



ભારતીય સૌંકેલિક વિજ્ઞાન સંસ્કૃત હૈડ્રેબાદ  
ભારતીય પ્રૌદ્યોગિકી સંસ્થાન હૈદરાબાદ  
Indian Institute of Technology Hyderabad

# Biomolecular Simulation

# BT2123

## Lecture 1 : Introduction

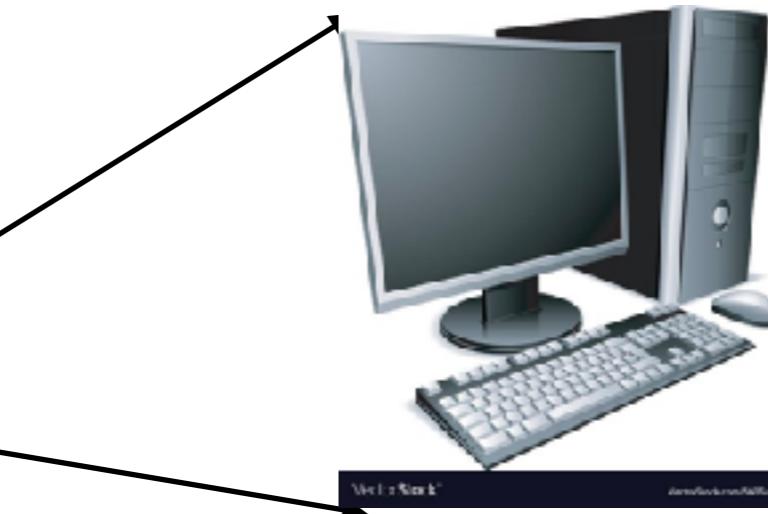
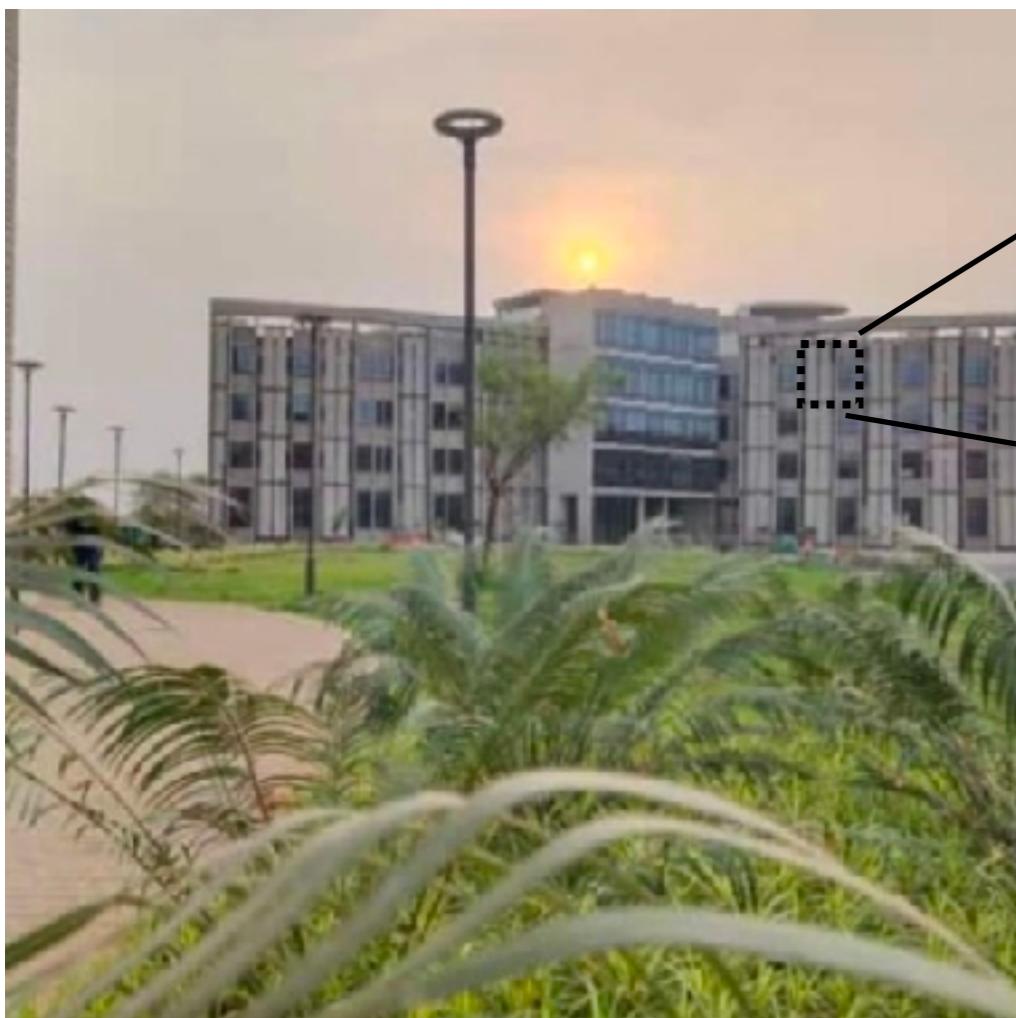
Himanshu Joshi 02 January 202

