Protein Molecules
A Kinematics Perspective

Kazem Kazerounian & Horea Ilies

Mechanical Engineering
University of Connecticut
Storrs, CT 06269-3139

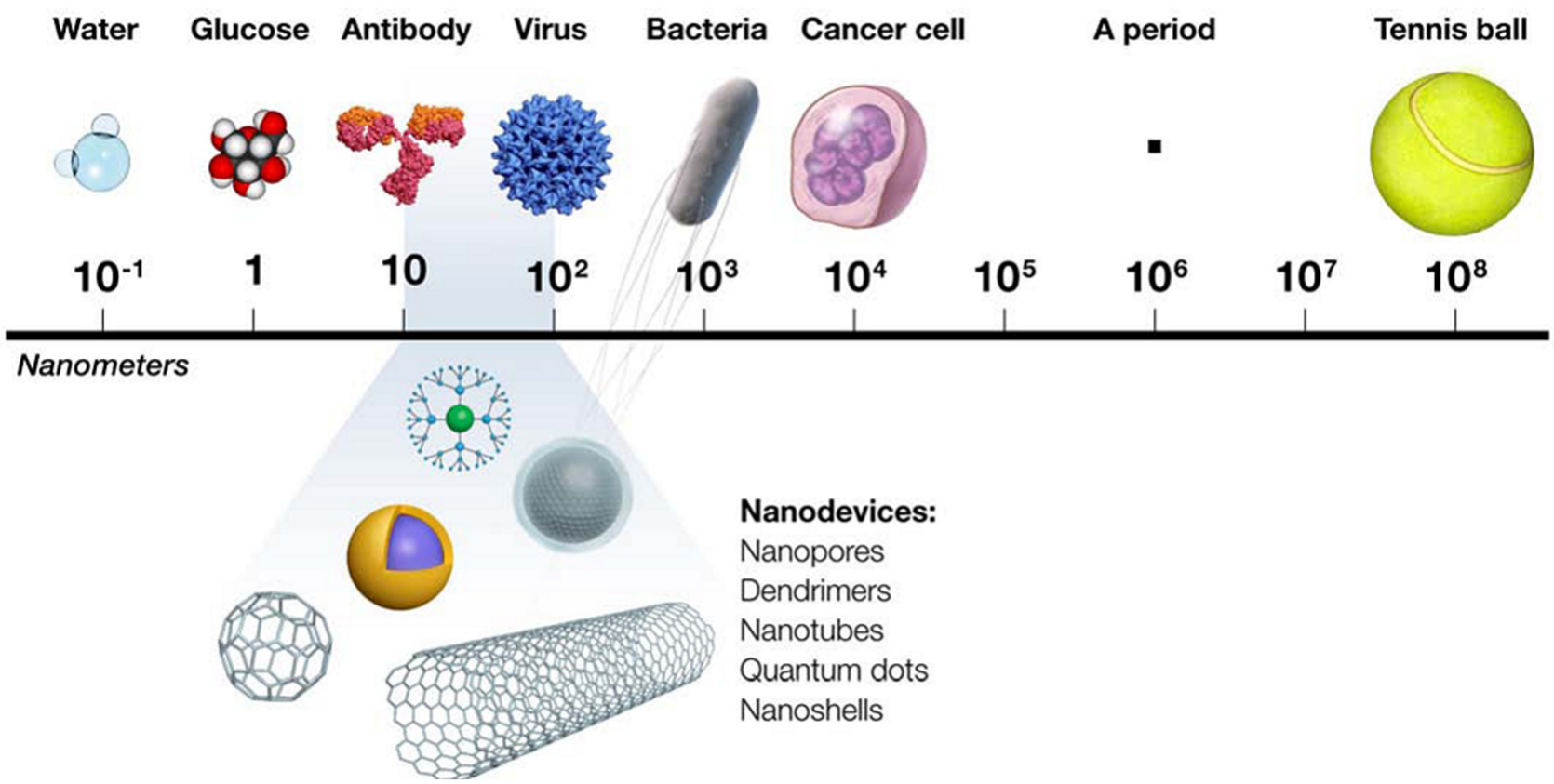
Acknowledgements:
NSF SGER 0733107
NSF CMMI 0856401

National Science and Technology Council (NSTC)

- … the ability to create, control and manipulate organized matter at nanoscales will lead to an industrial and technological revolution.
- … one of the *strategic national priorities* identified in the NSTC report is the development of “new mathematical and simulation capabilities and tools with high spatial and temporal resolution to guide experimental investigations” at nanoscale.

Nano Mechanisms and Sensors

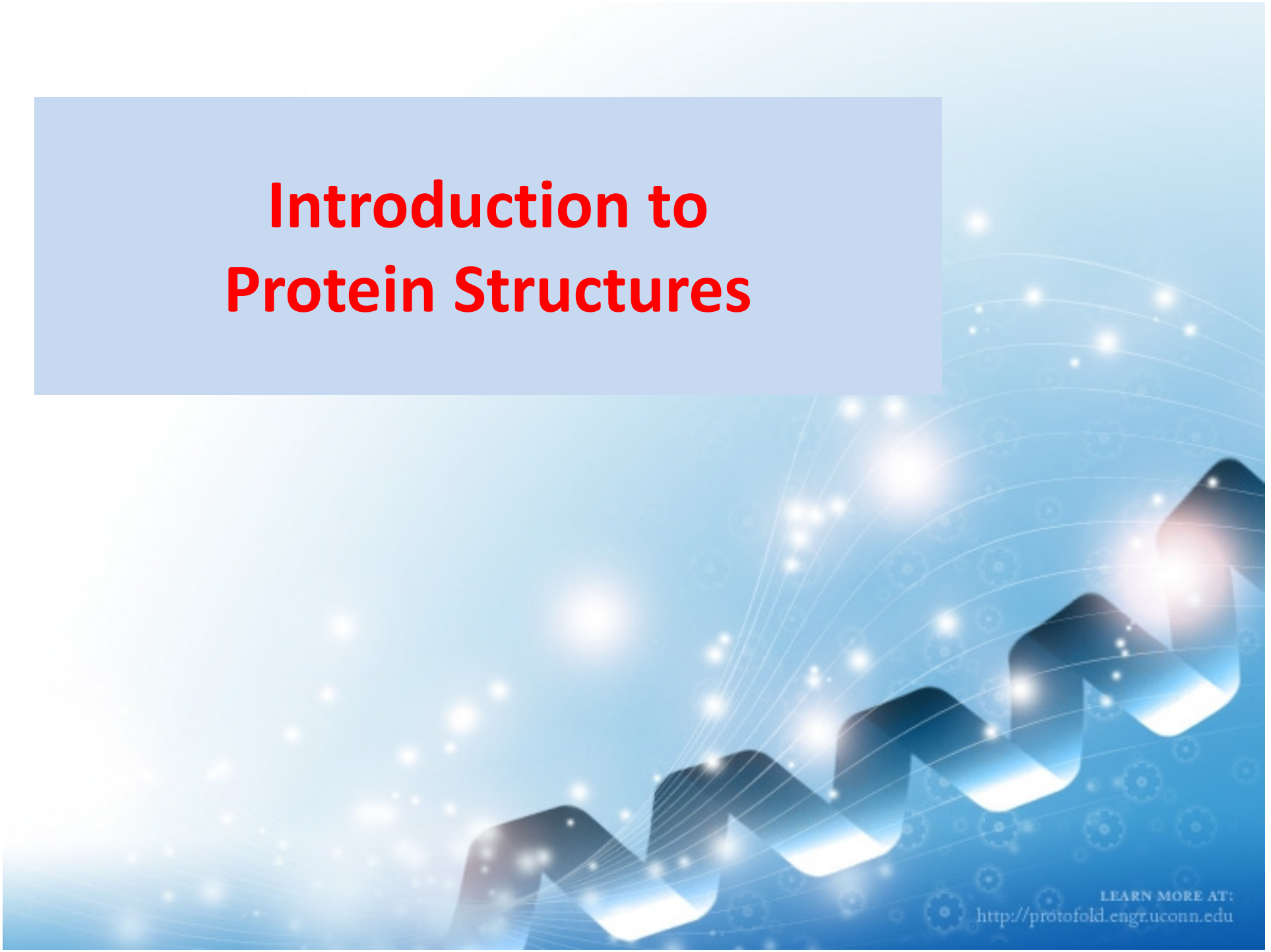
Devices that are in size in billionth of meters (10-9 m) and therefore are built necessarily from atoms.



Nano Mechanisms and Sensors

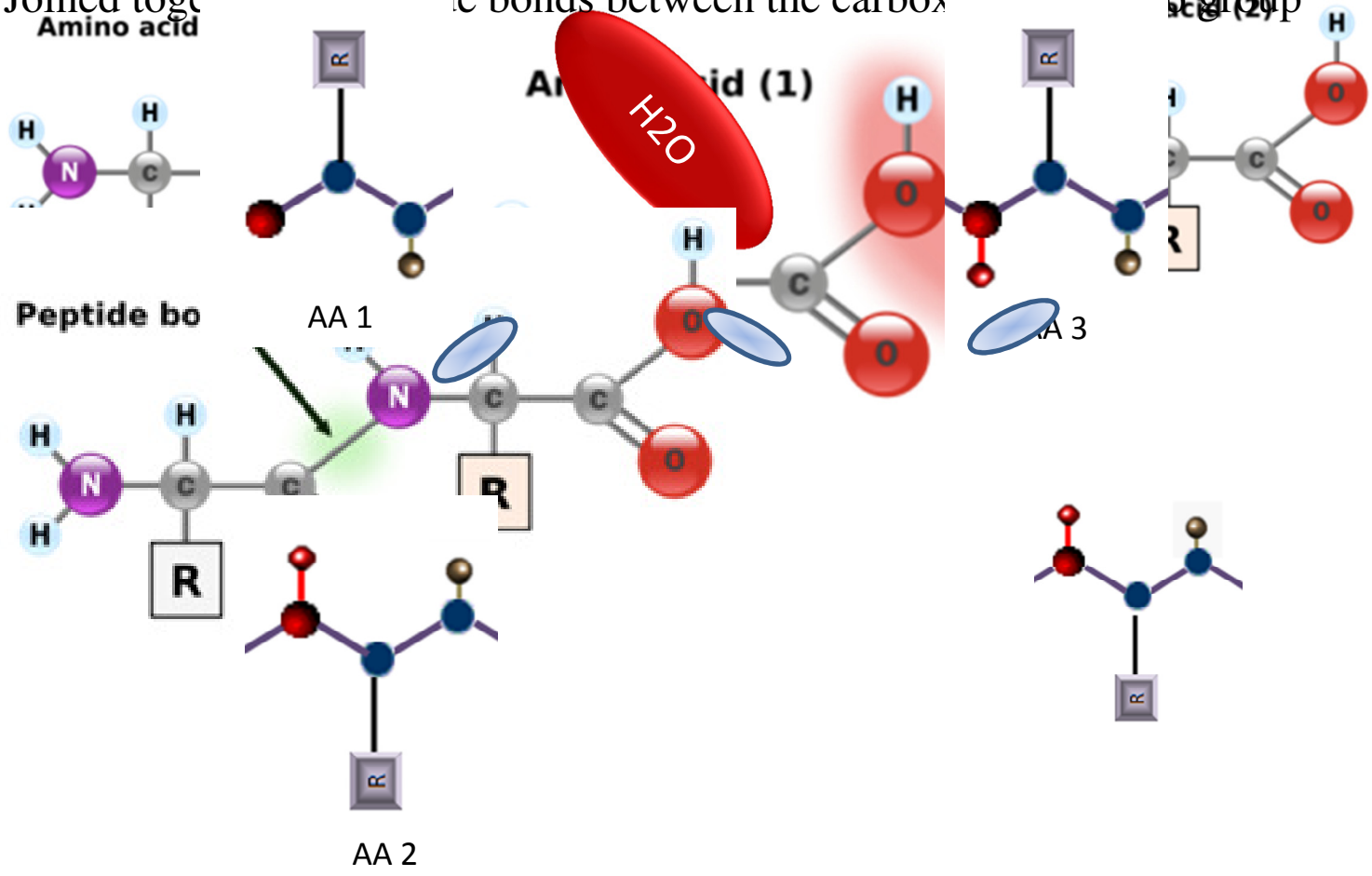
- These devices will have intrinsic mobility that results in their geometry change and hence enable them to perform specific functions.
- Proteins are the nano machines of choice for evolution.

Introduction to Protein Structures

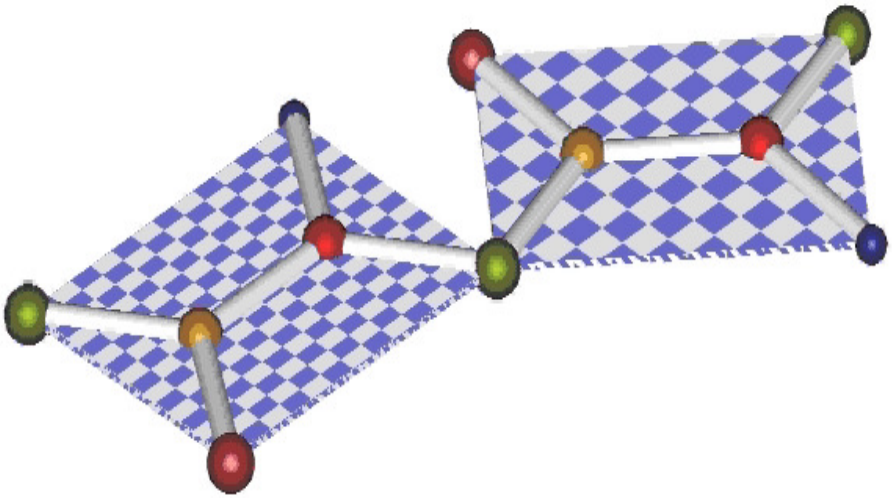


Introduction - Protein Structures

- Large Organic Molecules
- Made of Amino Acids arranged in a linear chain
- Joined toge le bonds between the carbox o group

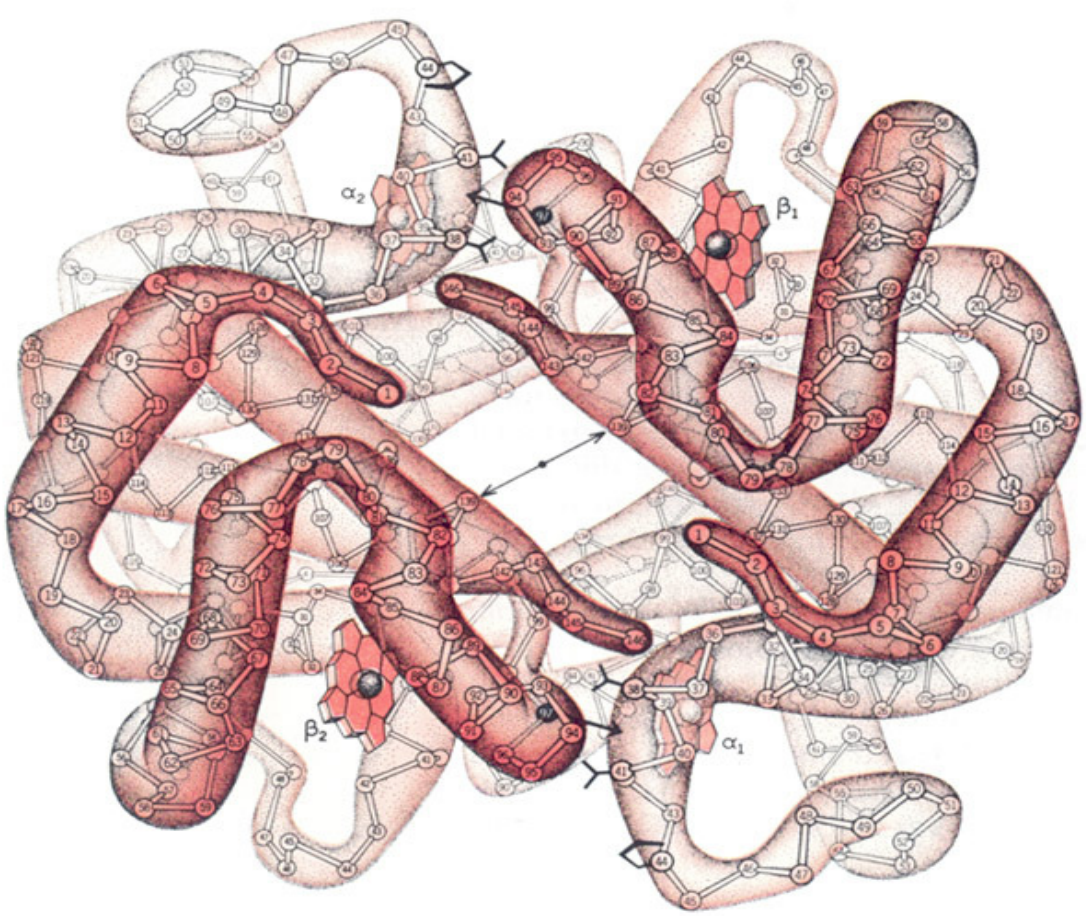


Amino Acids DOF



Example of a protein structure

hemoglobin

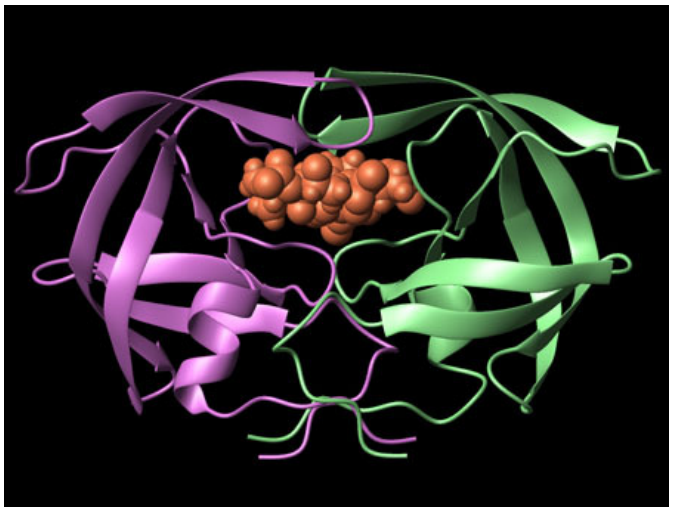


(From Campbel M. 1991)

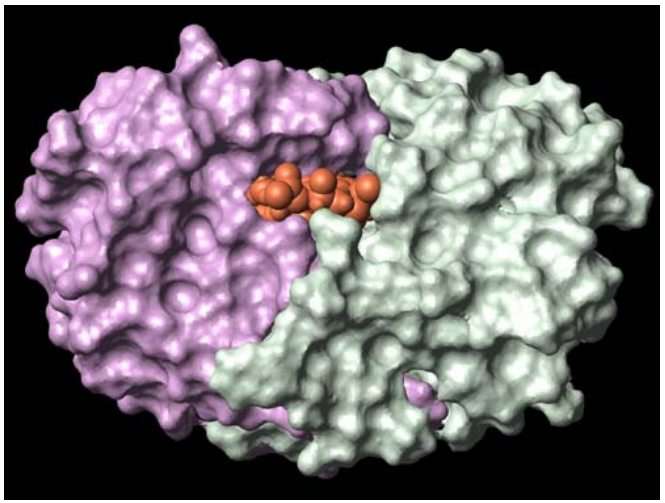
Protein Function

(*protein docking*) → key and lock

HIV-1 protease bound to an inhibitor



Cartoon representation



Surface representation

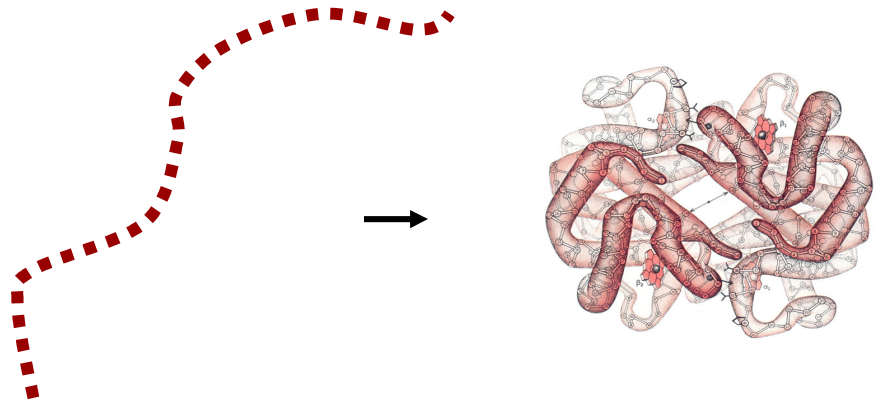
Protein Function

Induced fit:

Sometimes a small flexibility and compliance is needed in both the lock and the key (*receptor* and the *ligand*) for the protein *docking* to take place.

