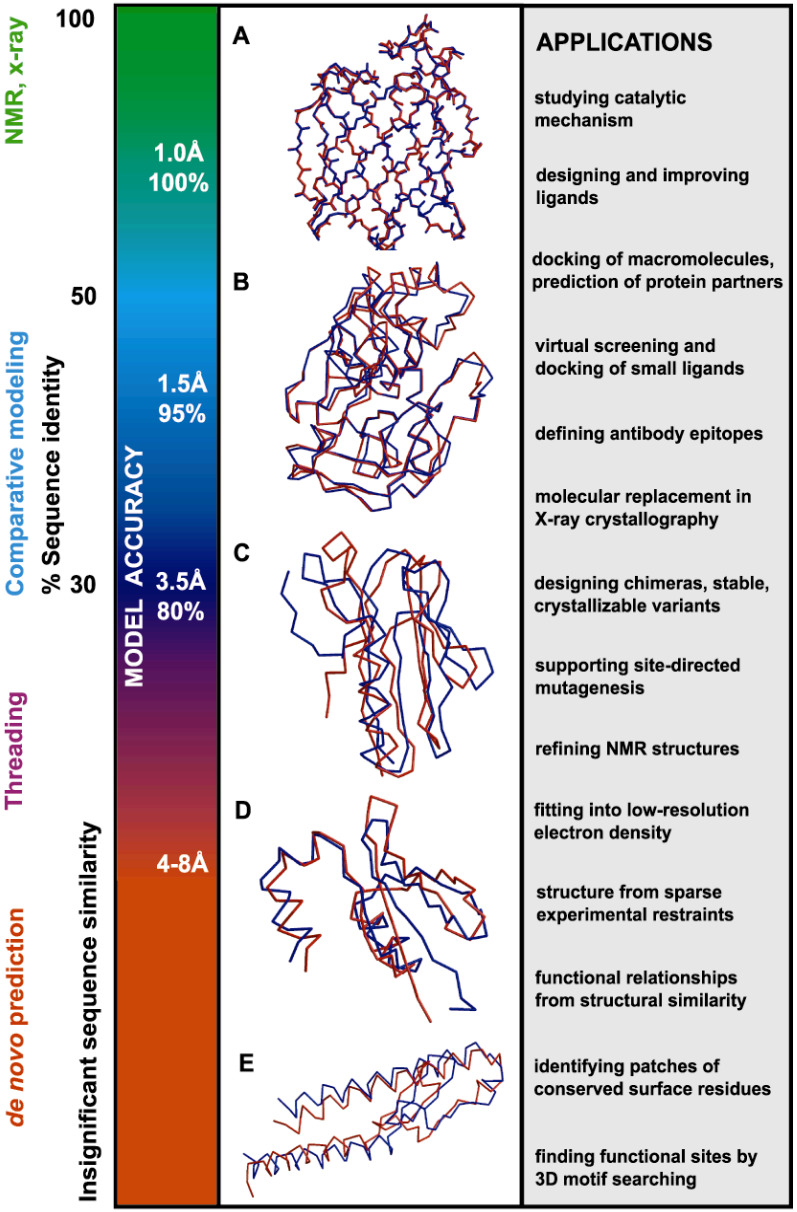
Utility of protein structure models, despite errors



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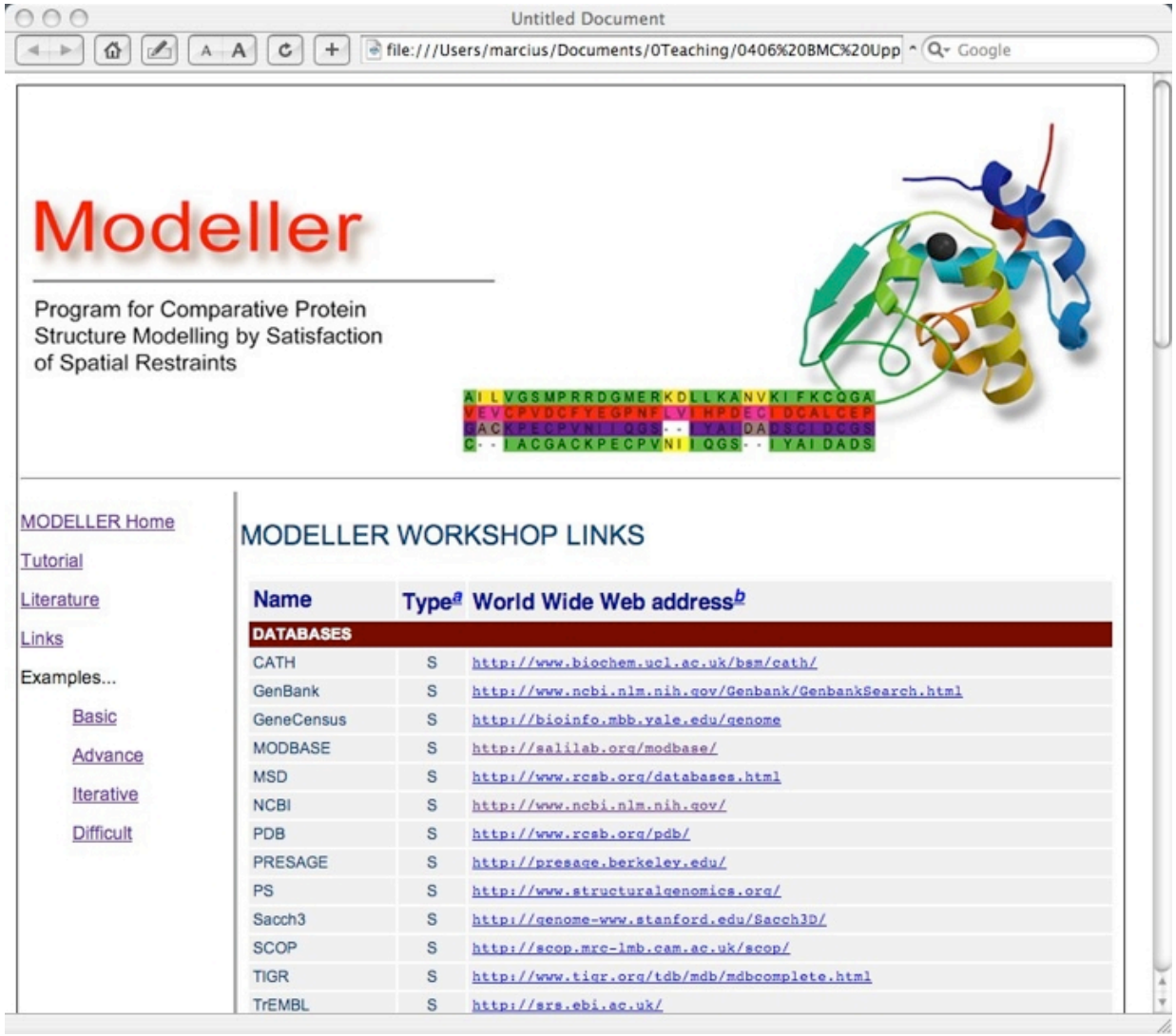