# About the instructor

Himanshu Joshi

Laboratory of computational Bionanotechnology

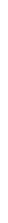
Department of Biotechnology



The screenshot shows a webpage for the "molecular-simulation-lab". At the top, there's a navigation bar with links for Home, Group Members, Research Projects, Publications, and Opportunities. The main header is "Laboratory of Bionanotechnology". Below the header, there's a section titled "About the lab" with a detailed description of their research focus on molecular simulation at the nanoscale. There are also several small images illustrating molecular structures and simulations.

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Web:  
<https://sites.google.com/view/molecular-simulation-lab>



## About students

- Name and introduction
- Background
- Future Interest
- Contact information

## Course contents

- Historical perspective
- Statistical ensembles
- Quantum Mechanics (QM)
- Foundations of Molecular Mechanics (MM),
- Introduction molecular dynamics simulations
- Equation of motion,
- Force-fields, Scheme of integrations,
- Langevin Dynamics,
- Non-bonded Computations,
- Brownian Dynamics,
- Monte Carlo Techniques,
- Coarse Graining Models

# Exam and evaluation

| Segments                               |    |    |            |
|--|----|----|------------|
| 2 Jan                                  |    |    | 1 May      |
| 1                                      | 2  | 3  | 4          |
| HW                                     | QZ | MT | HW         |
| 5                                      |    |    | 6          |
| QZ                                     |    |    | FT         |
| Homeworks/ Assignments/Reading project |    |    | 10         |
| 2 quizzes before and after midterm     |    |    | 10         |
| 1 midterm                              |    |    | 30         |
| 1 final term exam                      |    |    | 30         |
| Course project and presentation        |    |    | 20         |
| <b>Total</b>                           |    |    | <b>100</b> |



## Reference Books

1. Molecular modelling and simulation: An interdisciplinary guide by Tamar Schlick
2. Statistical mechanics : theory and molecular simulation by Mark Tuckerman
3. Computer Simulations of Liquids by M.P. Allen and D. J. Tildesly
4. Understanding molecular: From Algorithms to Applications by Daan Frenkel and Berend Smit
5. "Molecular Modelling Principles And Applications" by Andrew Leach
6. The art of Molecular dynamics by D. C.Rappaport

# **Objective of the course**

- The course is designed to introduce the idea of biomolecular simulations.
- Using computers to reveal the information and knowledge about the forces that govern the bimolecular assembly and function of biomolecules.
- Students will learn the theory of molecular simulations and are expected to write basic codes to get started with the dynamics of bimolecular simulations.
- Biology by numbers