Protein Folding (Conformation)

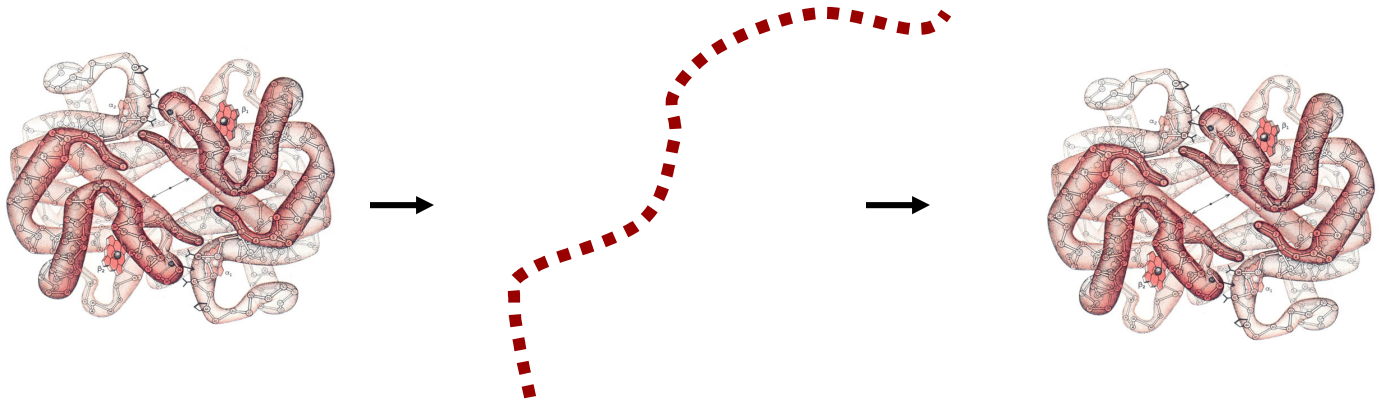
- *The folding occurs under the effect of nuclear forces (among protein atoms as well as between protein atoms and the solvent's atoms).*
- *The final conformation is a relatively stable configuration for which the total potential energy is globally minimized.*



Protein Folding (Conformation)

The final three dimensional structure (*secondary structure*) of the protein is intrinsic to its *primary structure*

Native state → Denatured state → native state



Prediction of Protein Fold

- To date, the structure of about 70,000 proteins are experimentally observed (either through x-ray crystallography or Nuclear Magnetic Resonance (NMR) technologies.
- There are an estimated 200,000 proteins in the human body. Many of these, due to their complicated structure or denaturing tendencies in crystallization, will not be accurately determined with current technologies.

Prediction of Protein Fold

3 major categories of methods for predicting protein folding:

1. Comparative modeling,
   - significant similarity between the primary structure (sequence) of protein of interest and a protein of already known structure : predicted structure is assumed to have significant similarities to the know structure.
2. Fold recognition
   - no significant sequence similarity, but the target proteins structure turns out to have similar structural aspects to a known protein
3. *ab initio* methods.
   - does not assume a priori knowledge of the structure, and attempts to predict the final fold based on the principles of physics in conjunction with various optimization and computational techniques.

Prediction of Protein Fold

"The **Grand Challenge**"

Despite more than 50 years of intense work on this subject, the protein prediction problem remains largely unsolved.

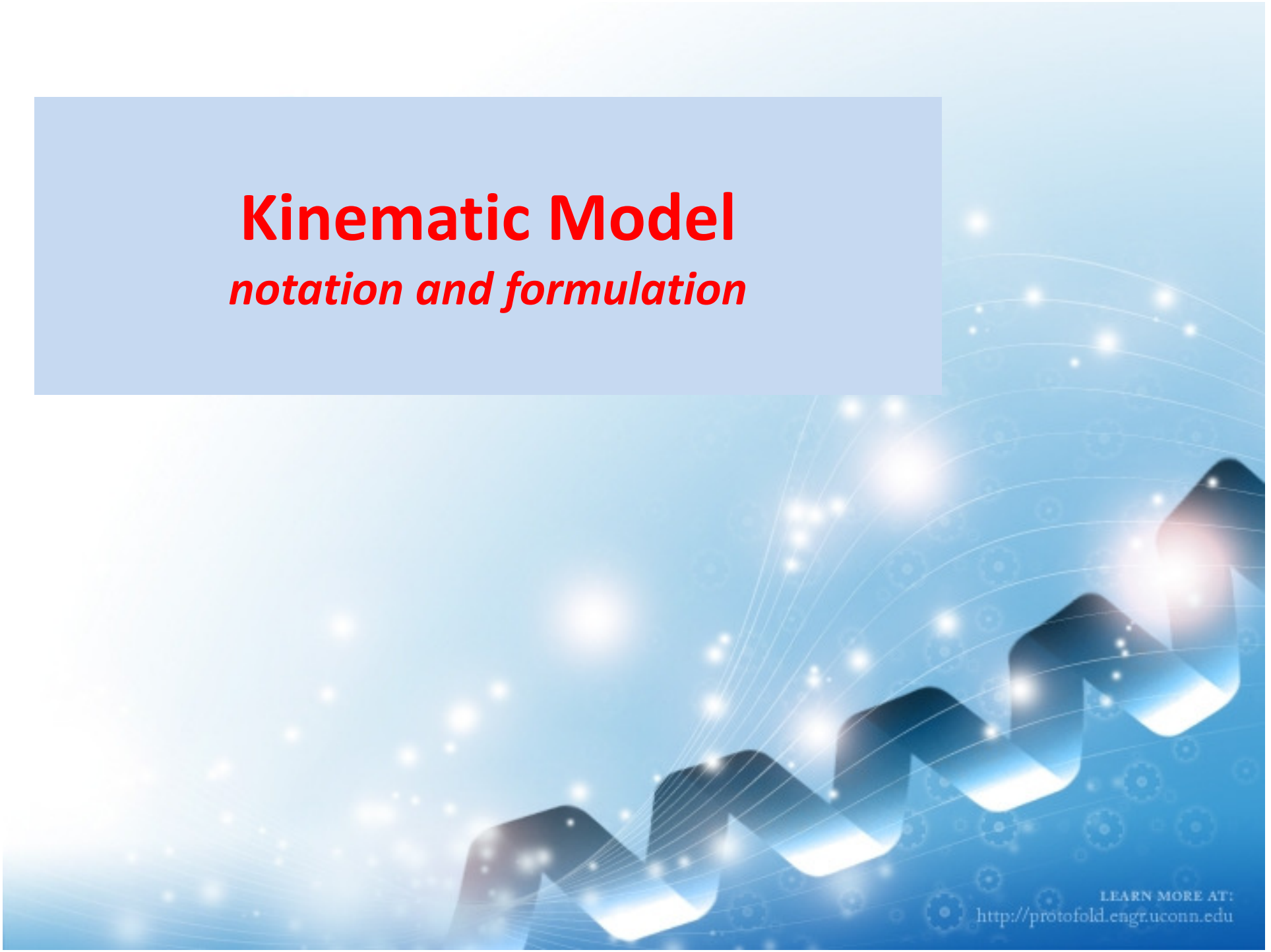
- Model
- Notation
- Direct Kinematics
- Inverse Kinematics
- Geometry agents
- Conformation prediction
- Force field model

- Benchmarking
- Parametric Calibrations
- Mobility Analysis
- Workspace analysis
- Mechanical Compliance
- Computer Aided Design (CAD)
- Energy maps

http://protofold.engr.uconn.edu

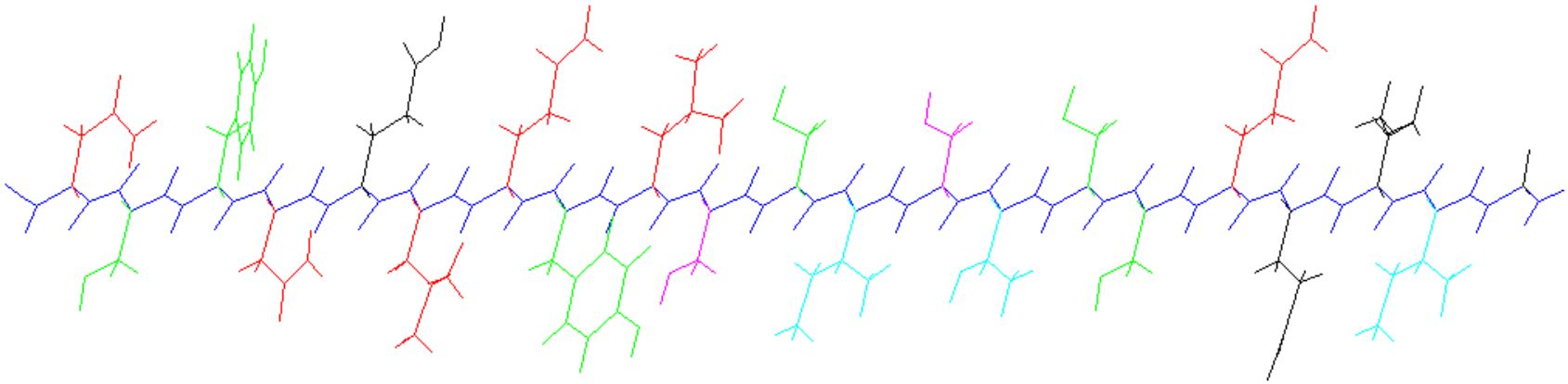
Kinematic Model

notation and formulation



Protein Kinematic Model

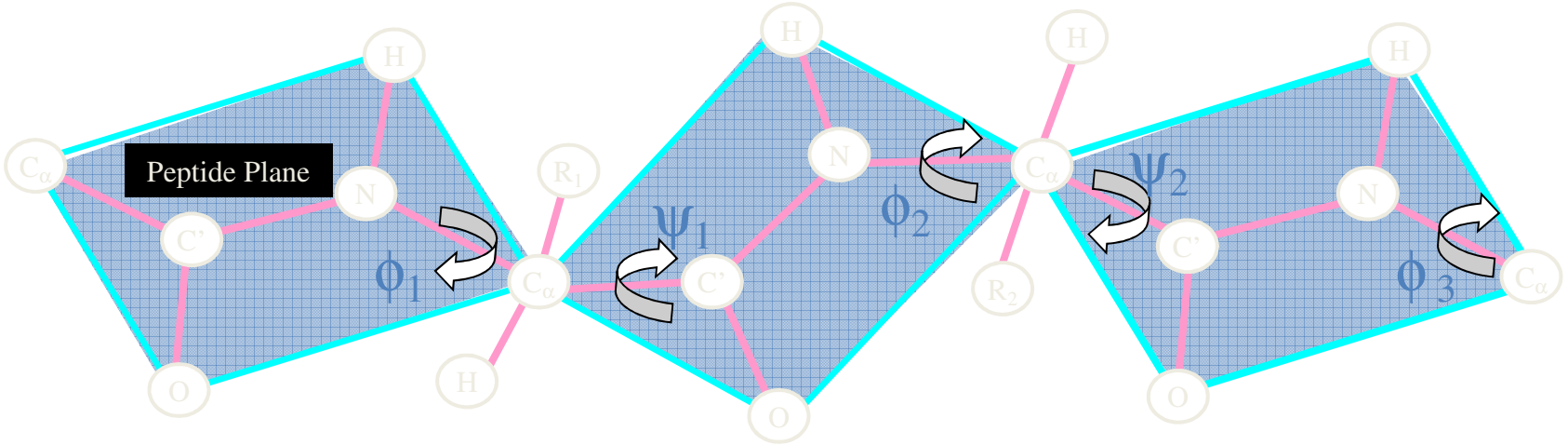
Multi branch serial linkage of many nano rigid bodies connected by revolute joints



- protein in *denatured state:*

  serial linkage with N+1 solid links connected by N revolute joints.

- The side chains are shorter serial linkages with any where between zero to a few revolute joints connected to the main links of the serial linkage (back bone).



Notation

- Commonly used method: Cartesians coordinates of the atoms

- **Potentially useful methods:**
  - Denavit-Hartenberg notation (1955),
  - Vector notation and analysis (Chase, M. 1964),
  - Tensor methods (Kislitsin A. P.1954; Osman & Mansour1971),
  - Screw coordinates (Yuan and Freudenstein, 1971),
  - Dual numbers (Yang and Freudenstien, 964),
  - Quaternion operators (Sandor, 1968),
  - Constant distance equation method (Osman and Sergev, 1972),
  - Spherical trigonometry method (Duffy, 1980),
  - Zero Position Method (Gupta, 1984) and
  - Train components method (Osman *et al*, 1981).

Notation

- Computational Cost Comparison of Rotation Operators

  1) Rotation Matrix

$$\vec{b}_j = R_{1-N} * \vec{b}_{0j}$$

  2) Quaternions

$$\vec{b}_j = q_{1-N} * \vec{b}_{0j} * q_{1-N}^{-1} \quad \text{and} \quad \vec{b}_j = Q_{1-N} * \vec{b}_{0j}$$

  3) Rodrigues

$$\vec{r}_j = \vec{r}_{0j}\cos(\phi_j) + \vec{u}_j \times \vec{r}_{0j}\sin(\phi_j) + (\vec{r}_{0j} \bullet \vec{u}_j)\vec{u}_j(1-\cos(\phi_j))$$

- Direct Kinematics of a Protein molecule
- Dynamic Simulation of Protein Folding

Results of Computational Cost Comparison of Rotation Operators

Rotation Matrix (N=number of joints, M_j=number of atoms in side chain j)

$$\sum_{i=1}^{N} 25 + \sum_{i=2}^{N} 45 + \sum_{j=1}^{M} 15M_j \quad \text{or} \quad 70N - 45 + \sum_{j=1}^{M} 15M_j$$

Quaternions

$$\sum_{i=1}^{N} 6 + \sum_{i=2}^{N} 28 + \sum_{j=1}^{M} 41M_j \quad \text{or} \quad 34N - 28 + \sum_{j=1}^{M} 15M_j$$

Quaternion Matrix

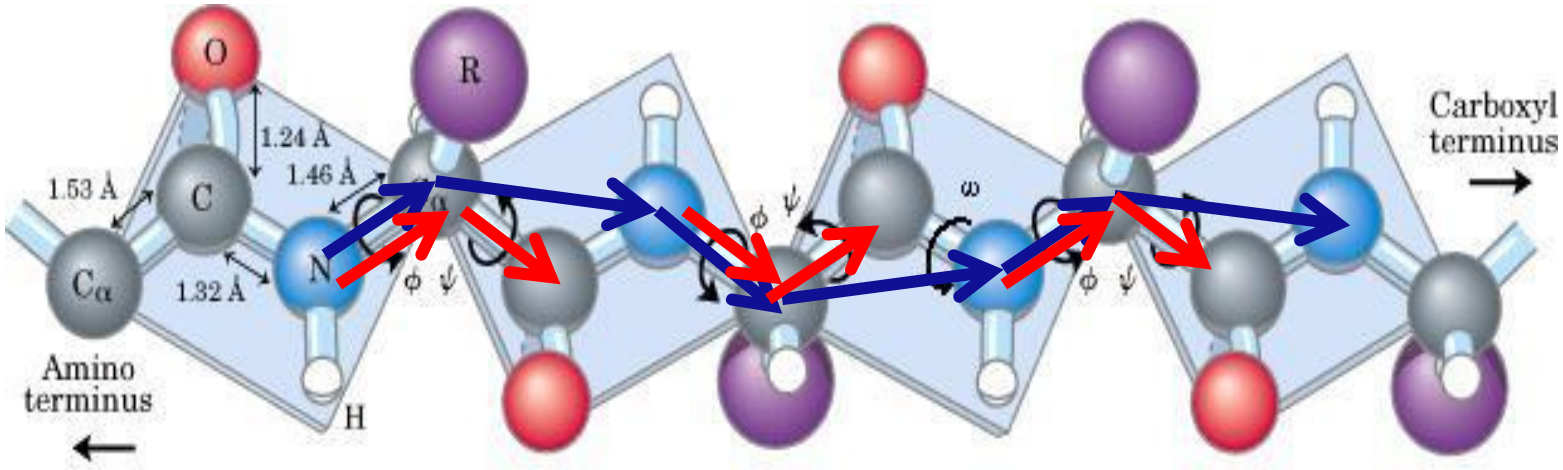
$$\sum_{i=1}^{N} 29 + \sum_{i=2}^{N} 45 + \sum_{j=1}^{M} 15M_j$$

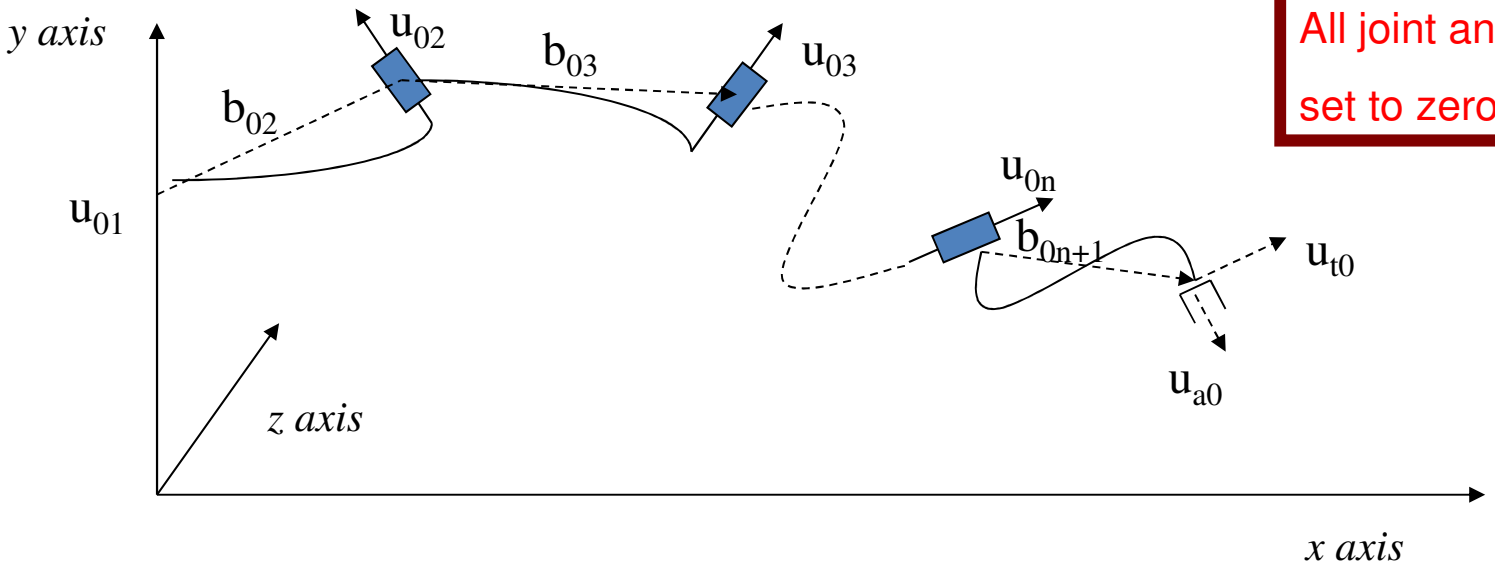
Rodrigues

$$\sum_{i=1}^{N} 33i - \sum_{j=1}^{M} 26 + \sum_{j=1}^{M} 26M_j$$

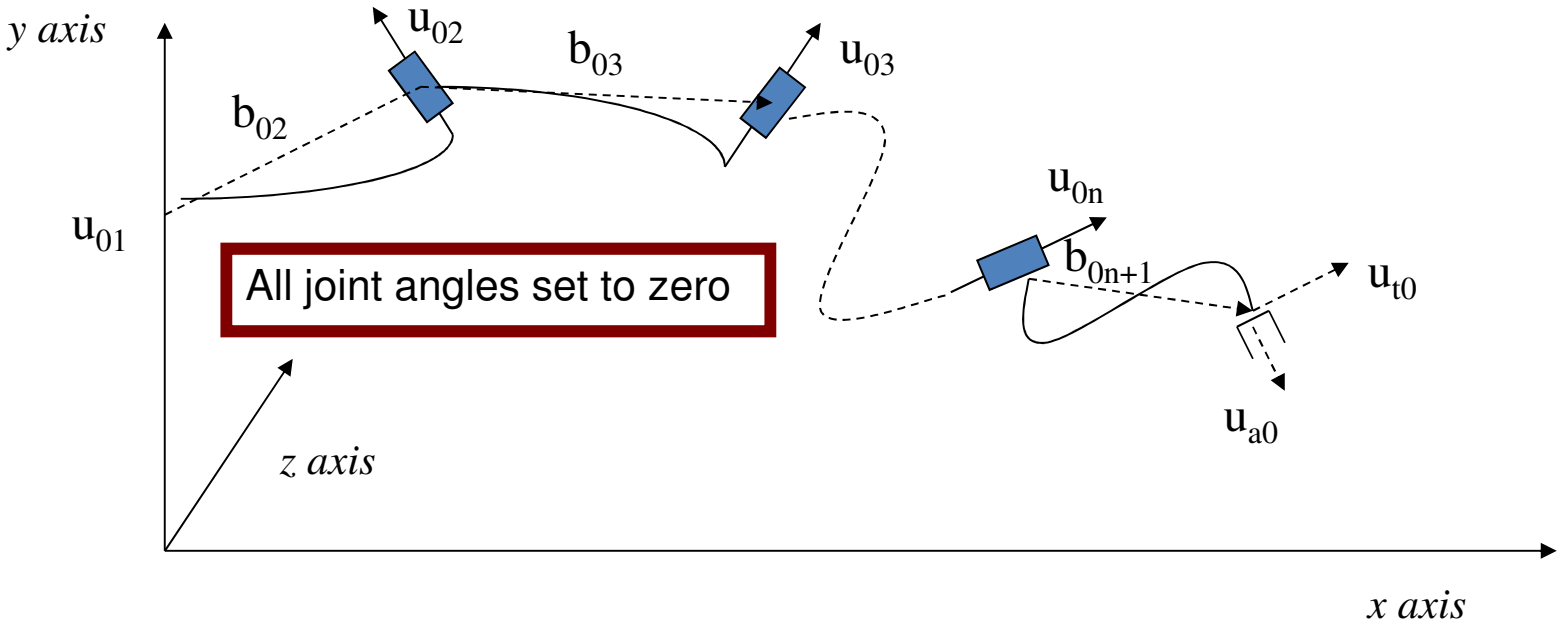
Note: Assuming addition and multiplication Operation costs to be the same.