Web site...

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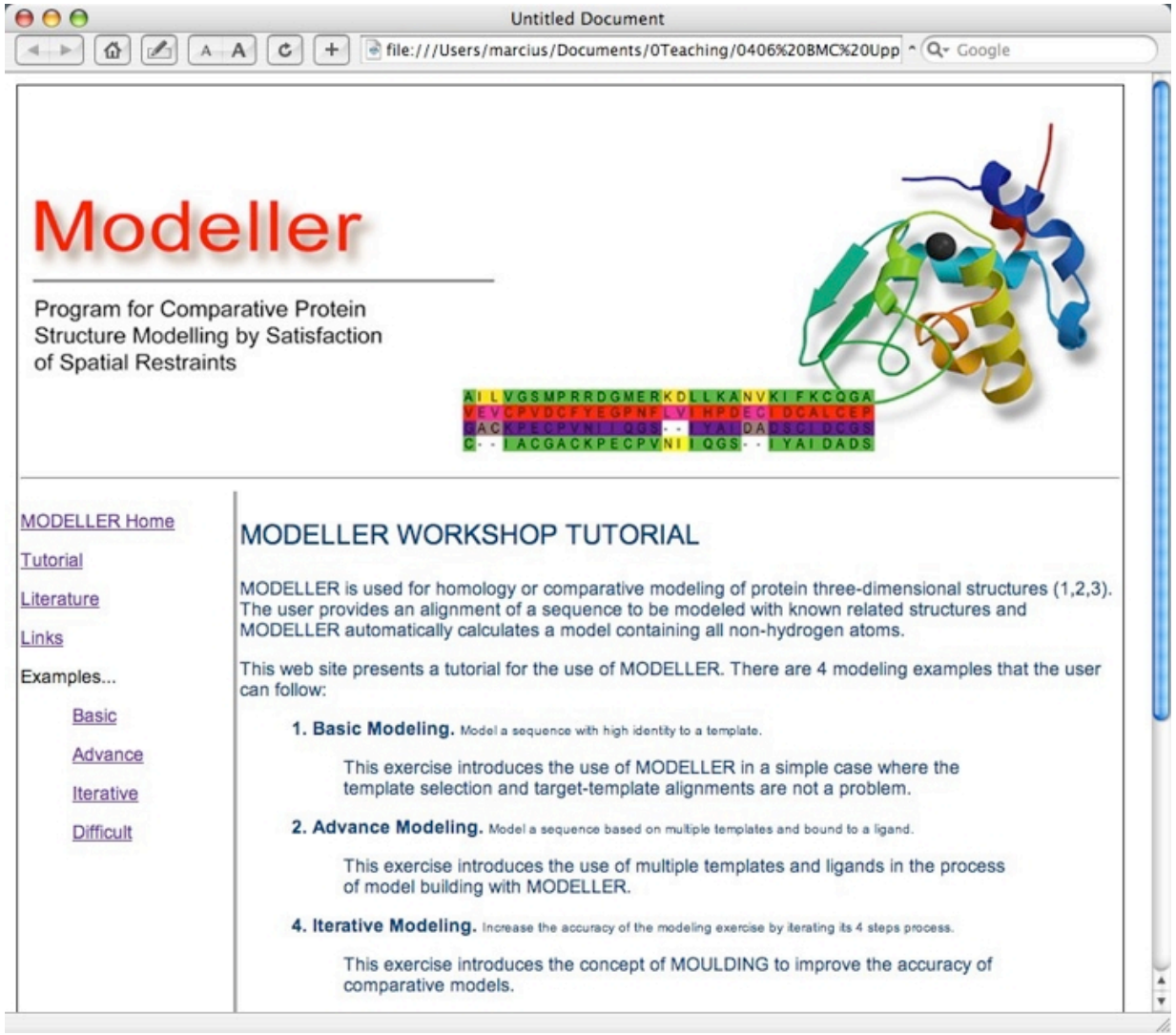

Acknowledgments

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