# Introductory video

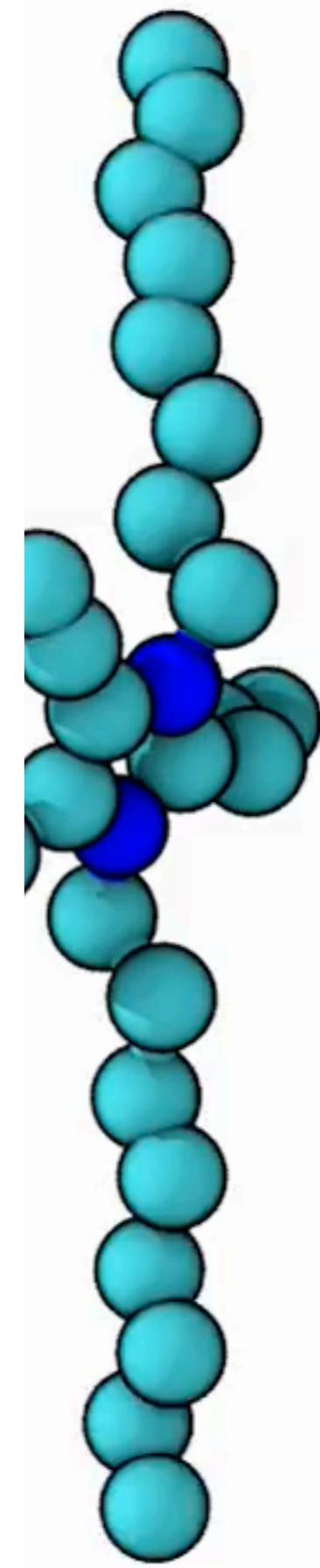
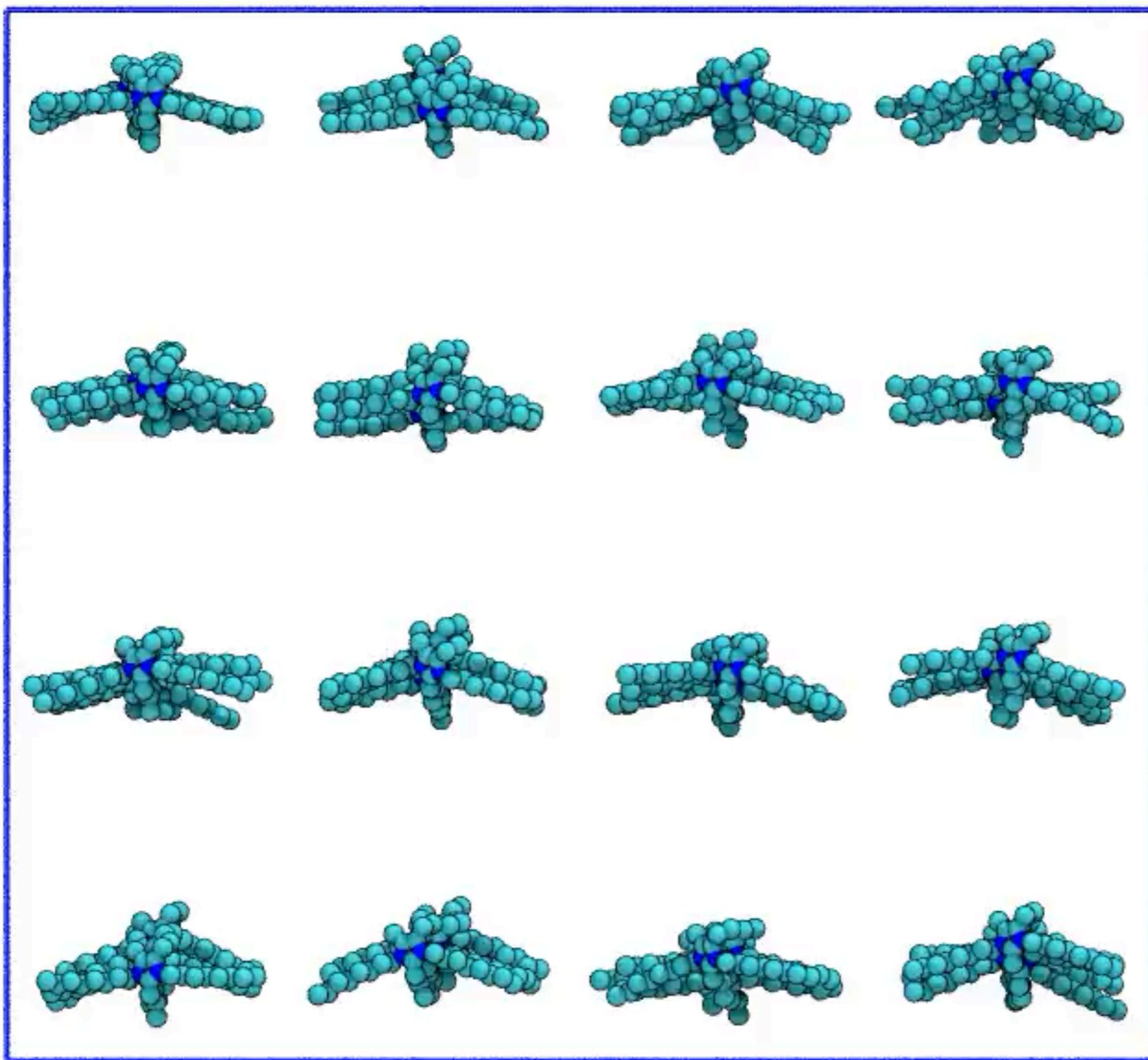
[https://www.youtube.com/watch?v=ipRnvs7\\_CxA](https://www.youtube.com/watch?v=ipRnvs7_CxA)