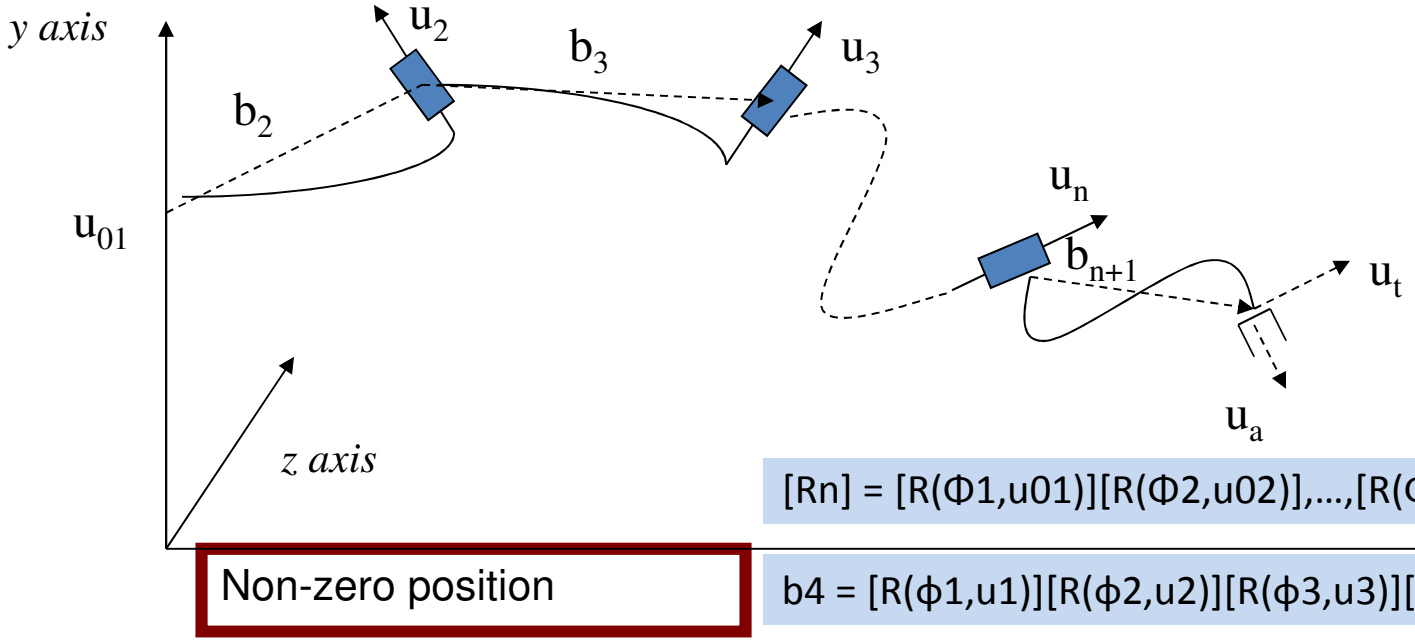
Zero-Position Notation
(from Robot Kinematics)





All joint angles are set to zero



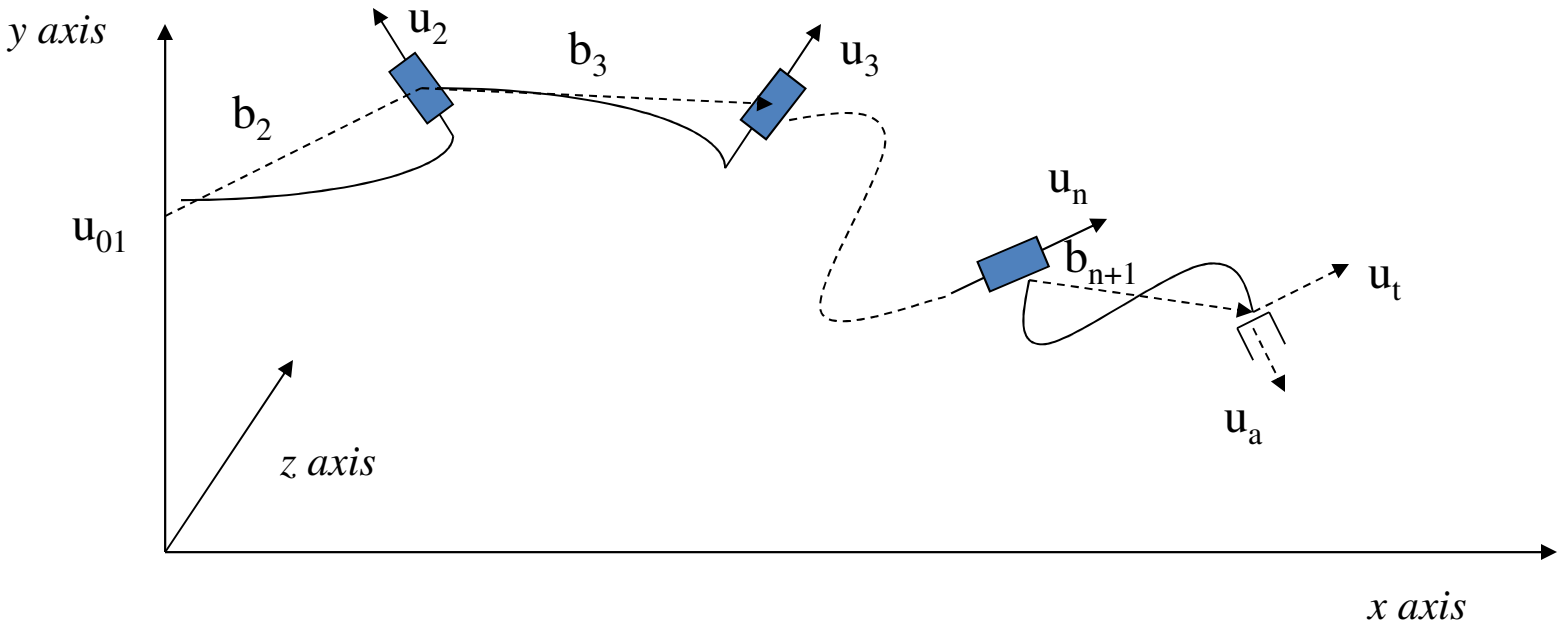


$$u_k = [R_k]u_{0k}$$
$$b_{k+1} = [R_k]b_{0k+1}$$

[Rn] = [R(Φ1,u01)][R(Φ2,u02)],…,[R(Φn,u0n)]

b4 = [R(ϕ1,u1)][R(ϕ2,u2)][R(ϕ3,u3)][R(ϕ4,u4)]b04

Direct Kinematics



$$u_k = [R_k] u_{0k}$$

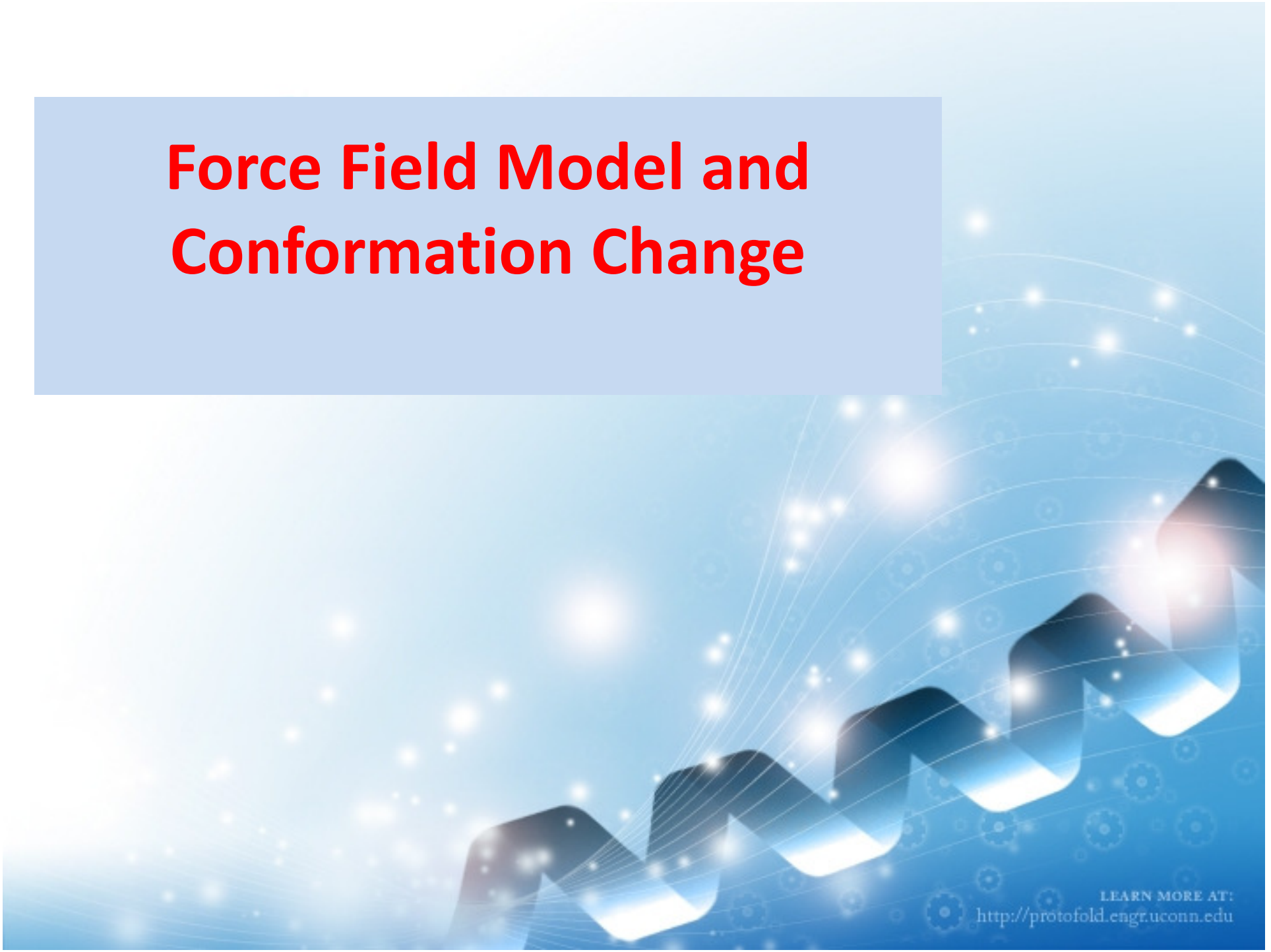
$$b_{k+1} = [R_k] b_{0k+1}$$

[Rn] = [R(Φ1,u01)][R(Φ2,u02)],…,[R(Φn,u0n)]

b4 = [R(ϕ1,u1)][R(ϕ2,u2)][R(ϕ3,u3)][R(ϕ4,u4)]b04

Questions on Kinematic Model?

Force Field Model and Conformation Change



Amber Potential Field Model:

$$E_{total} = E_{bond\text{-}length} + E_{bond\text{-}angle} + E_{torsion} + E_{van\ der\ Waals} + E_{Electrostatic}$$

$E_{bond\text{-}length}$ = Bond energy calculated by Hook's law = $\Sigma\ k_b\ (l\text{-}l_0)^2$ where k_b is experimentally known and l and l_0 are actual and ideal bond lengths.

$E_{bond\text{-}angle}$ = Bond angle (bending) energy calculated by Hook's law = $\Sigma\ k_\theta\ (\theta\text{-}\theta_0)^2$ where k_θ (angular stiffness of the bond) is experimentally known and θ and θ_0 are actual and ideal bond angles.

$E_{torsion} = \Sigma\ A\ (1+ \cos(n\varphi\text{-}\varphi_0))$ = where *A* is an experimentally determined constant and φ is the torsion angle (the rotation angle around the bond between the 2nd and the 3rd atom in any serially connected four atoms). The torsion energy is mainly used to correct the bond and bending energies to make the results agree with experimental results.

$E_{van\ der\ Waals}$ = The energy due to non-bonded forces between two atoms *i* and *j* =

$$\Sigma\ \Sigma\ (-a_{ij} / r_{ij}^{6} + b_{ij} / r_{ij}^{12})$$

where *a* and *b* are experimentally known and *r* is the distance between the two atoms.

$E_{Electrostatic}$ = Electrostatic energy between two atoms = $\Sigma\ \Sigma\ q_i q_j / r_{ij}$ where *q* and *s* are known and *r* is the distance between the two atoms.

ab initio Prediction Methods

(computational complexity)

- Computation procedure of the potential energy or forces: straight forward
- computational complexity: mind bugling
- Example:
  - protein molecule with 100 residues (200 revolute joints).
  - If samples on the joint angles @ 36 degrees (10 per joint)
  - Energy calculations 10^{-20} seconds (using many parallel super computers)

Computation time= $(360 / 36)^{200} * 10^{-20} = 10^{180}$ seconds = $3.16 * 10^{172}$ years

Conformation Prediction

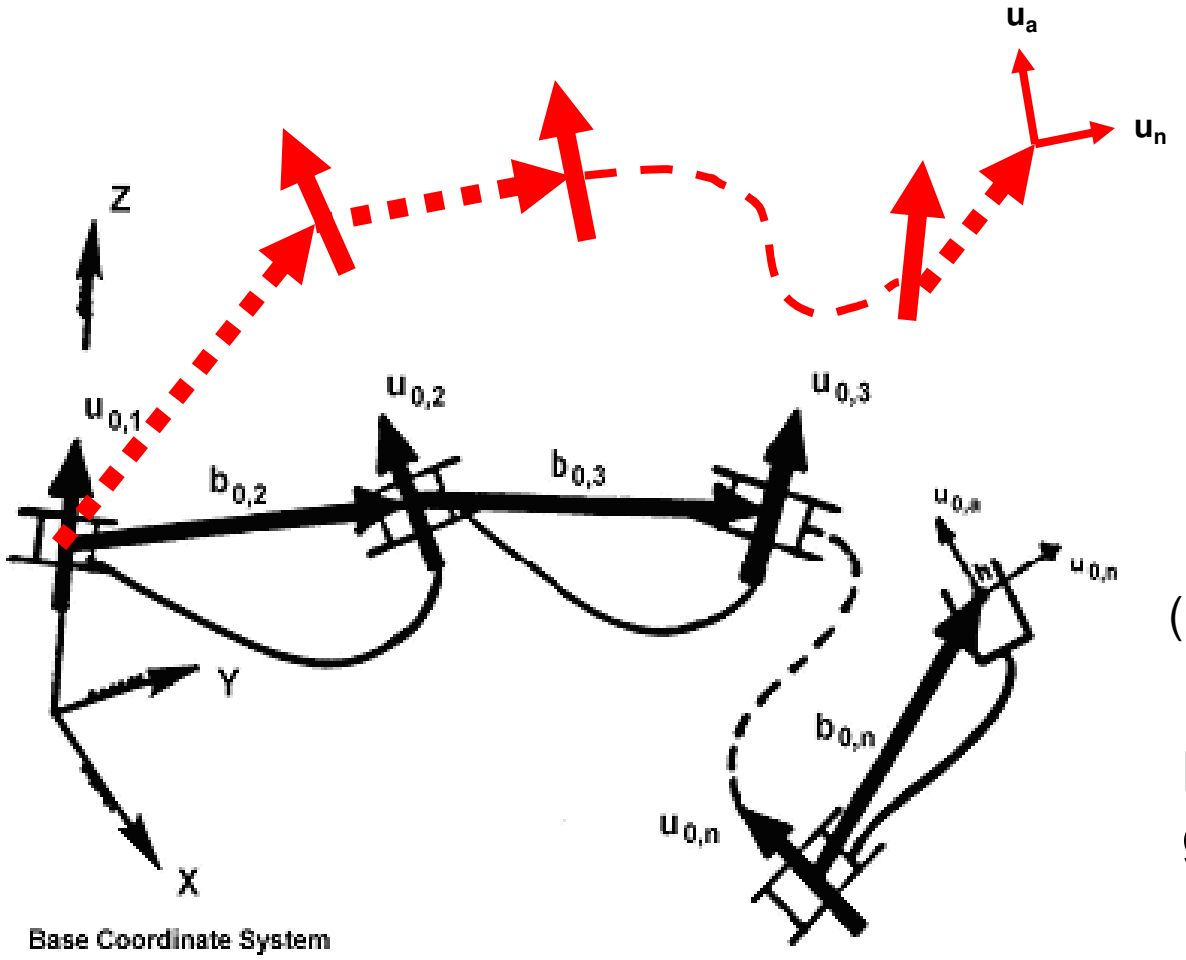
Successive Kinetostatic Compliance Method

Question:

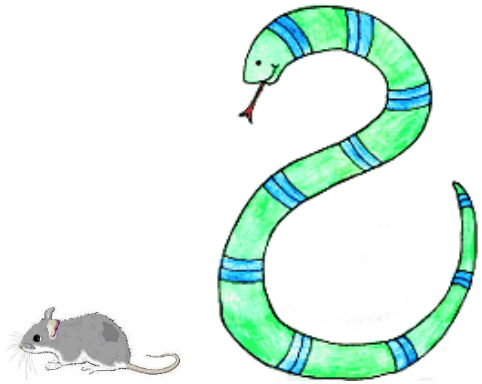
Under the effect of the force field, what is the conformation change of the protein molecule?

Conformation Prediction

Target Tracking = Successive Kinetostatic Compliance Method

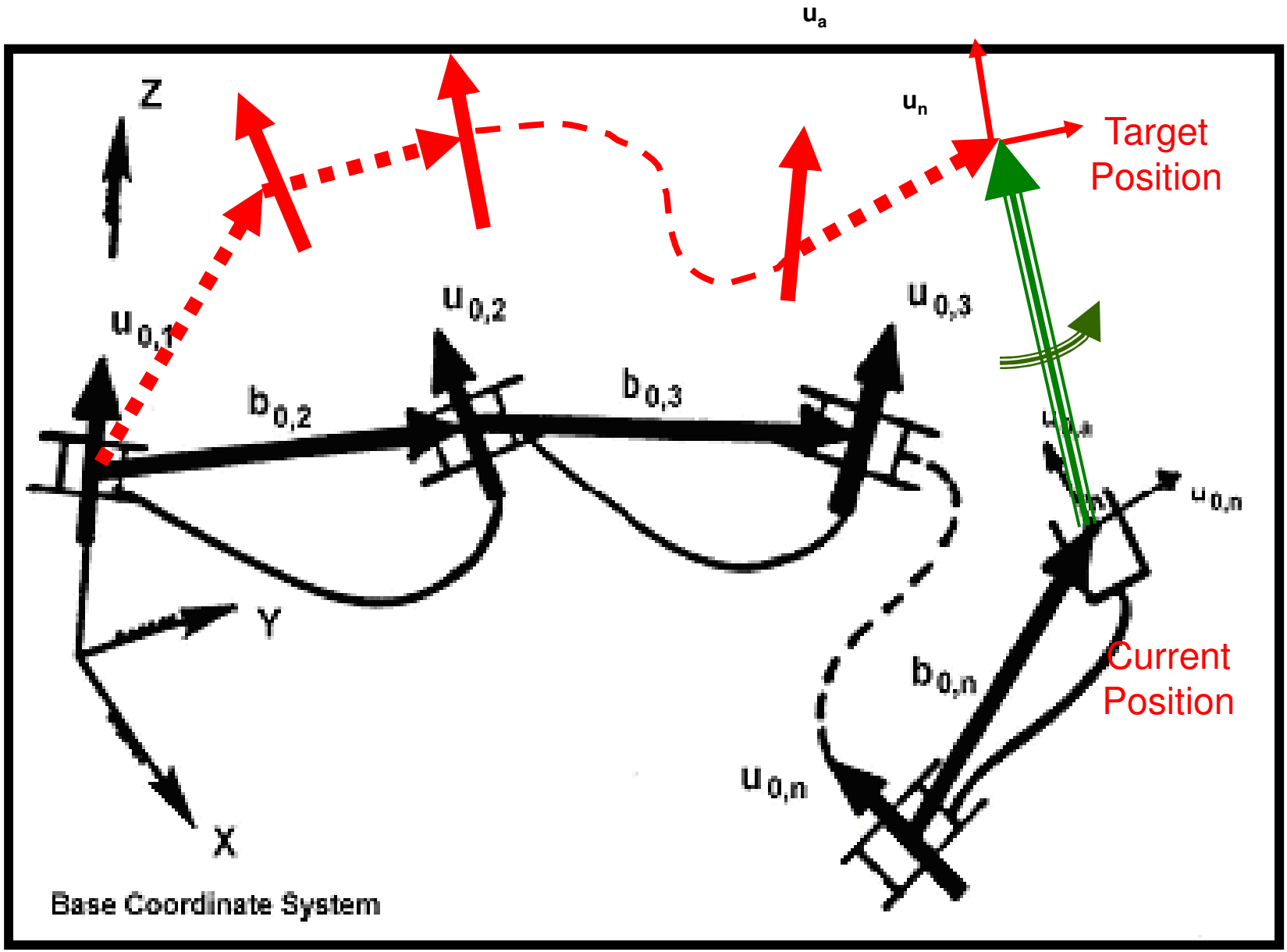


Target Position (Prey)



Current Position (Predator)