The diagram illustrates the derivation of Newton's second law from a potential energy function. It consists of three main parts:

- Left Box (1):** Contains two sets of variables:
  - $\{\vec{r}_i\}_{i \in [1, N]}$
  - $\{\vec{v}_i\}_{i \in [0, N]}$
- Middle Box (2):** Contains:
  - A potential energy function  $U_{ij}(r_{ij})$ .
  - The formula  $U_{tot} = \sum_{i > j} U_{ij}$ .
- Bottom Box (3):** Contains:
  - Newton's second law:  $\vec{a} = \frac{\vec{F}_i}{m_i}$ .
  - The formula  $\vec{F}_{j \rightarrow i} = -\vec{g} \nabla_{\vec{r}_i} U_{ij}$ .
  - The formula  $\vec{F}_i = \sum_{j \neq i} \vec{F}_{j \rightarrow i}$ .

Arrows indicate the flow of information: an arrow points from the left box to the middle box, and another arrow points from the middle box to the bottom box.

Is that all ?





Anees Rahman (1927–1987) in a picture taken in 1967  
(Springer)

## Correlations in the Motion of Atoms in Liquid Argon\*

A. RAHMAN

*Argonne National Laboratory, Argonne, Illinois*

(Received 6 May 1964)

A system of 864 particles interacting with a Lennard-Jones potential and obeying classical equations of motion has been studied on a digital computer (CDC 3600) to simulate molecular dynamics in liquid argon at 94.4°K and a density of 1.374 g cm<sup>-3</sup>. The pair-correlation function and the constant of self-diffusion are found to agree well with experiment; the latter is 15% lower than the experimental value. The spectrum of the velocity autocorrelation function shows a broad maximum in the frequency region  $\omega = 0.13(k_B T/\hbar)$ . The shape of the Van Hove function  $G_s(r,t)$  attains a maximum departure from a Gaussian at about  $t = 3.0 \times 10^{-11}$  sec and becomes a Gaussian again at about  $10^{-10}$  sec. The Van Hove function  $G_v(r,t)$  has been compared with the convolution approximation of Vineyard, showing that this approximation gives a too rapid decay of  $G_v(r,t)$  with time. A delayed-convolution approximation has been suggested which gives a better fit with  $G_v(r,t)$ ; this delayed convolution makes  $G_v(r,t)$  decay as  $t^2$  at short times and as  $t$  at long times.

### I. INTRODUCTION

In recent years considerable use has been made of large digital computers to study various aspects of molecular dynamics in solids, liquids, and gases.<sup>1</sup> The following is a description of a computer experiment on liquid argon (using the CDC 3600) to study the space and time dependence of two-body correlations which determine the manner in which slow neutrons are inelastically scattered from the liquid. If neutron scattering data of unlimited accuracy and completeness was available, then the kind of work presented here would serve the useful though unexciting purpose of confirming the results already obtained with neutrons. At present, however, the situation is that theorists are trying to build models for these two-body dynamical correlations to account for the observed neutron spectra; the current interest in the work presented here is thus to throw some light on the validity of these models, and to suggest the manner in which some improvements can be made.

The calculations presented here are based on the assumption that classical dynamics with a two-body central-force interaction can give a reasonable description of the motion of atoms in liquid argon. For practical reasons, further assumptions have to be made, namely, the interaction potential has to be truncated beyond a certain range, the number of particles in the assembly has to be kept rather small, and suitable boundary conditions have to be imposed on the assembly. Finally, the equations of motion have to be solved as a set of difference equations, thus involving a certain increment of time to move one set of positions and velocities to

system, namely, 94.4°K and 1.374 g cm<sup>-3</sup>. A less exhaustive study, at 130°K and 1.16 g cm<sup>-3</sup>, is mentioned briefly at the end.

### II. METHOD OF COMPUTATION

The calculations reported here were based on the following ingredients.

Particles with mass  $39.95 \times 1.6747 \times 10^{-24}$  g (the mass of an argon atom) were assumed to interact in pairs according to the potential  $V(r) = 4\epsilon\{(\sigma/r)^12 - (r/\sigma)^6\}$ ,  $\epsilon/k_B = 120^\circ\text{K}$ ,  $\sigma = 3.4 \text{ \AA}$ ,  $r$  being the distance between the particles. This interaction was assumed to extend up to a range  $R = 2.25\sigma$ , so that a particle interacts with all particles situated within a sphere of that radius;  $V(2^{1/6}\sigma) = -\epsilon$  is the minimum of  $V(r)$  and at  $r = R$ ,  $V \sim -0.03\epsilon$ .

864 such particles were placed in arbitrary positions in a cubical box of side  $L = 10.229\sigma$ , thus providing a density of 1.374 g cm<sup>-3</sup>. Periodic boundary conditions were imposed, so that at any given moment a particle with coordinates  $x, y, z$  inside the real box implied the presence of 26 periodic images with coordinates obtained by adding or subtracting  $L$  from each Cartesian coordinate. The density was conserved because when a particle moves out across one face of the cube another moves in across the opposite face.