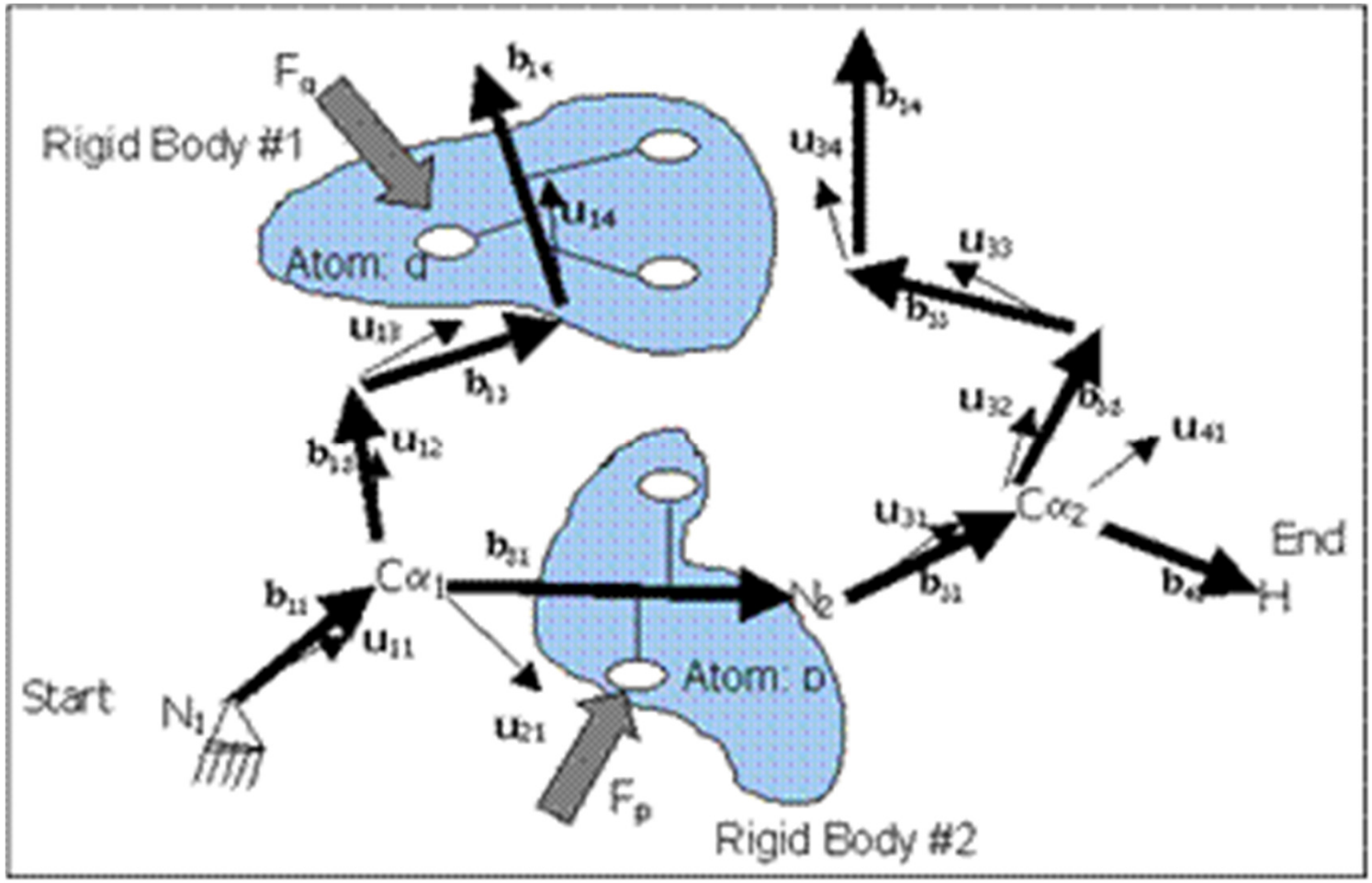
How does the Predator gets the Prey?


u_a
Z
u_n
Target Position
u_0,1
u_0,2
u_0,3
b_0,2
b_0,3
u_0,n
Y
b_0,n
Current Position
u_0,n
X
Base Coordinate System

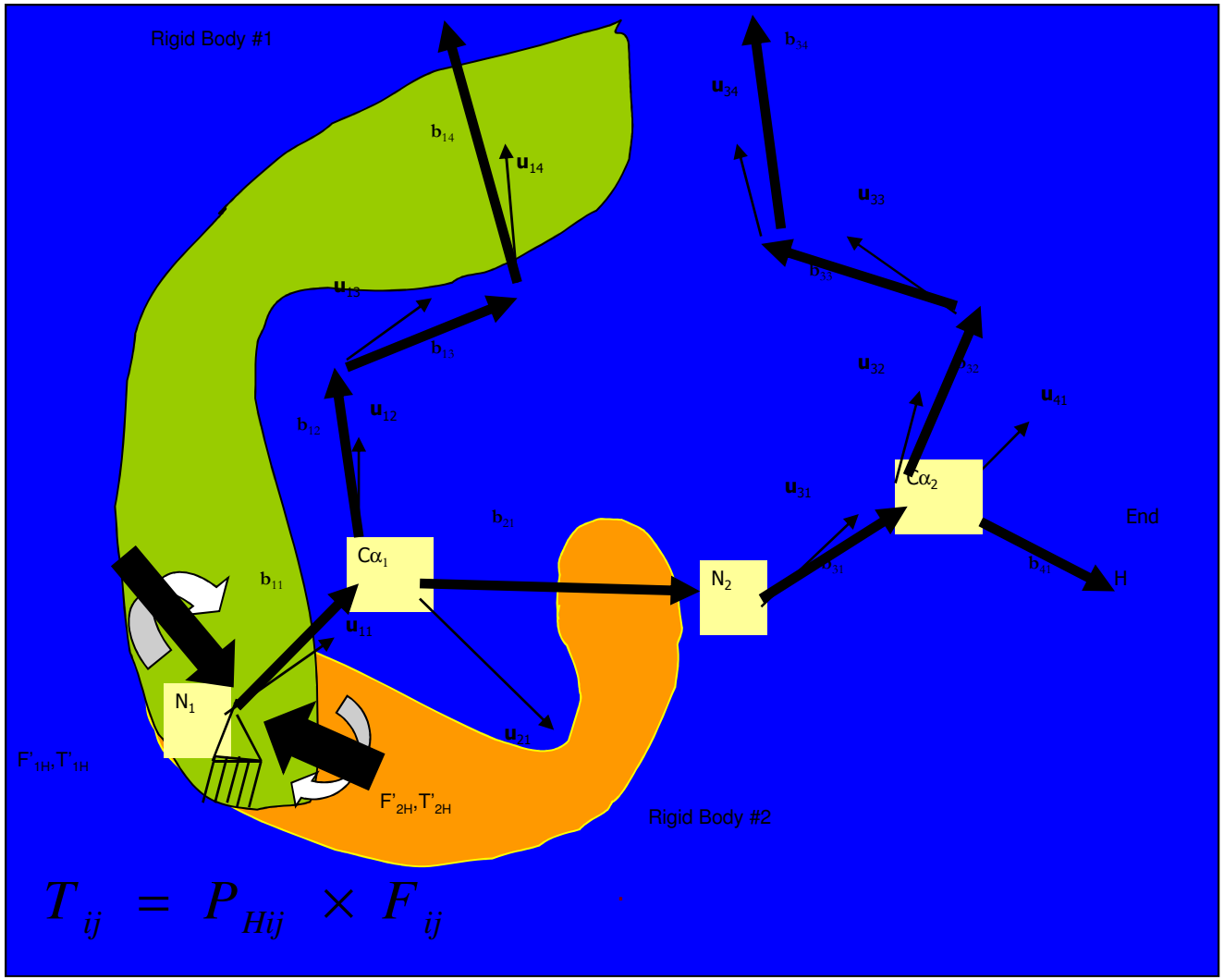
Joint motion:

$$\vec{\tau} = J^T \begin{Bmatrix} \vec{T}_H \\ \vec{F}_H \end{Bmatrix}$$

$$\Delta\theta = k * J^T \tau$$



Resultant Forces Fp and Fq are shown on atoms (points) p and q on two Rigid Bodies of the Kinematic Chain.



Equivalent force/torque couples at the base

$$J_i = \begin{Bmatrix} u_i \\ u_i \times P_i P_H \end{Bmatrix}$$

P_H is now the origin of the coordinate system for all atoms

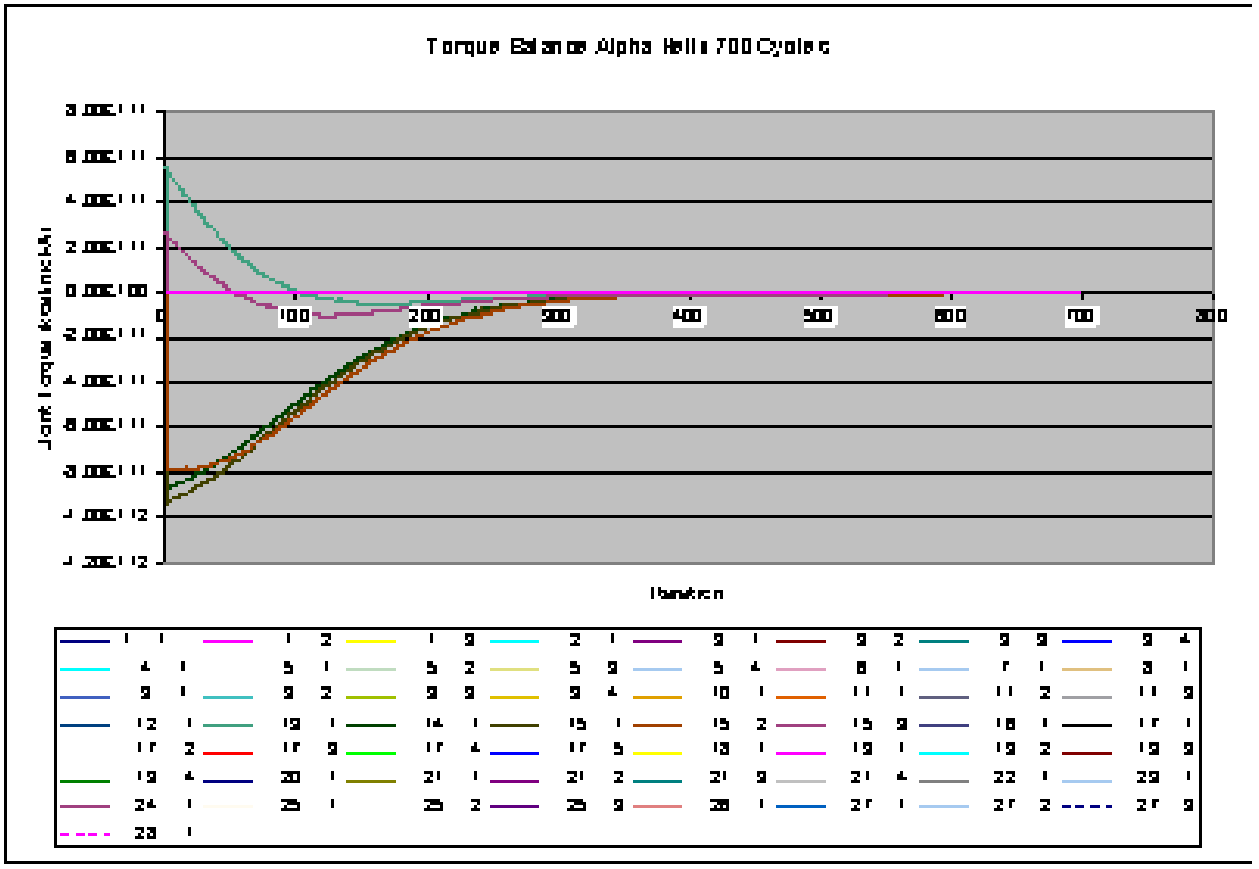
For every link, the contribution of the forces acting on the atoms of that link to the equivalent joint torques on all of the joints preceding that link are:

$$\tau_i = \begin{bmatrix} . & . & . & u_k & . \\ . & . & . & -u_k \times P_k & . \end{bmatrix}^t \begin{Bmatrix} T_i \\ F_i \end{Bmatrix}$$

These contributions are then combined to calculate the overall equivalent joint torques $\boldsymbol{\tau}$.

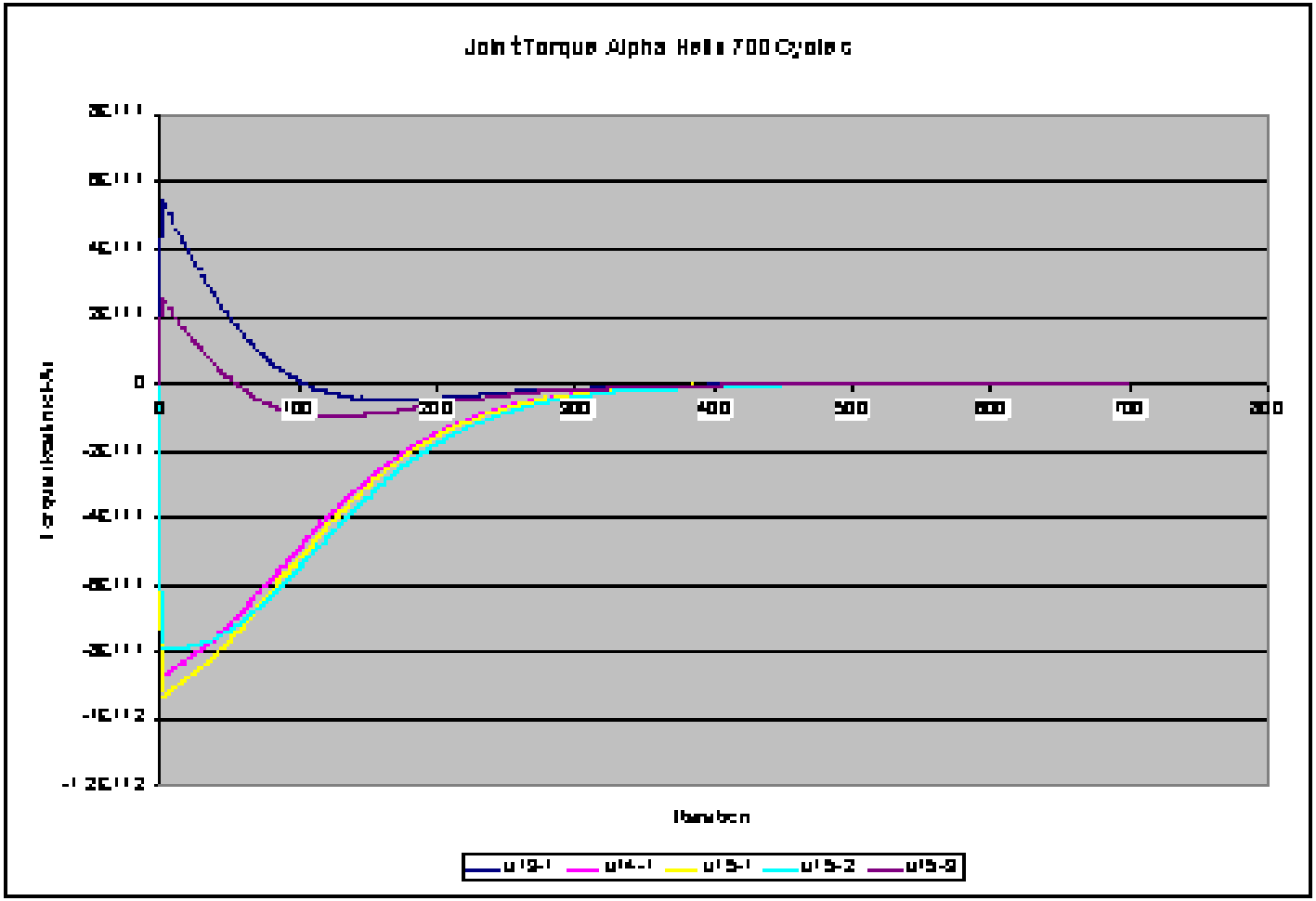
Numerical Experiments

LMEAQHALKMEAHL (Alpha Helix)



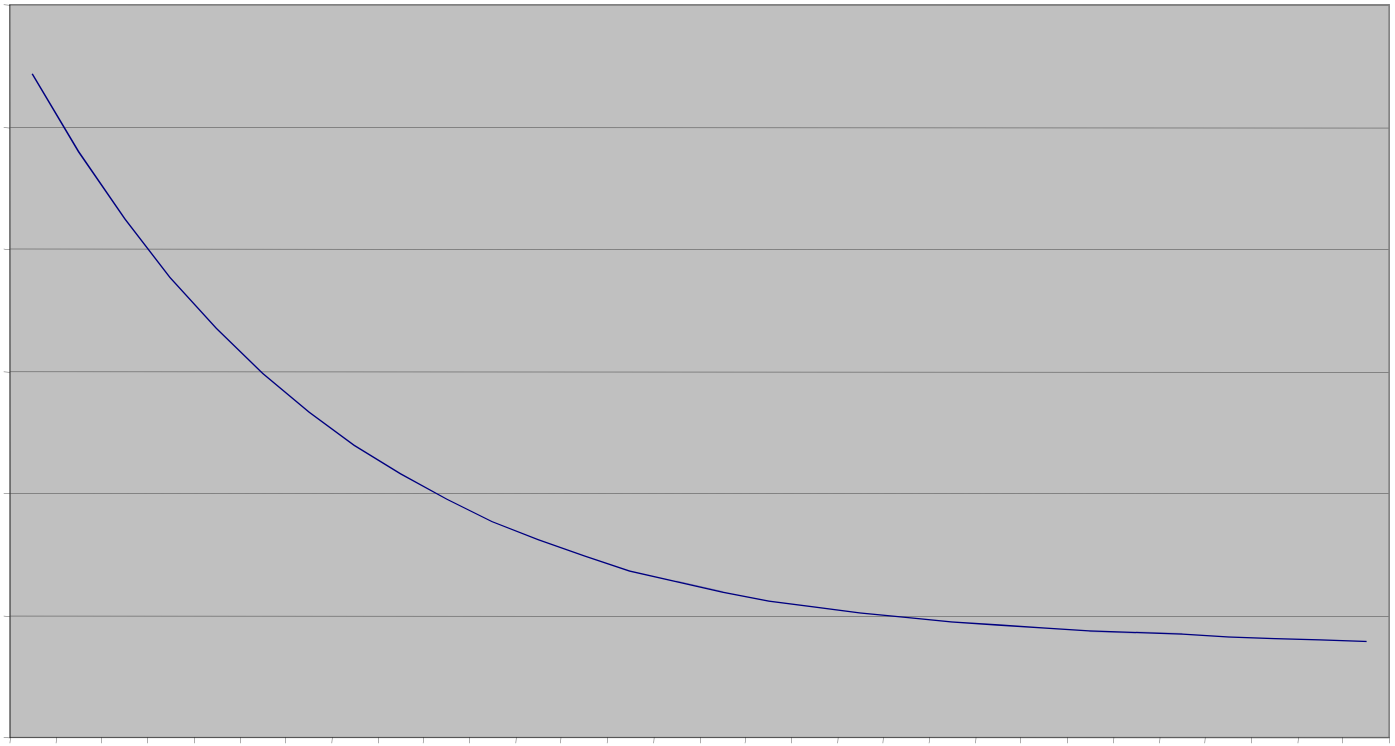
Numerical Experiments

LMEAQHALKMEAHL (Cont.)



Numerical Experiments

Potential Energy



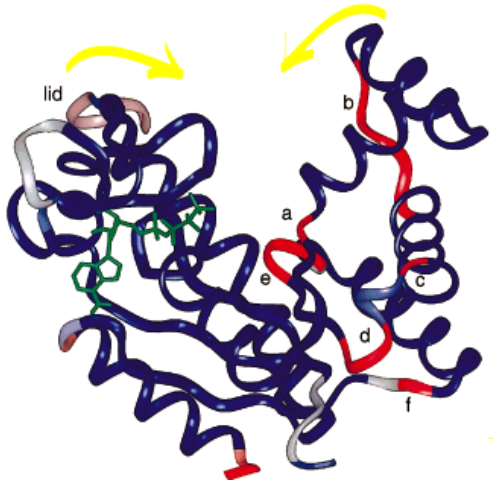
Questions on Force Field Model and Conformation Change?