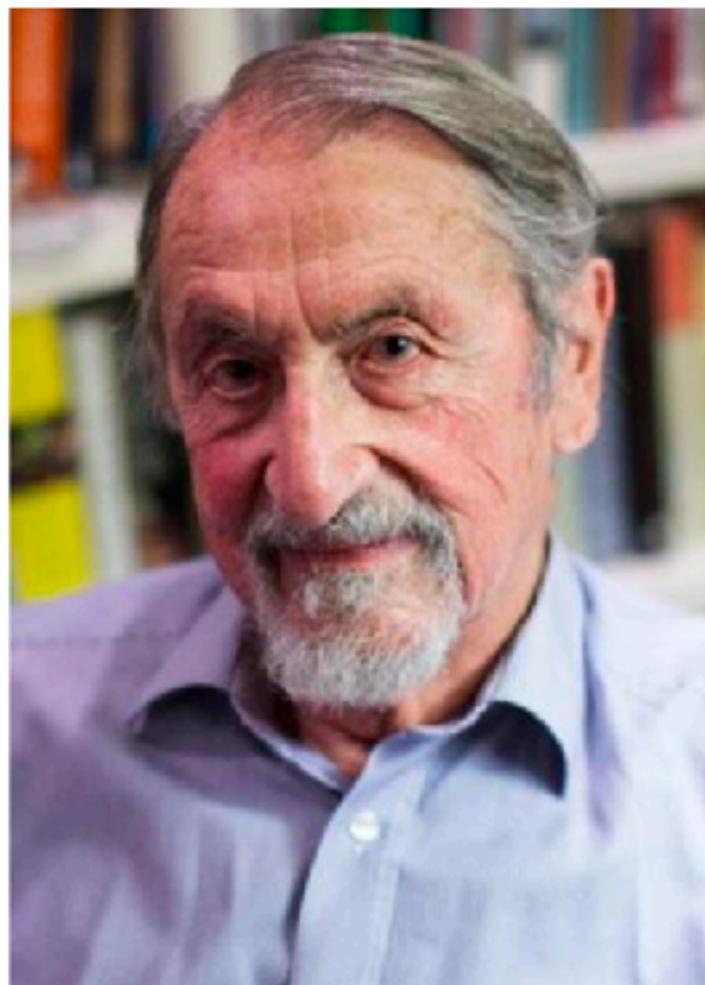
The particles were then allowed to move, and their motions were calculated using a set of difference equations with a time increment of  $10^{-11}$  sec. The details have been given in an Appendix. The positions and velocities obtained at successive moments were recorded on magnetic tape for later analysis. The calcu-

# A Multidisciplinary approach

13.7 billion year      After 200 m year later stars and galaxies      380,000 year later      Biology  
Physics      Chemistry      Biology

Quantum theory underlies atomic physics, which is the foundation of reagent chemistry and its specialized offshoot biochemistry, which interlock with molecular biology essentially, the chemistry of organic macromolecules and hence, through successively higher levels of organization, cellular, organismic, and evolutionary biology. . . . Such is the unifying and highly productive understanding of the world that has evolved in the natural sciences.

# Nobel Prize in Chemistry 2013



M. Karplus  
Chemistry  
Harvard



M Levitt,  
Structural Bio & Computer Science  
Stanford



A Warshel,  
Chemistry  
USC

"for the development of multiscale models for complex chemical systems"