Mobility Analysis

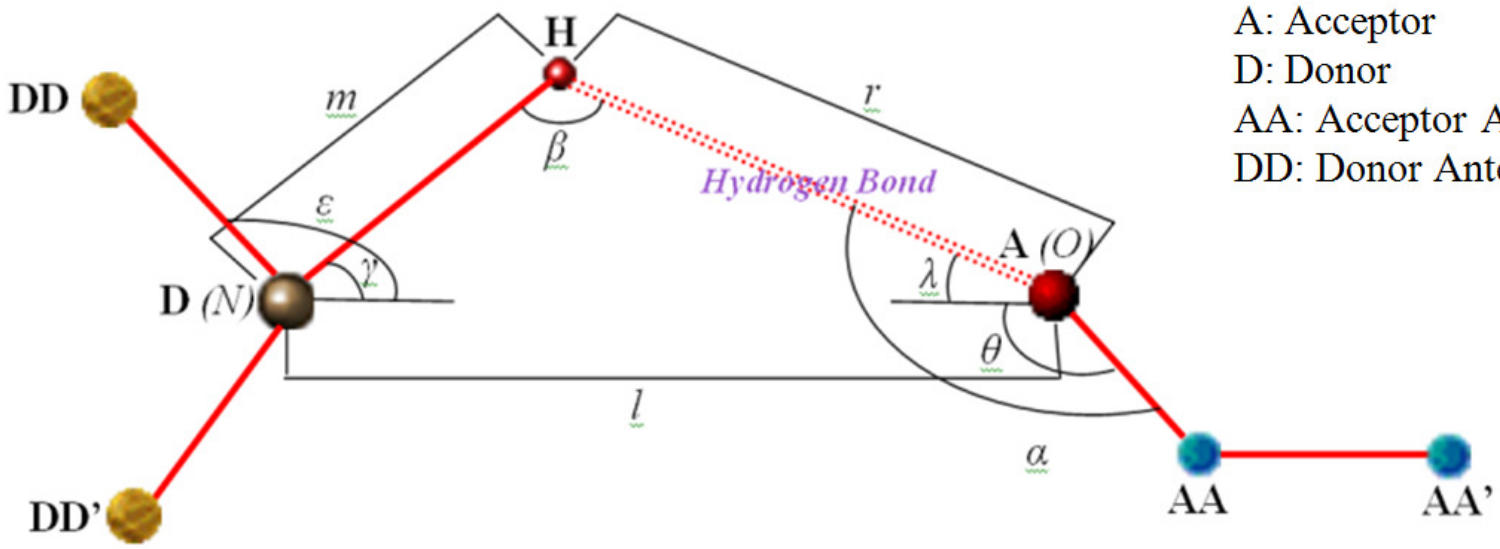
Identification of Rigid and Flexible domains

- Hydrogen Bonds: Interaction between a Hydrogen atom and an electro-negative atom (such as oxygen or nitrogen)

  - Establish rigidity
  - Improve faithfulness
  - Reduce DOF of the protein



Hydrogen Bonds

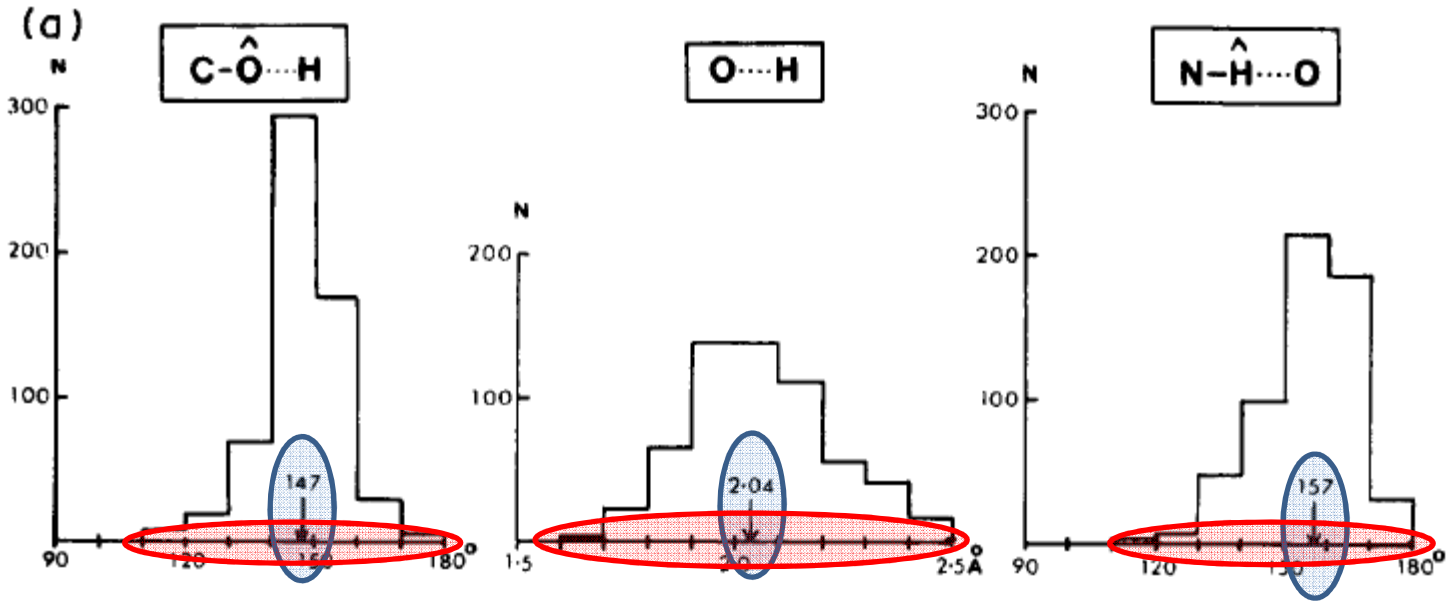


A: Acceptor
D: Donor
AA: Acceptor Antecedent
DD: Donor Antecedent

Hydrogen Bonds Geometric Criteria

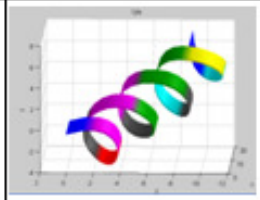
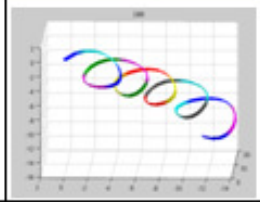
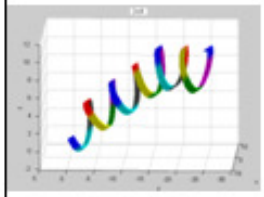
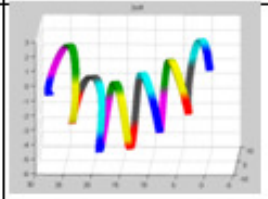
	α°	β°	θ°	γ°	r °A	l°A
E.N. Baker *et al.* [36]	147±9	155±11	153±8	17±8	2.06±0.16	2.99±0.14
Ian K.McDonald *et al.* [48]	>90	>90	>90		<2.5	<3.9
D. Xu *et al.*[51]	140±19.3	151.5±16.3	146.2±18		2.06±0.22	2.95±0.21
T. Kortemme *et al.* [38]	85 < ,<180	105<,<180			<2.6A	
Fleming *et al. [46]*	>90	>110				<4.5
Langkilde *et al.* [56]		>120				<3.07
Alexandescu *et al.*[40]		120<,<180			<2.5	
Artymiuk *et al.* [57]				18.5±9.6	2.05±0.18	2.96±0.17
Our Suggested criteria	110<, <180	110<, <180			<2.5	

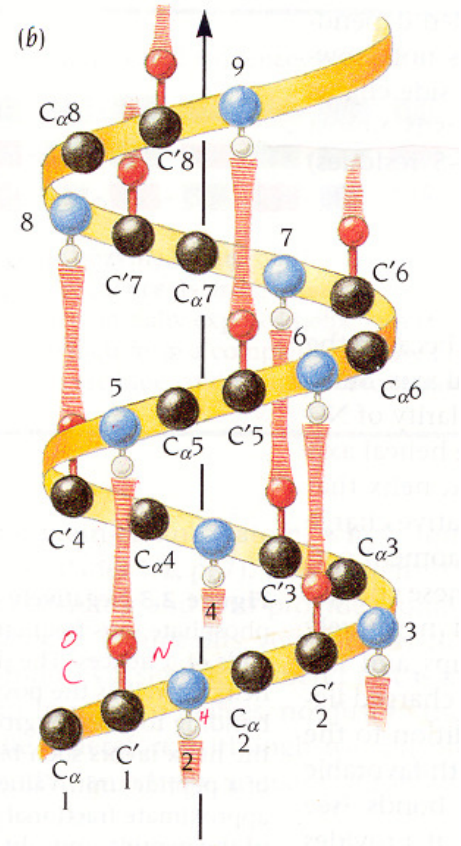
Baker Experimental Results



Baker, E. N., and Hubbard, R. E., 1984. “Hydrogen bonding in globular proteins”. Prog Biophys Mol Biol, 44(2), pp. 97–179

Sample Proteins

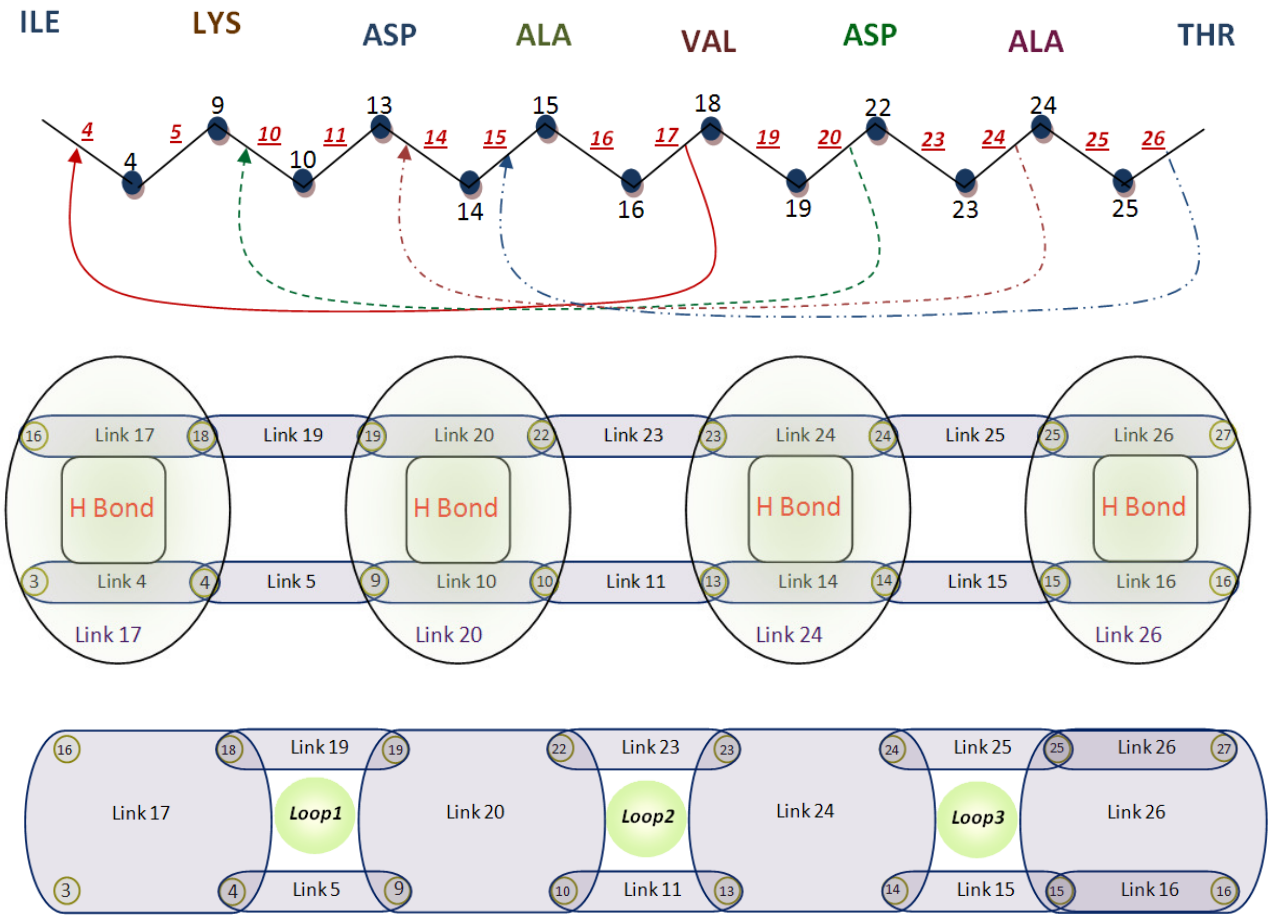
Protein (PDB code)	Amino Acids	Figure	Number of Amino Acids	Number of turns	Confirmed number of Hydrogen bonds in biology
1JILE	REAQKTLA EVTKFIH		15	4.16	11
2I88	IKDAVDAT VIFYLTLTL K		18	5	14
2IC8	SLMHILFNL LWWWYLG GAVEKR		22	6.11	18
2NR9	SNLHILFNL SWFFIFGG MIERT		22	6.11	18



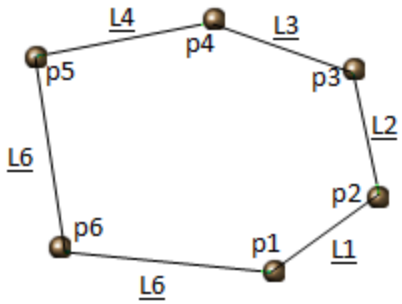
Criteria for Hydrogen bonds Proposed by:	Protein Name			
	1jile	2i88	2ic8	2nr9
	Number of Hydrogen bonds predicted by the criteria			
E.N. Baker *et al.*	7	6	9	6
Ian K.McDonald *et al.*	11	16	19	17
D. Xu *et al.*	10	8	14	8
T. Kortemme *et al.*	12	19	20	16
Fleming *et al.*	14	18	22	22
Langkilde *et al.*	11	11	17	14
Alexandescu *et al.*	11	15	18	16
Artymiuk *et al.*	9	8	14	9
T. Ackbarow *et al.*	15	18	22	22
Our Suggested criteria	11	14	17	15
Confirmed Observations	11	14	18	18

Zahra Shahbazi, Horea Ilies, Kazem Kazerounian, "Hydrogen Bonds and Kinematic Mobility of Protein Molecules", Journal of Mechanisms and Robotics, 2009.

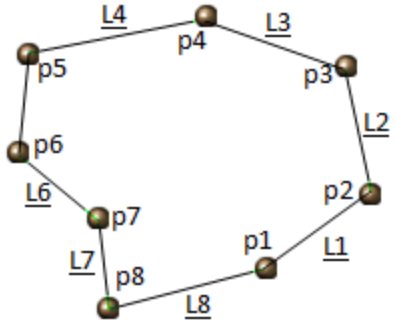
Hydrogen Bonds form Closed Loops



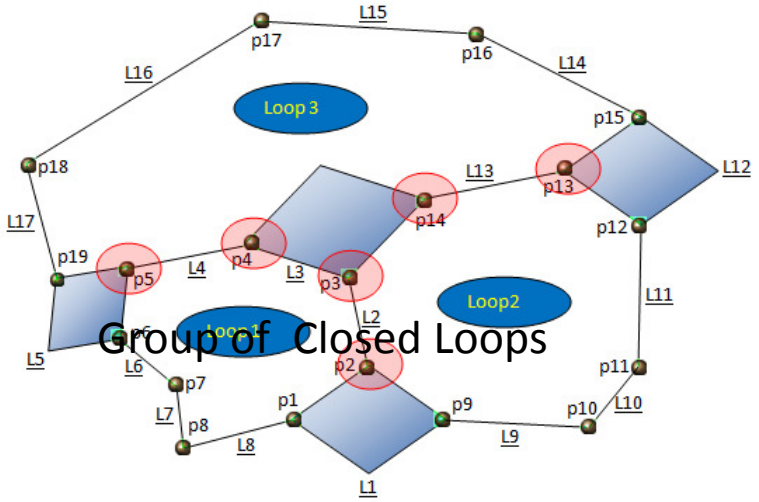
Closed Loops



Rigid Single Closed Loop



Non-rigid Single Closed Loop



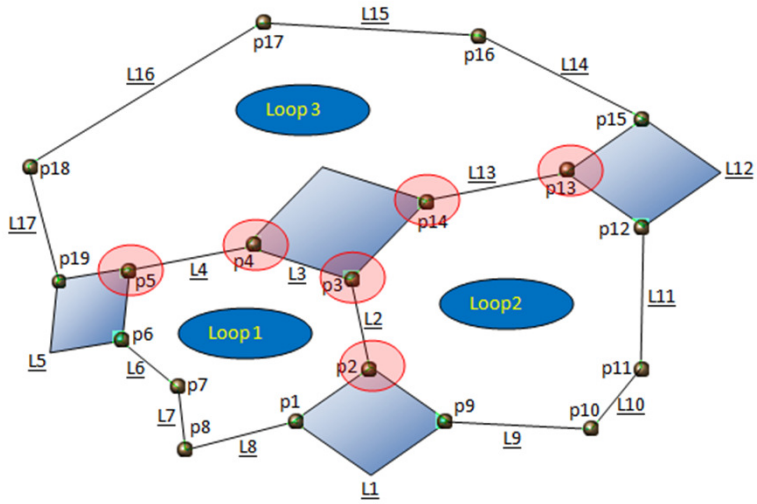
Group of Closed Loops

Grubler-Kutzbach criterion

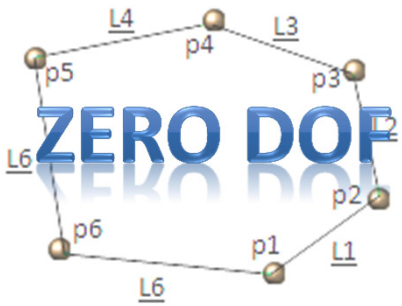
$$DOF = 6(L-1) - 5J_1 - 4J_2 - 3J_3 - 2J_4 - J_5$$

- L: number of links
- Ji=number of joints with i degrees of freedom

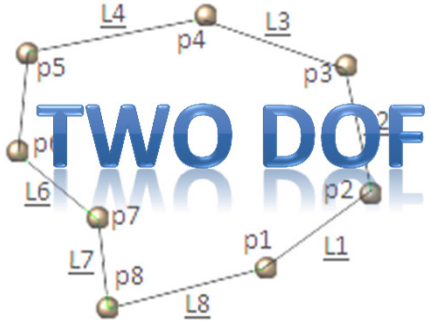
$$DOF = \sum_{i=1}^{m} (DOF)_i - \sum_{j=1}^{n} P_j$$



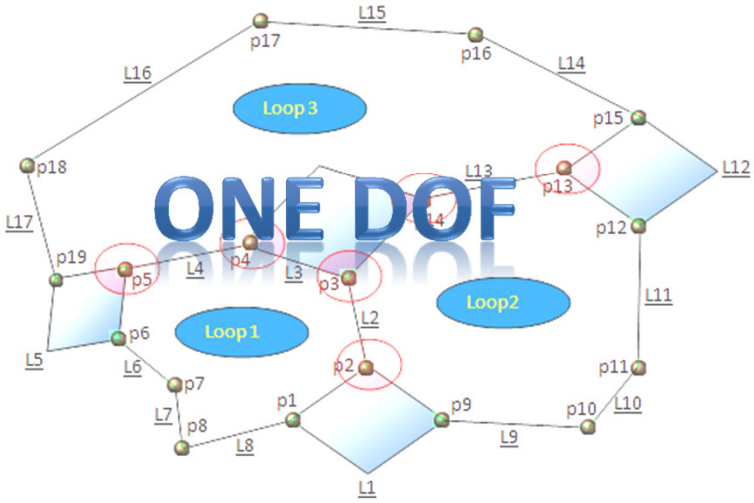
Closed Loops



Rigid Single Closed Loop

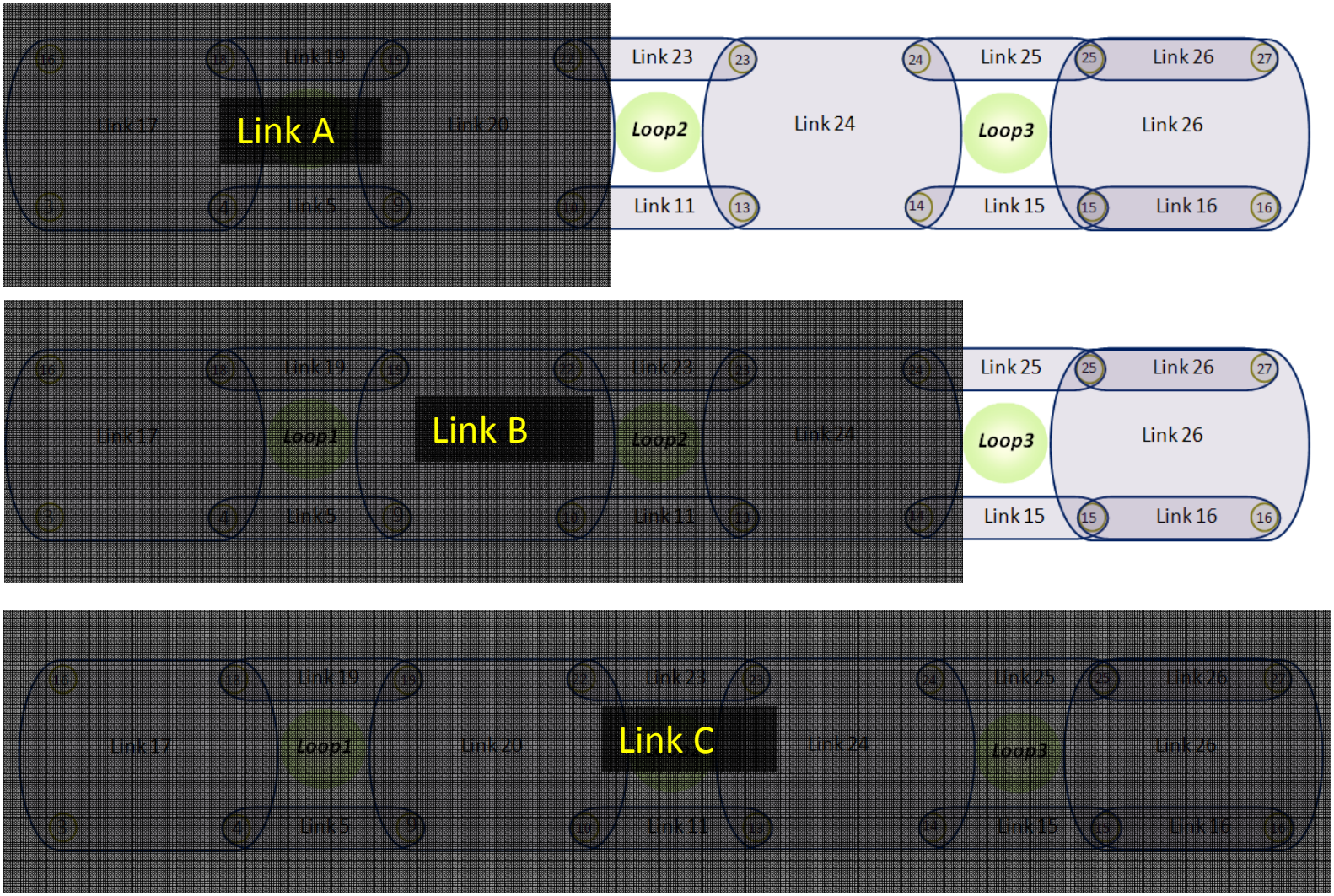


Non-rigid Single Closed Loop

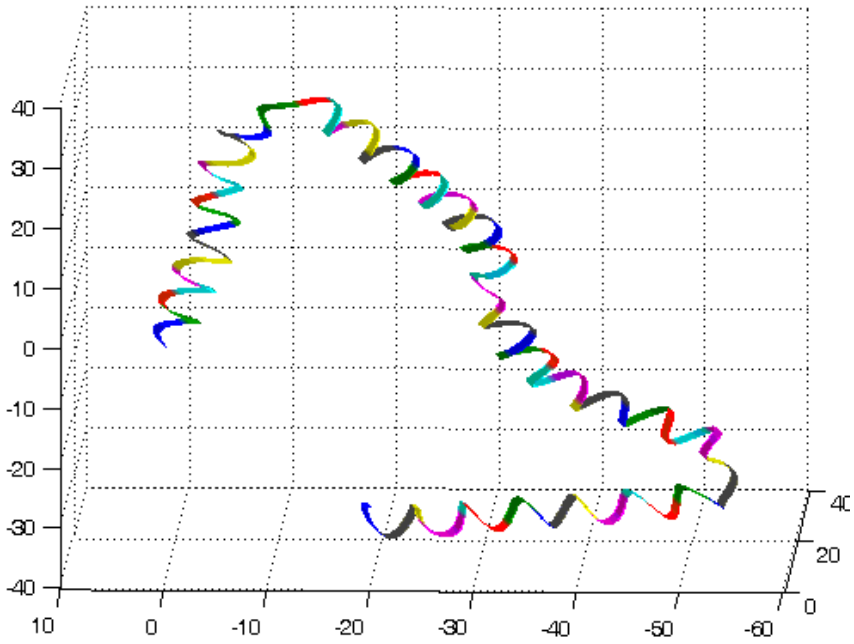


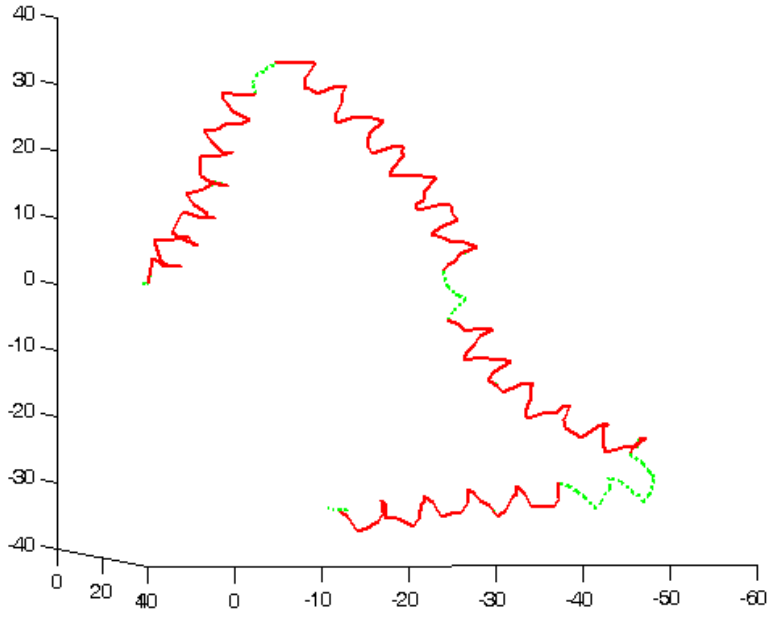
Group of Closed Loops

Rigid loops


Link 19
Link 17
Link A
Link 20
Link 5
Link 23
Loop2
Link 24
Link 11
Link 25
Loop3
Link 26
Link 15
Link 16
Link 19
Link 17
Loop1
Link B
Link 23
Loop2
Link 24
Link 5
Link 11
Link 25
Loop3
Link 26
Link 15
Link 16
Link 19
Link 17
Loop1
Link 20
Link C
Link 23
Link 24
Link 5
Link 11
Link 25
Loop3
Link 26
Link 15
Link 16

Rigid and flexible regions for 1U7M



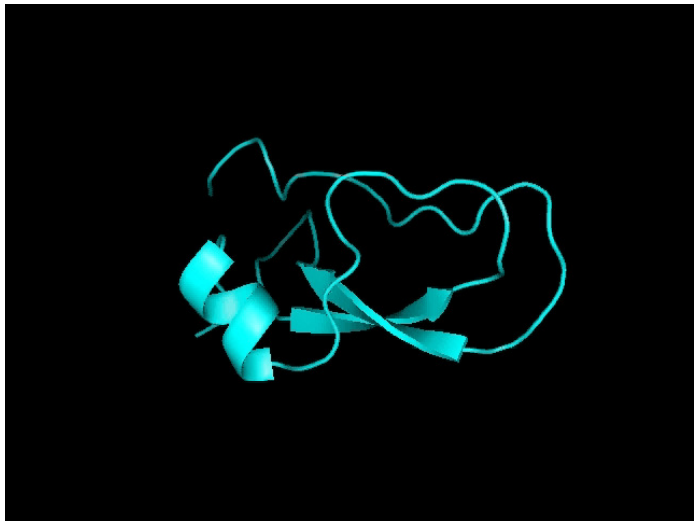


Red: Rigid regions
Green: Flexible region

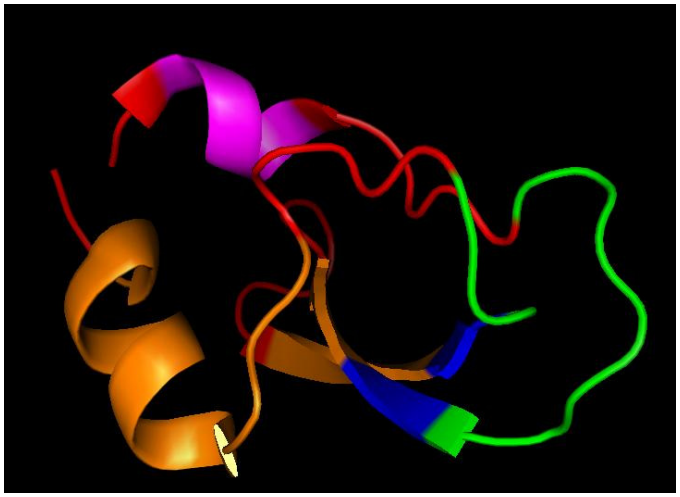
Zahra Shahbazi, Horea Ilies, Kazem Kazerounian, "Hydrogen Bonds and Kinematic Mobility of Protein Molecules", Journal of Mechanisms and Robotics, 2009.

Mobility Analysis

Identification of Rigid and Flexible domains



Movie: 1K6U Protein for Visual check



Red Portions are flexible. Other colors are all Rigid Domains

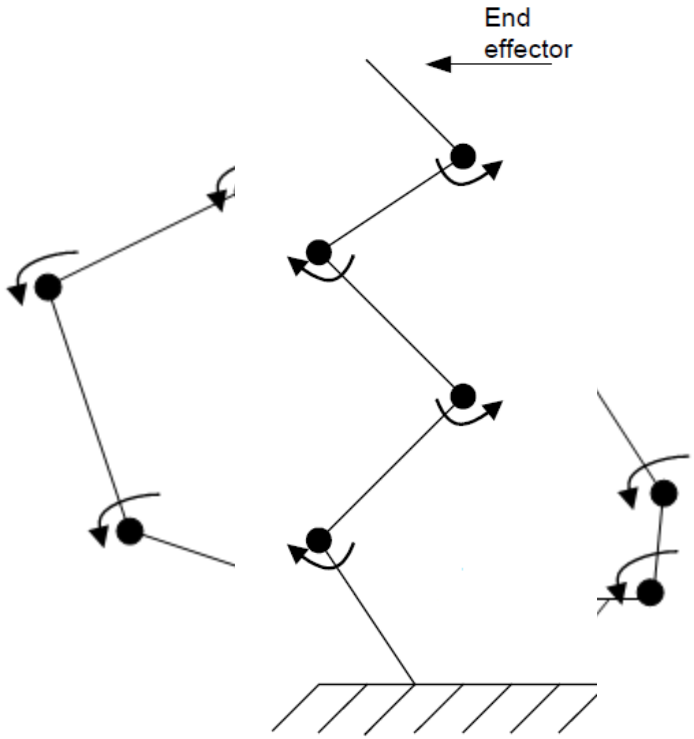
Non-Rigid Loops

$$\dot{\mathbf{X}} = J\dot{\mathbf{q}}$$

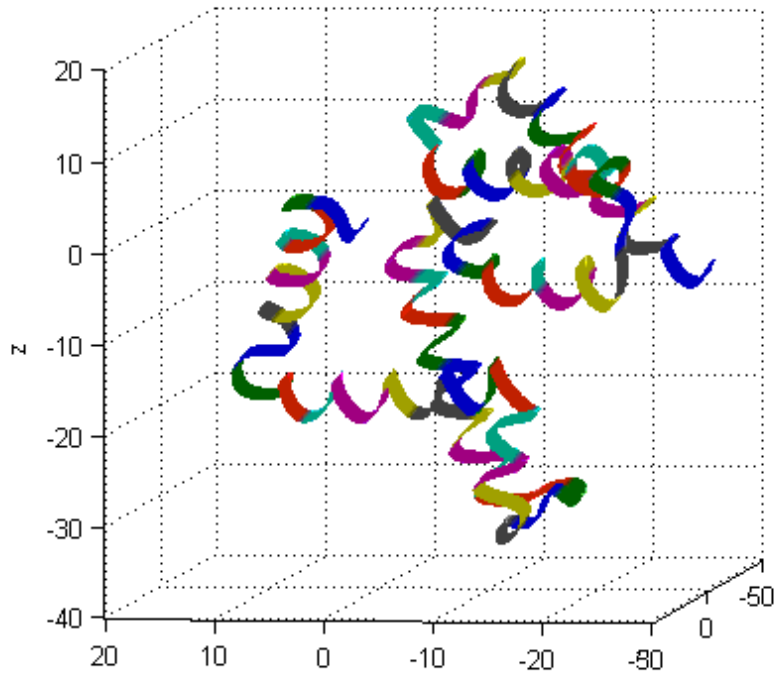
$$J = \begin{pmatrix} u_i \\ \\ u_i * P_i P_H \end{pmatrix}$$

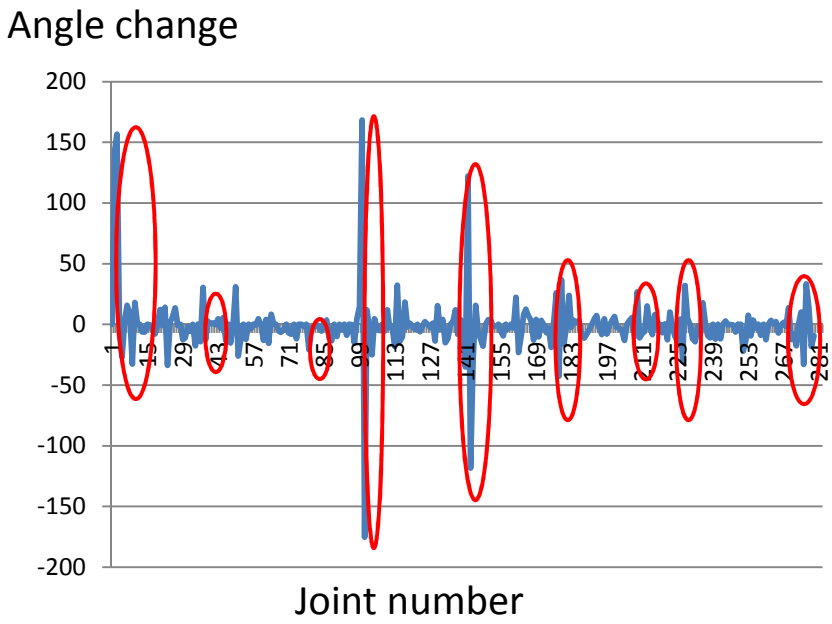
$J\dot{q} = 0$ Closed loop

$J(\Delta\theta) = 0$ Small Displacement



Results





2HHB, 141 AA, 282 DOF
95 Hbond, 59 DOF (79% Reduction)

Zahra Shahbazi, Horea Ilies, Kazem Kazerounian, “Kinematic Motion Constraints of the Protein Molecule Chains", submitted to Journal of Mechanisms and Robotics, 2011.

DOF

		Protein Name			
		1YVQ	2I88	1Z15	2HHB
I	No. of amino acids	141	176	342	141
II	Total No. of DOF	282	352	684	282
III	No. of MC-MC Hbonds	90	98	140	82
IV	No. of DOF considering just MC-MC Hbonds	52	79	303	64
V	No. of all types of Hbonds	106	110	191	95
VI	No. of DOF considering all types of Hbonds using new mobility analysis	39 (86%)	37 (89%)	254 (62%)	59 (79%)

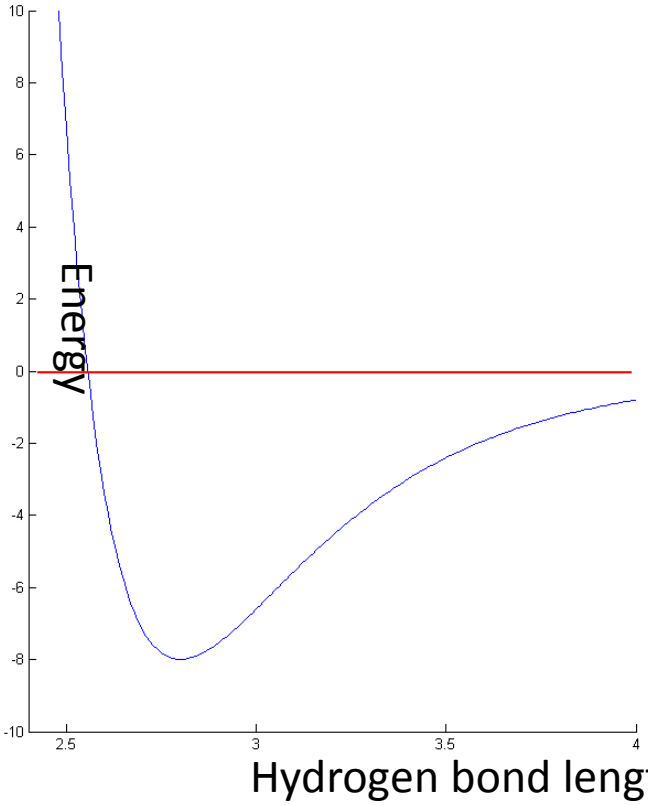
Average of 80%

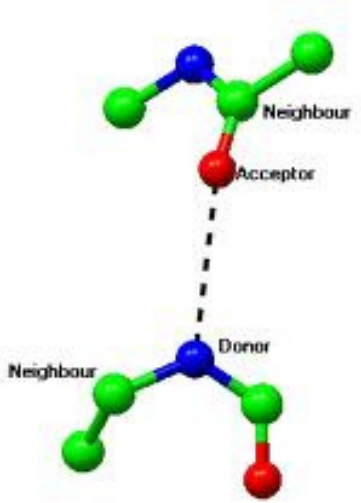
Questions on Mobility Analysis?

Stiffness Analysis

Energy of hydrogen bonds

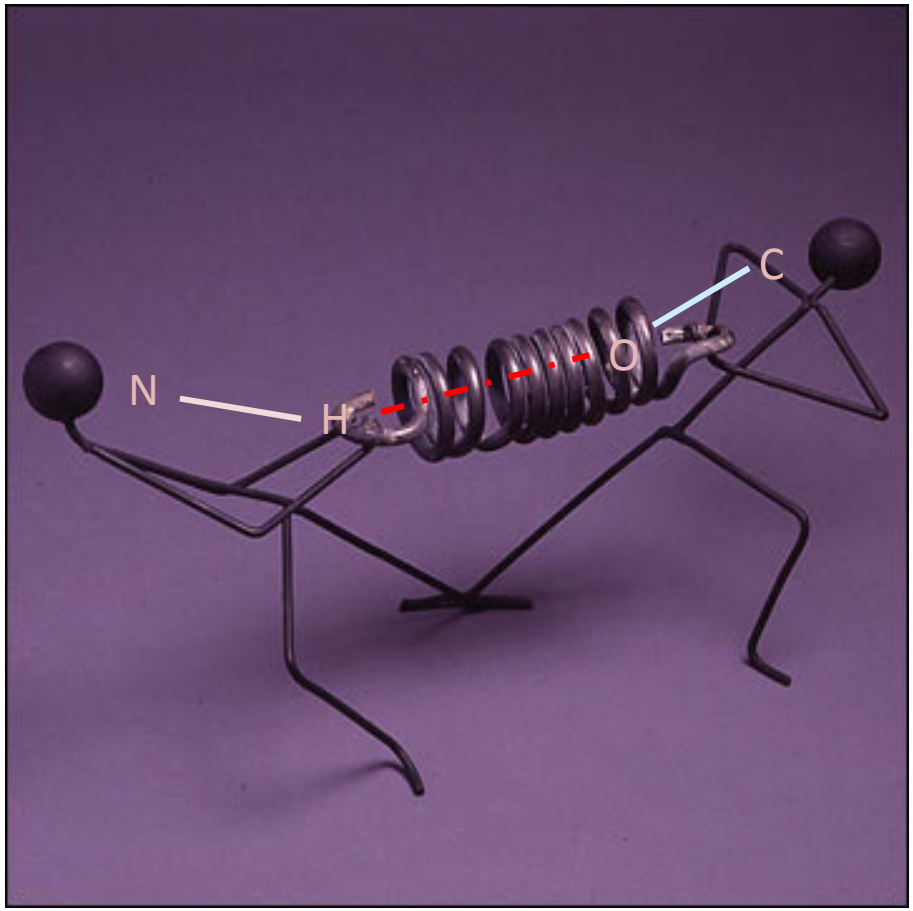
$$E_{HB} = v0[5(d_0/d)^{12} - 6(d_0/d)^{10})]g(\theta, \phi, \Phi)$$





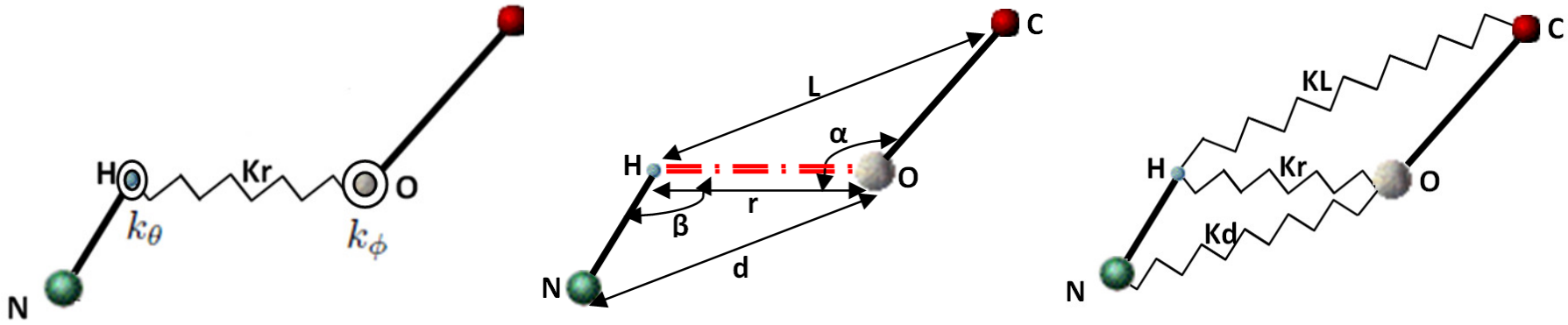
Dahiyat, B. I., Gordon, B., and Mayo, S. L., 1997. “automated design of the surface positions of protein helices”. Protein Science, 6, pp. 1333–1337.