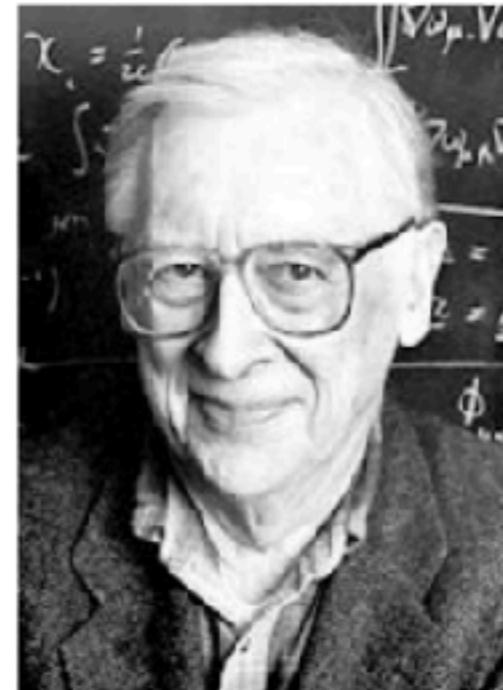
Nobel lecture by Martin Karplus

<https://www.nobelprize.org/prizes/chemistry/2013/summary/>

# Nobel Prize in Chemistry 1998



**Walter Kohn**  
Physics, University of California, Santa Barbara,



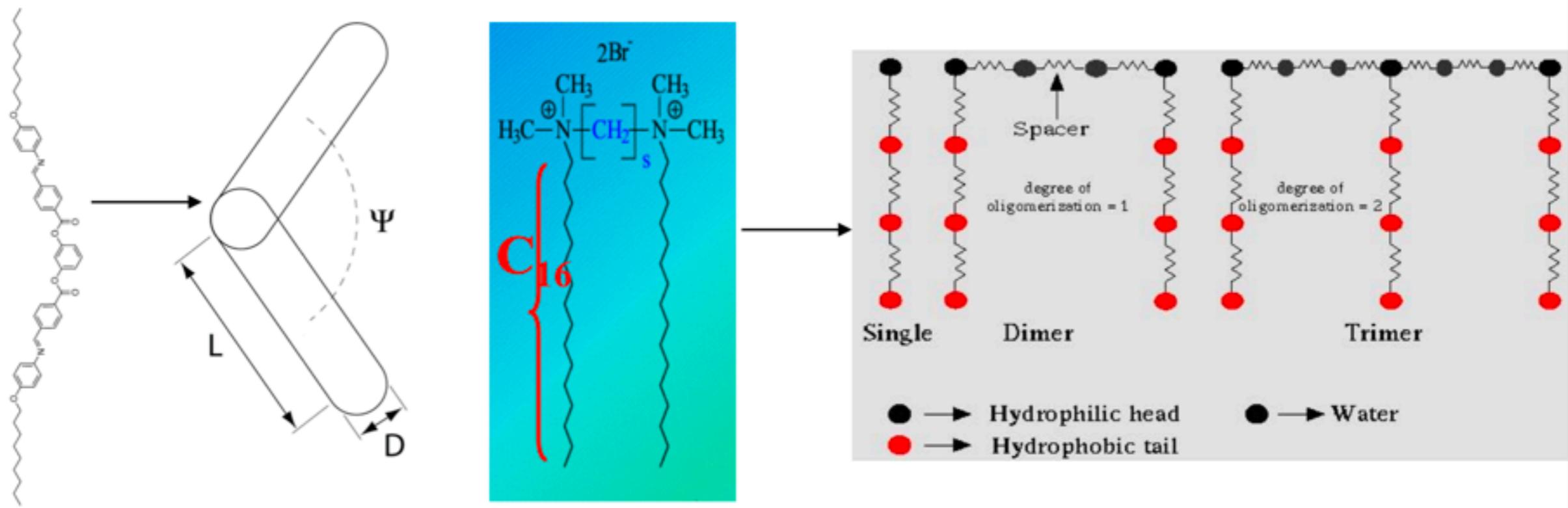
**John A. Pople**  
Chemistry, Northwestern University, Evanston

Walter Kohn "for his development of the density-functional theory" and John A. Pople "for his development of computational methods in quantum chemistry".