Spring Model of Hydrogen Bonds



Energy Function of Hydrogen bonds

$$E_{HB} = v0[5(d_0/d)^{12} - 6(d_0/d)^{10})]g(\theta,\phi)$$



$$E_{HB}(d,\theta,\phi) = 0.5k_l(l_1 - l_0)^2 + 0.5k_r(r_1 - r_0)^2 + 0.5k_d(d_1 - d_0)^2$$

Optimization Problem

$$M = 0.5k_l(l_2 - l_0)^2 + 0.5k_r(r_2 - r_0)^2 + 0.5k_d(d_2 - d_0)^2 - E(d2, \alpha 2, \beta 2)$$

$$H1 = 0.5k_l(l_1 - l_0)^2 + 0.5k_r(r_1 - r_0)^2 + 0.5k_d(d_1 - d_0)^2 - E(d1, \alpha 1, \beta 1)$$

$$H2 = k_l - dE_l/(l_1 - l_0)$$

$$H2 = k_l - dE_l/(l_1 - l_0)$$

$$H3 = k_r - dE_r/(r_1 - r_0)$$

$$H4 = k_d - dE_d/(d_1 - d_0)$$

$$-k_d + s^2 \leq 0$$

$$-k_d + p^2 \leq 0$$

$$-k_l + q^2 \leq 0$$

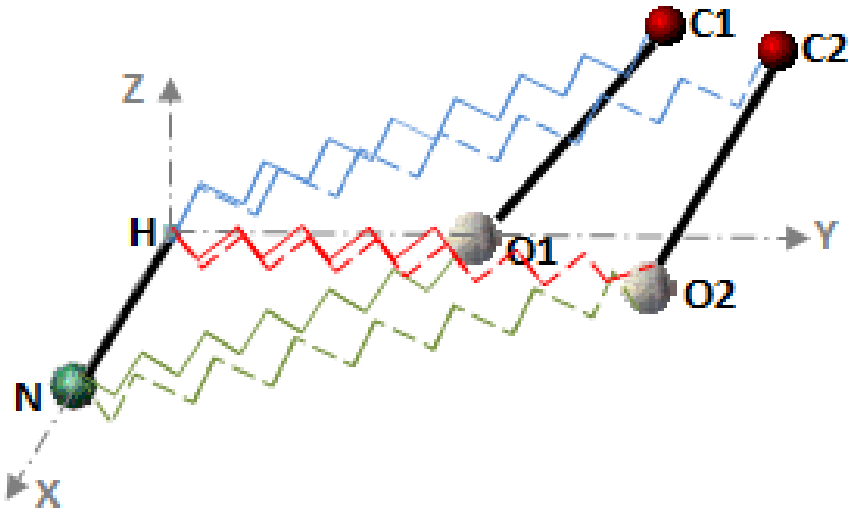
$$-l_0 + m^2 \leq 0$$

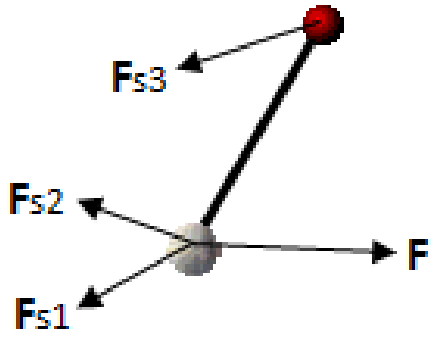
$$-r_0 + n^2 \leq 0$$

$$-d_0 + o^2 \leq 0$$

$$-k_d + s^2 \leq 0$$

Small Displacement



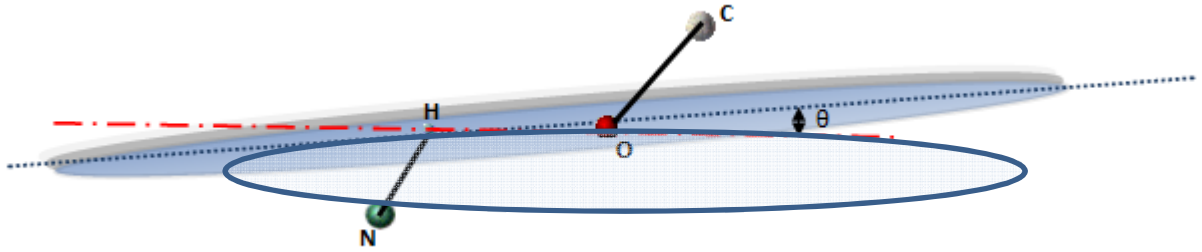


$$\begin{pmatrix} F_x \\ F_y \\ F_z \end{pmatrix} = \begin{pmatrix} k_{11} & k_{12} & k_{13} & k_{14} & k_{15} & k_{16} \\ k_{21} & k_{22} & k_{23} & k_{24} & k_{25} & k_{26} \\ k_{31} & k_{32} & k_{33} & k_{34} & k_{35} & k_{36} \end{pmatrix} * \begin{pmatrix} dx_o \\ dy_o \\ dz_o \\ dx_c \\ dy_c \\ dz_c \end{pmatrix}$$

Table 1: Hydrogen bond stiffness for some sample bonds

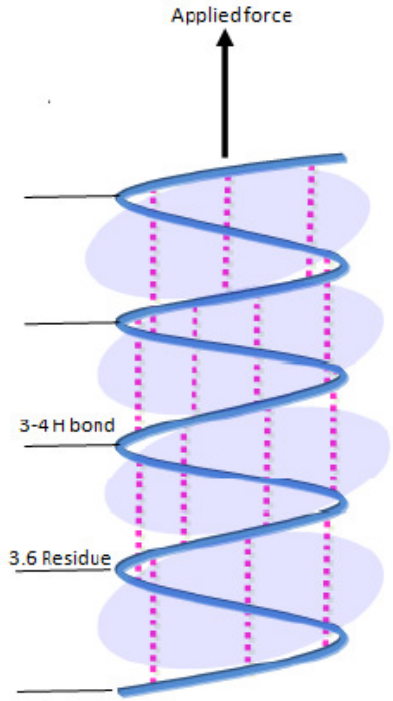
E(energy)	k_l	k_r	k_d	l_0	r_0	d_0	max k	mean k	min k	θ^*	k^{**}
-2.303	51	26.3	4.8	2.9	2.2	3	54.53	1.82	0.14	6.9	3.36
-2.29	40.9	8	1.7	2.8	2	2.9	34.16	0.49	0.07	10	1.19
-3.576	68.3	23.6	3	2.8	2	2.9	64.68	1.61	0.07	5.4	2.1
-3.232	111.2	37.9	6.9	2.8	1.9	2.8	104.51	2.03	0.14	7.9	4.83
-4.791	87.9	26.6	3.3	2.8	2	3	80.43	1.19	0.14	5.5	2.31
-4.843	127.7	28.8	3.9	2.8	1.8	2.9	109.69	1.26	0.21	6.4	2.73
-3.676	69.6	22.7	3.5	2.8	2	3	64.82	1.19	0.14	6.8	2.45
-2.238	57.1	41.9	6.5	2.9	2.2	3	70.56	3.15	0.14	5.1	4.55
-2.043	45.3	22.1	4.6	2.9	2.2	3	47.39	1.33	0.14	8.2	3.22
-3.04	62.1	26.4	4.4	2.9	2.1	3	62.23	1.61	0.21	6.7	3.08
-1.37	46.9	49.6	8.2	3.1	2.4	3.1	69.51	4.2	0.14	4.6	5.74
-2.856	60.1	27.7	4.8	2.9	2.1	3	61.81	1.61	0.14	6.9	3.36
-3.765	109.3	29.8	5.3	2.8	1.9	2.8	97.44	1.33	0.14	8	3.71
-1.172	39	37.3	7.7	3	2.4	3.1	54.53	2.87	0.28	6.1	5.39

Bond Type	Bond stiffness (N/m)

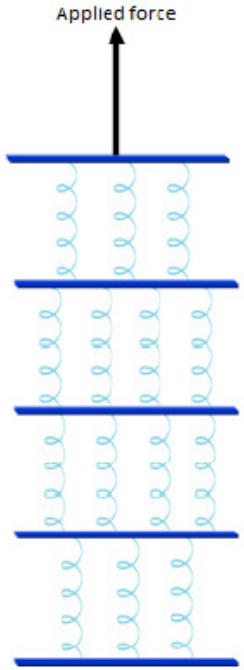


Ashby, M., Shercliff, H., and Cebon, D., 2007. Materials: engineering, science, processing and design. Butterworth-Heinemann.

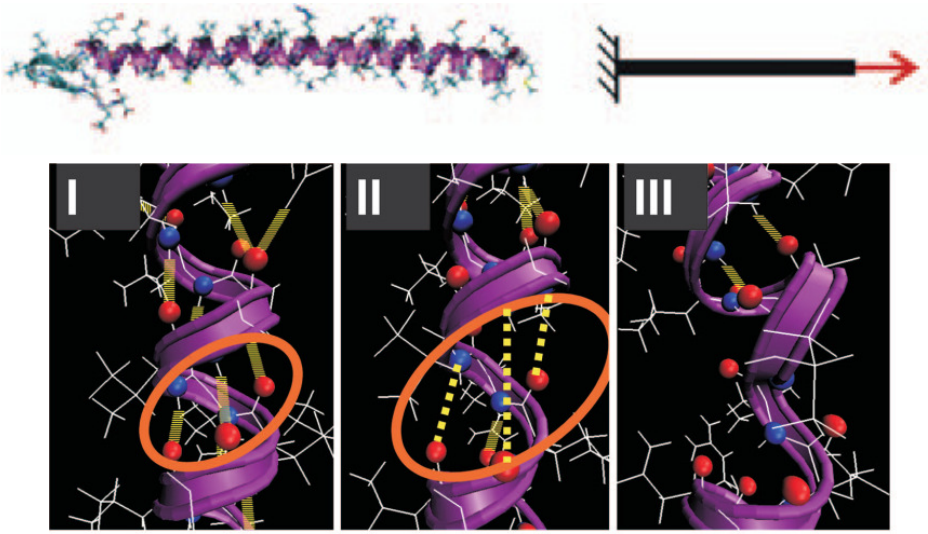
Calculating the stiffness of protein molecules



A: Schematic Biological System



B: Mechanical Equivalent Model



$$K_{eq} = 1/(1/k_{turn1} + 1/k_{turn2} + ... + 1/k_{turn-end})$$

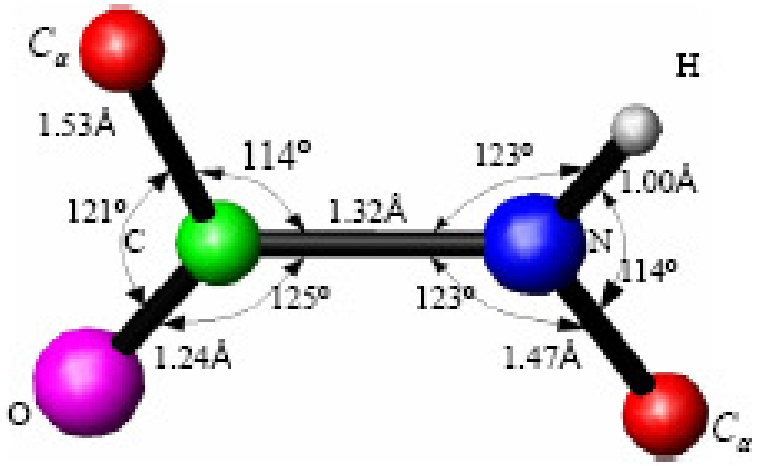
$$(1/2)K_{eq}(d_l)^2 = \Sigma(1/2)k_i(d_x)^2$$

PDB code	K from method # 1	K from method # 2	k reported in litrature
Synthetic peptide	380	384	300-400 [3]
1gk6	520	524	571 [7]
1nkn	83	66	60-80 [6]

Questions on Stiffness Analysis?

Parameter Calibrations

Parametric Calibration of the Geometric Features of a Peptide Plane

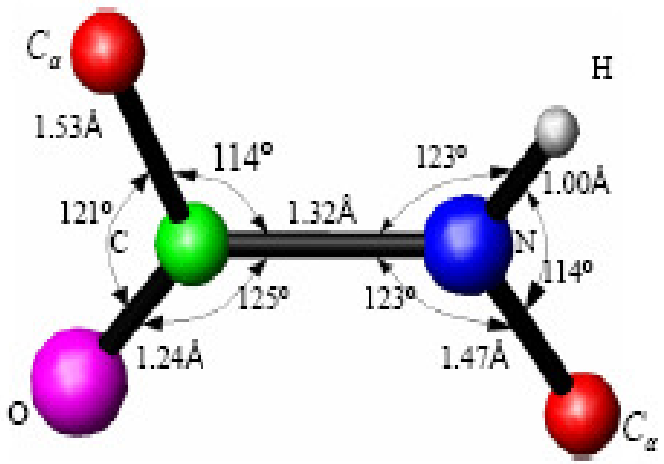


The geometric model of a Peptide plane with standard dimensions reported by Pauling and Corey (1951)

In search of the best values of the bond lengths and bond bending angles in a Peptide plane that offers a better structural definition of the proteins in terms of their Dihedral angles

Parametric Calibration of the Geometric Features of a Peptide Plane

Bond Lengths:
N-C(A): 1.3841Å,
C(A)-C: 1.4544Å,
C-N: 1.1893Å,
C=O: 1.0714Å
N-H: 0.8686Å



Bond Bending Angles:
N-C(A)-C: 111.164 degrees
C(A)-C=0: 107.4012 degrees
C(A)-C-N: 120.2981 degrees
O=C-N: 132.2735 degrees
C-N-H: 121.3974 degrees
C-N-C(A): 127.3087 degrees
C(A)-N-H: 111.2785 degrees

Peptide bond torsion angle:
179.128 degrees

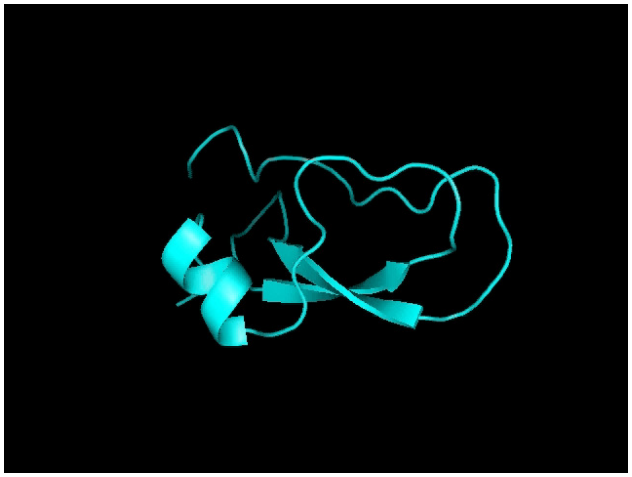
- A systematic optimization approach
- Minor changes (0.5% to 13.5%) in the bond length and bond angles to the standard form reported by Pauling and Corey leads to significant reduction in the Euclidian norm error (3.5% to 64.5%).

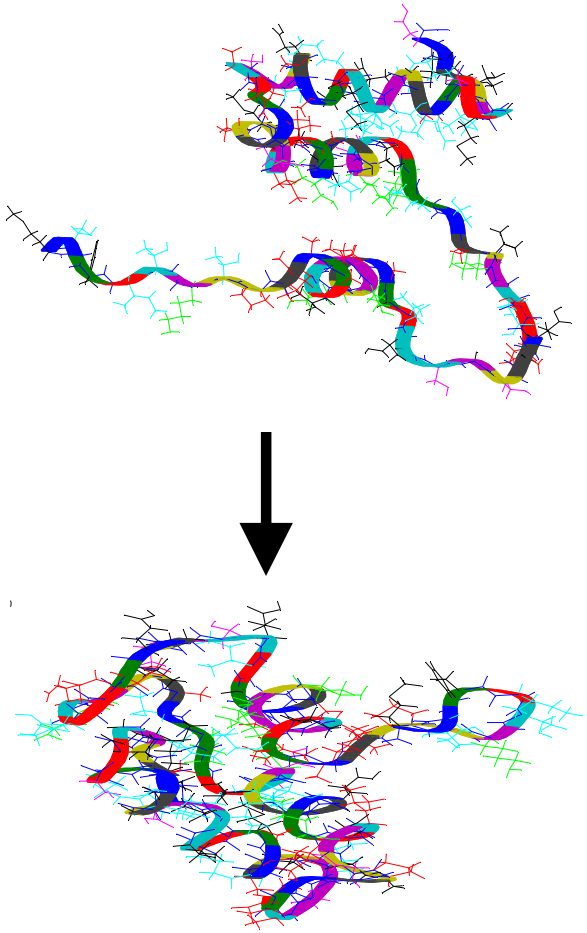
Conformation Pathways

Understanding Pathways

Graduate Student: Peter Bohnenkamp

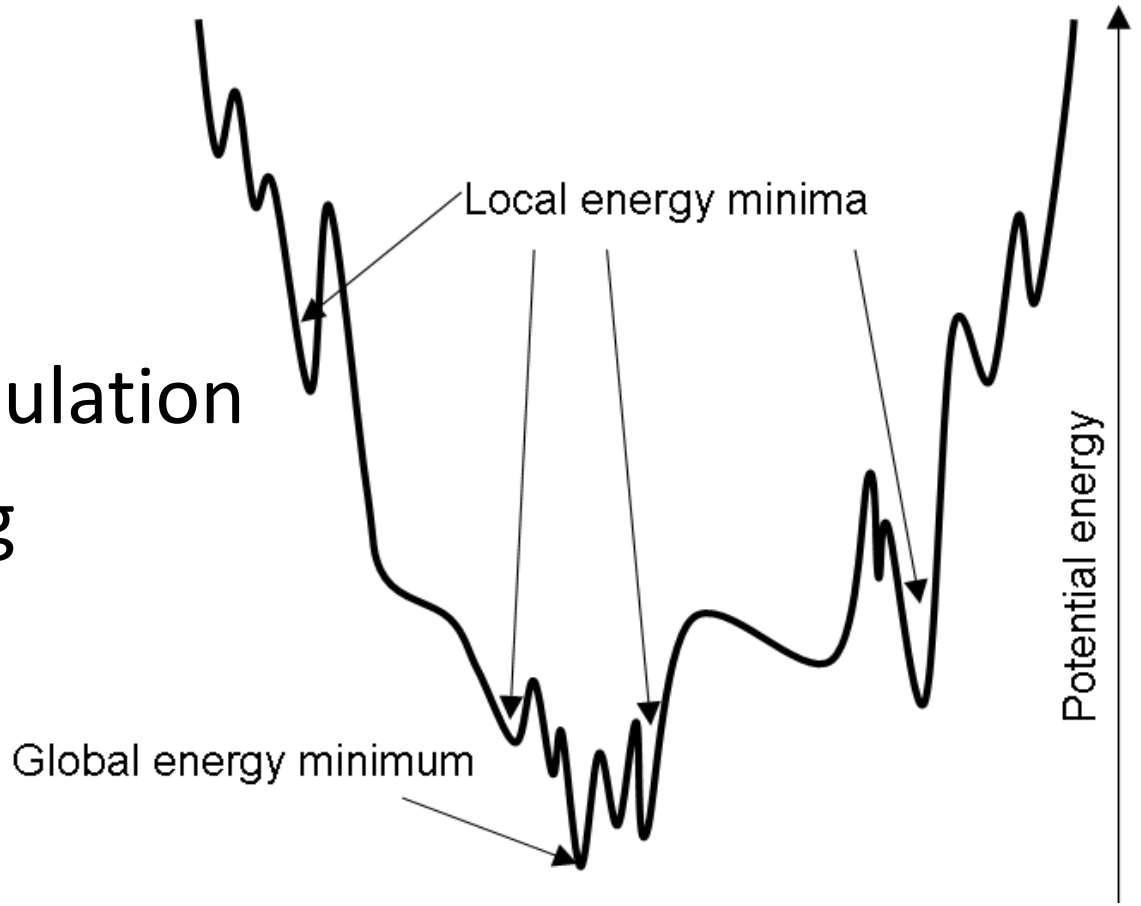
- Single protein – multiple conformations; depend on environment
- What are intermediate steps (pathway) in transition between conformations?





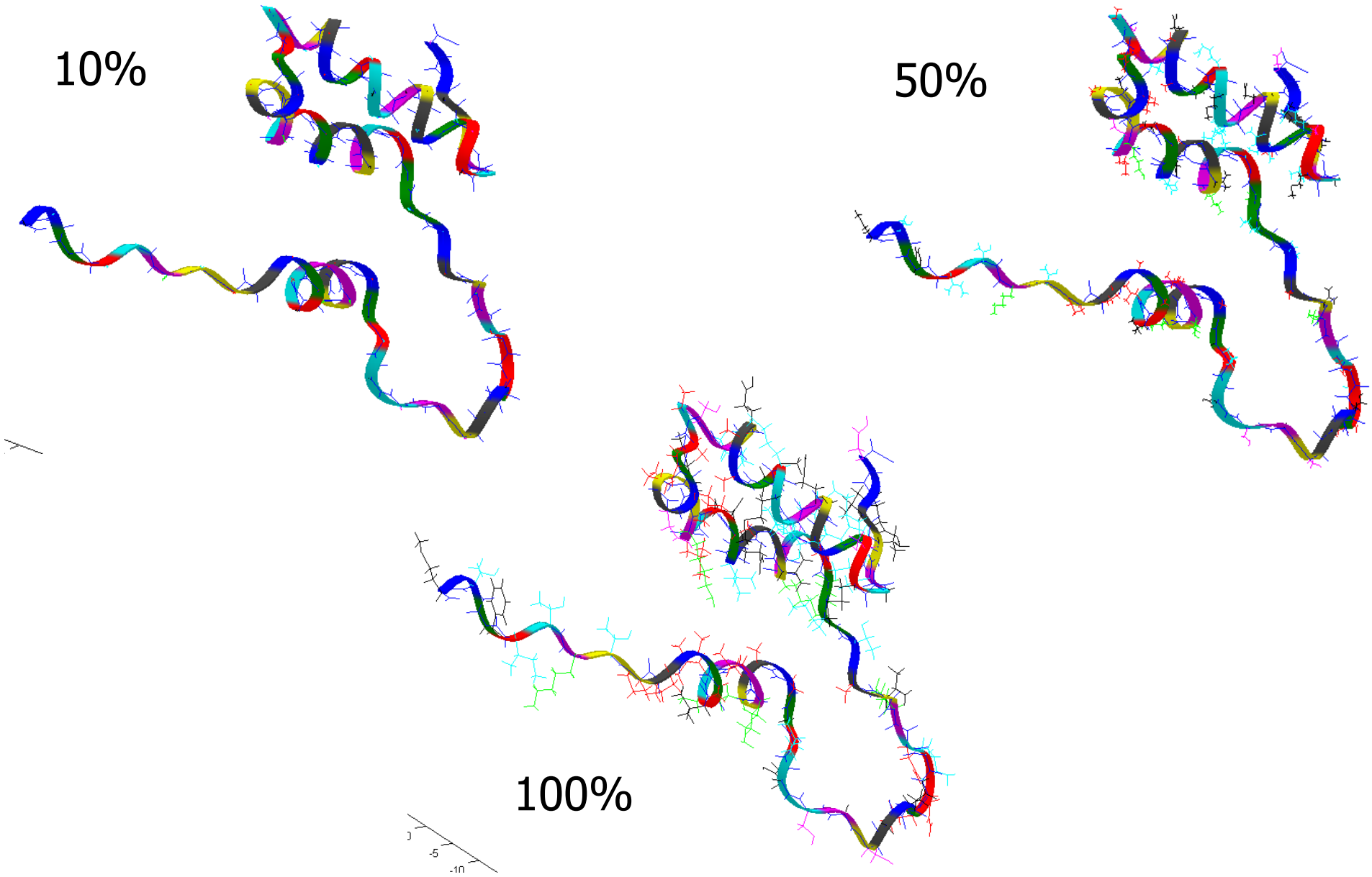
Energy Landscape

- Folding funnel
- Avoid “traps” of local energy minima

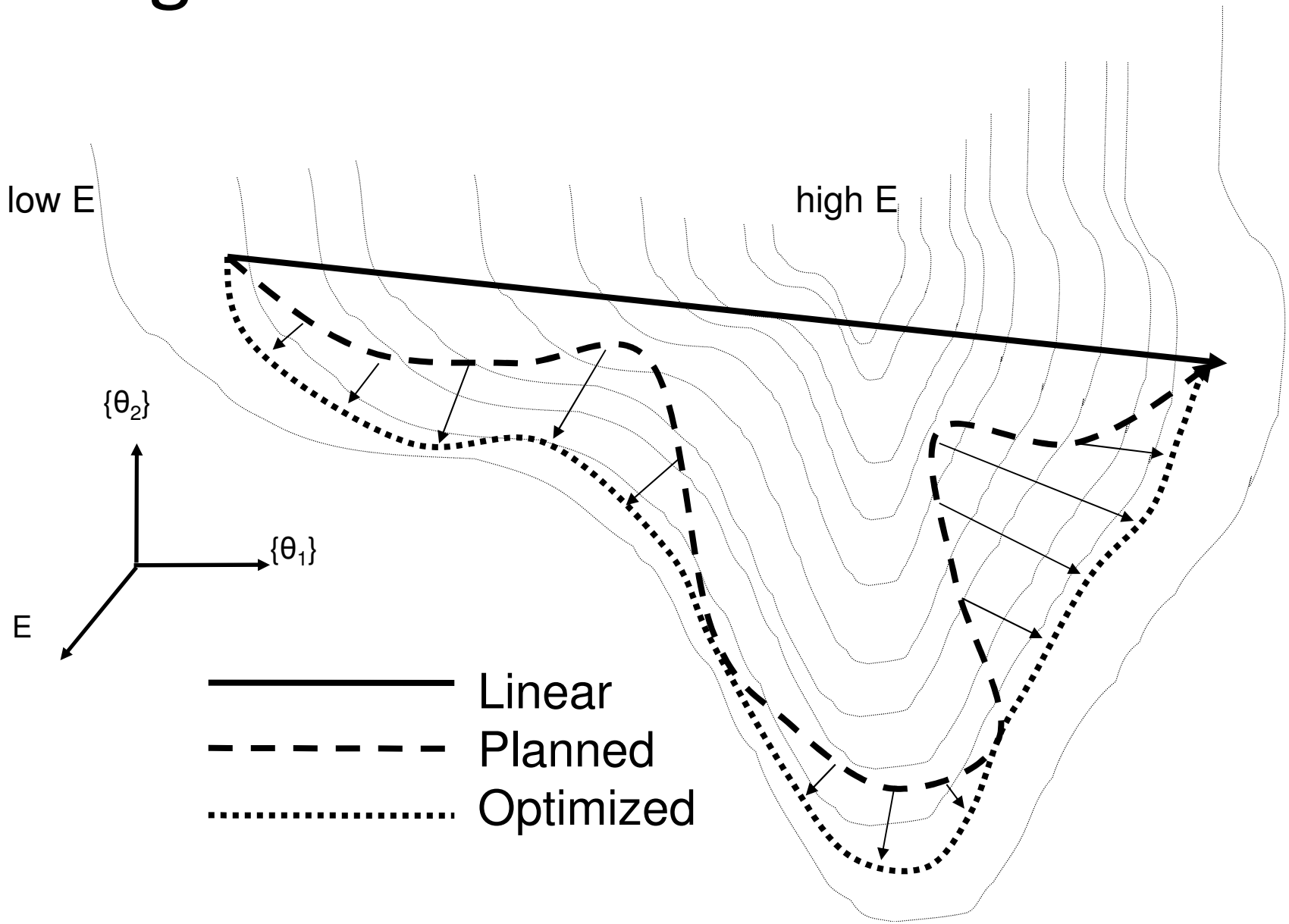


- Segmental Manipulation
- Side Chain Scaling

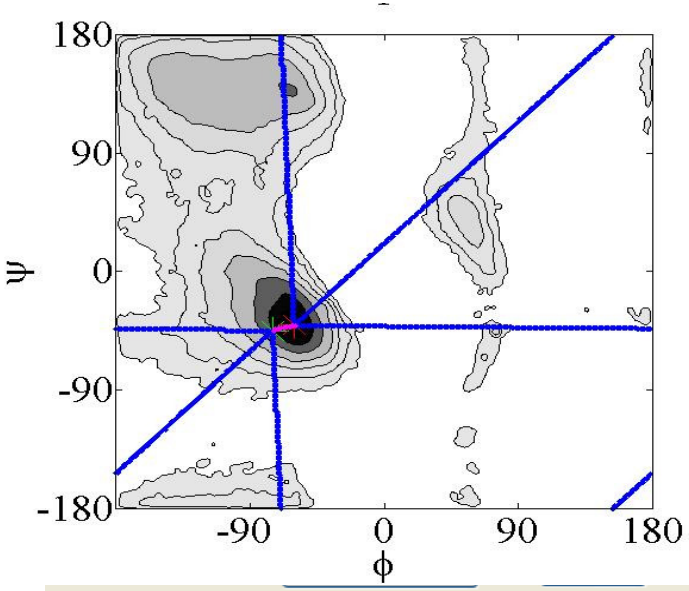
Side Chain Scaling

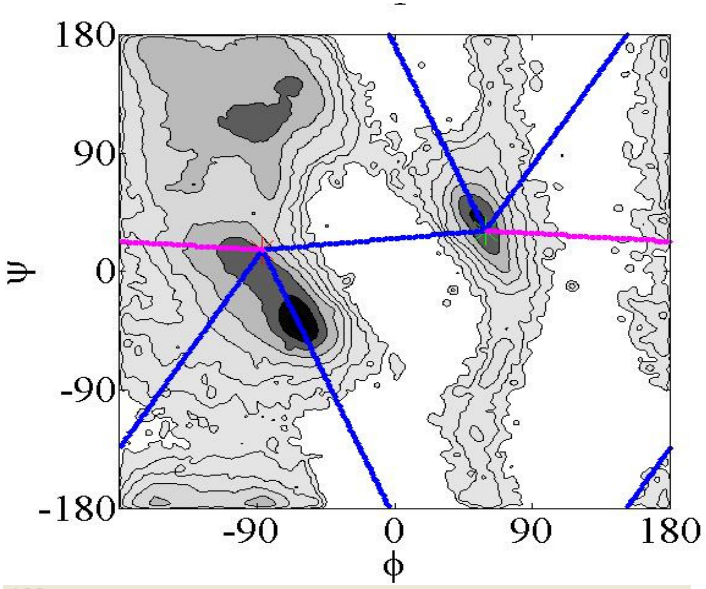


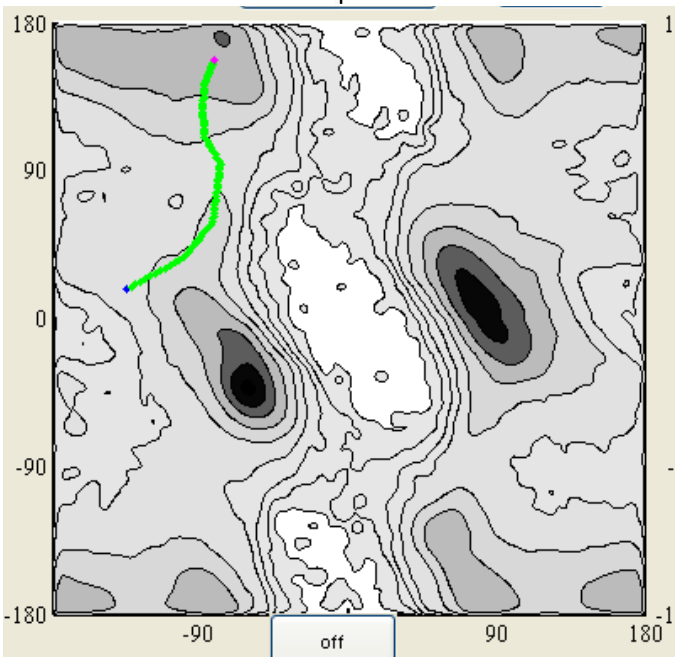
Design of Feasible Conformations

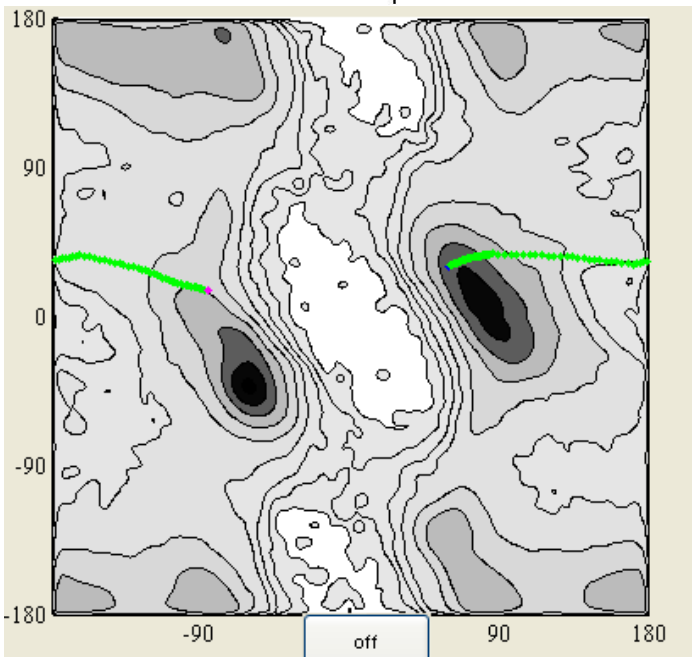


Path Planning

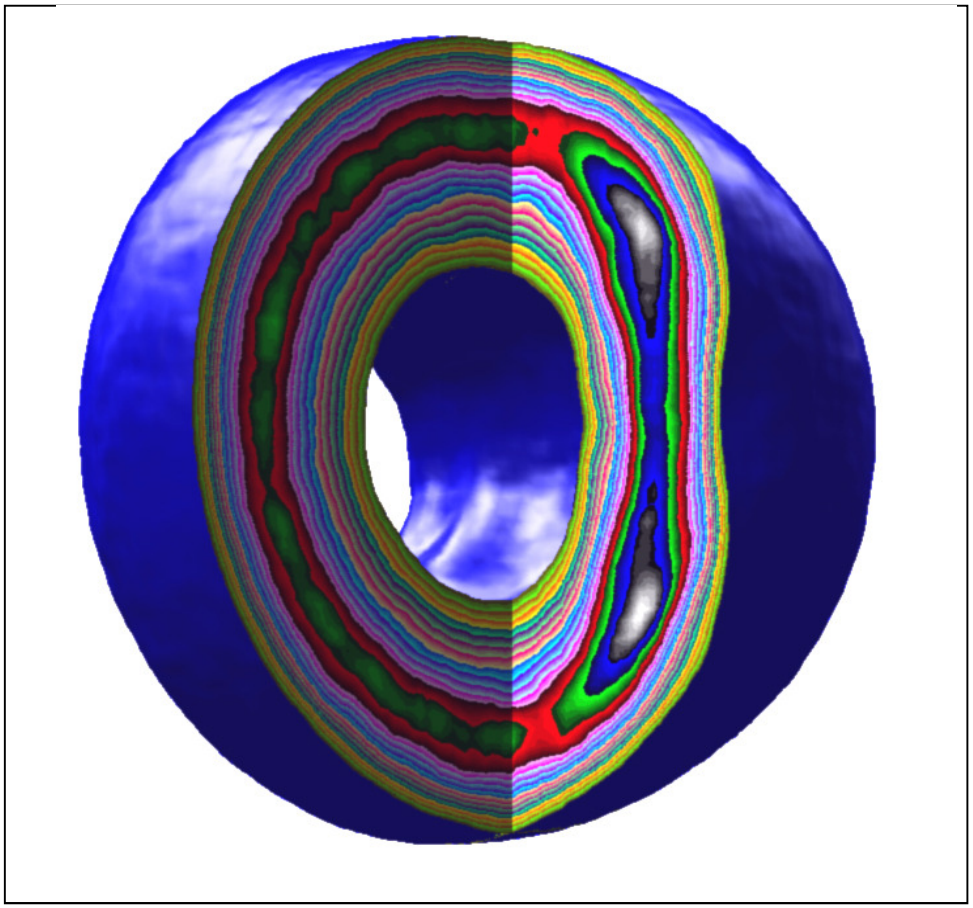






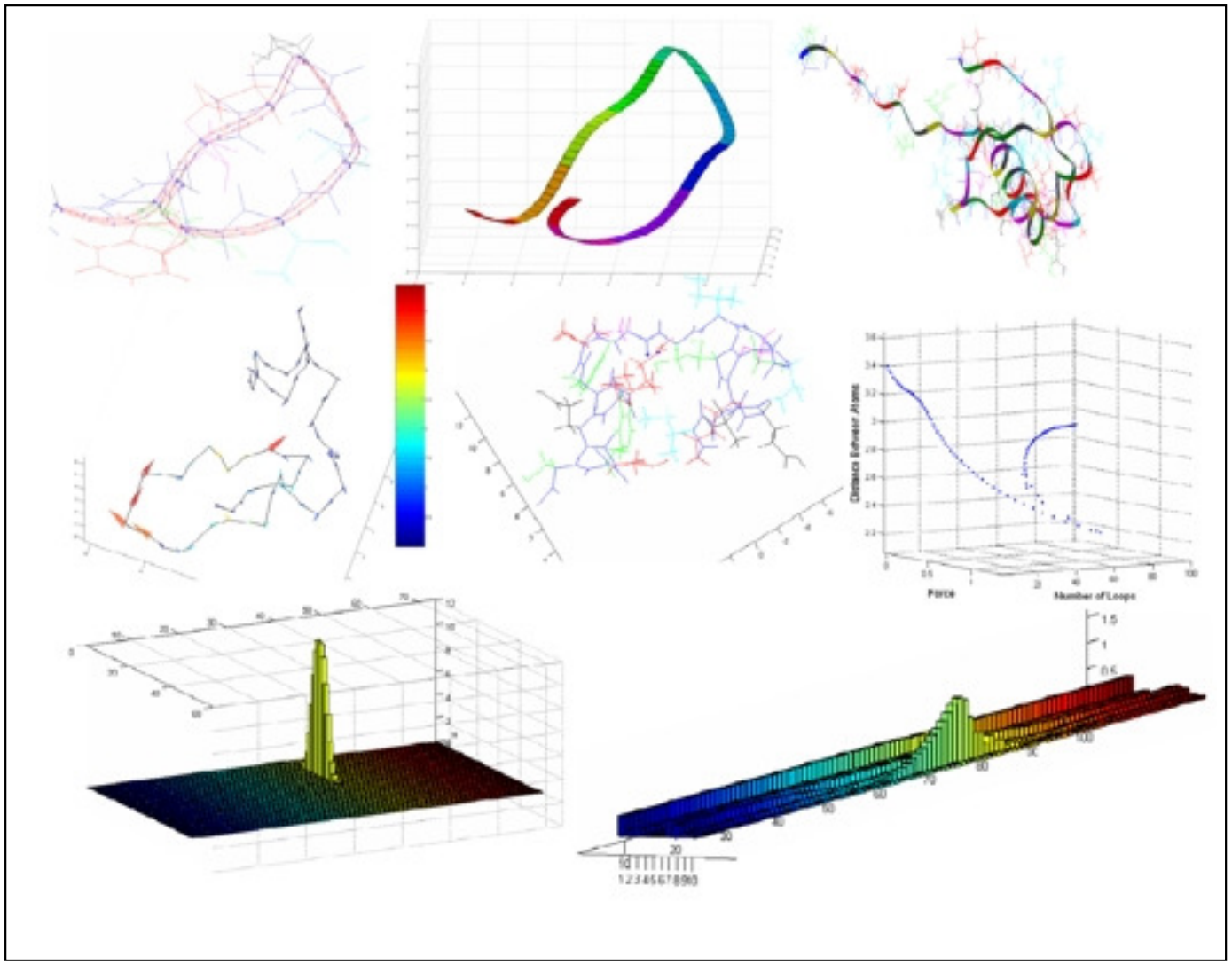


Work Space Analysis

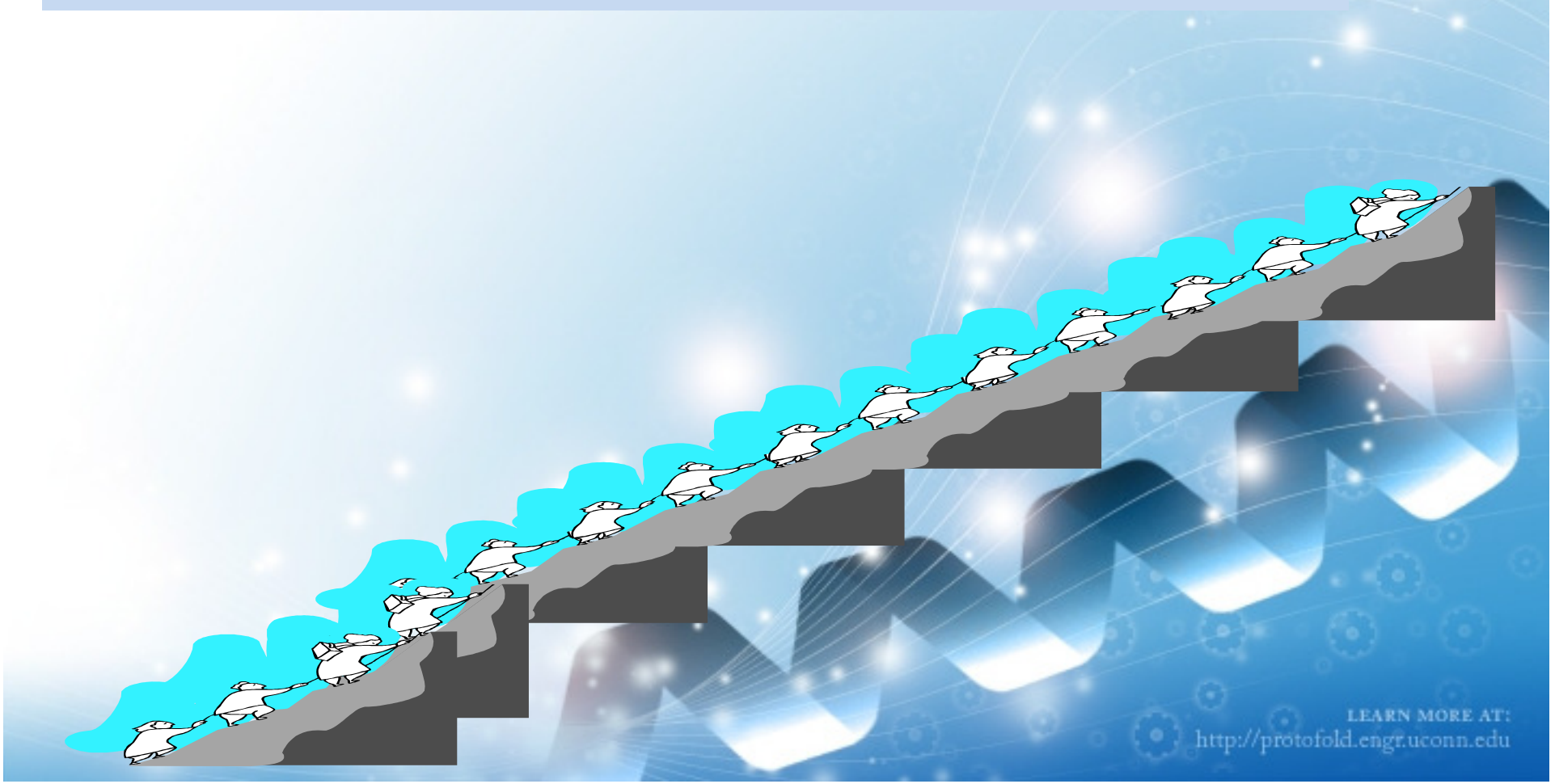


The workspace of the backbone of a three residue peptide chain

CAD Kernel



Concluding Thoughts



- Similarities of the protein folding in biological systems and the manipulation of mechanisms and robotics linkages
- Tremendous opportunities for contribution by kinematics
- Mind bugling analysis and computational complexities

- Protofold:
  - A comprehensive model for fold and motion prediction of protein polypeptide chains
  - Stable kinematic notation and analysis
  - Efficient kineto-static force analysis
  - Motion prediction without the need for molecular dynamics simulations

Acknowledgements

LEARN MORE AT:
http://protofold.engr.uconn.edu

Work of Graduate Students:

- Carlos Alvarado
- Morad Behandish
- Peter Bohnenkamp
- Hima Khoshreza
- Khalid Latif
- Chris Madden
- Jessie Parker
- Karla Rodrigues
- Zahra Shahbazi
- Raghav Subramanian
- Pouya Tavousi

Financial support:

- University of Connecticut

- NSF support acknowledged by K. Kazerounian
  - CMMI 0856401
  - CNS 0923158
  - CMMI 1053077

- NSF support acknowledged by H. Ilies
  - CMMI 0555937
  - CMMI 0644769
  - CMMI 0856401
  - CMMI 0927105


Thank You!