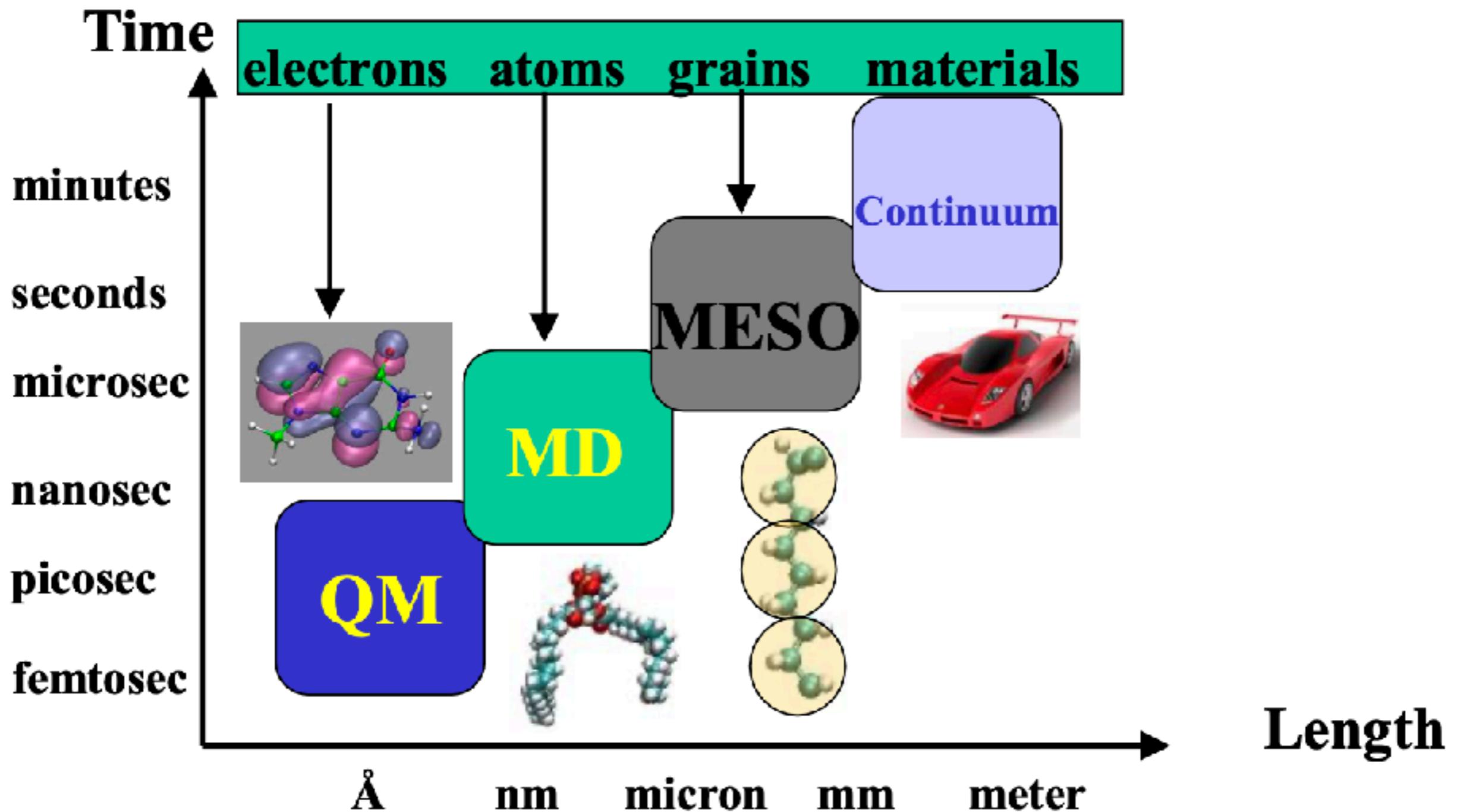
# What is molecular simulation

Molecular modeling is the science and art of studying molecular structure and function through model building and computation.

Model building could be as simple as representing molecule by hard/soft sphere (beads) , rigid rods, or other geometrical shape, sphere/beads connected through springs or molecule with full chemical details.



# Multi-scale Modeling strategy



# High quality multi-scale simulations

- Quantum Mechanical calculation
- First Principles force fields
- Large scale Molecular Dynamics (MD) simulations
- Mesoscopic modeling (Coarse-grained MD, DPD, BD)
- Macroscopic modeling (finite elements, continuum simulations, Lattice Boltzmann)

# Differential Equation

$$y = f(x)$$

Sometime it is easy to write the derivative  $y'$ ,  $y''$

$$m \frac{dv}{dt} = F \quad m \frac{d^2x}{dt^2} = F$$

$$x(t) = ??$$

# Classical and Quantum mechanics

$$m \frac{d^2x}{dt^2} = F = -\nabla U$$

$$i\hbar \frac{\partial}{\partial t} \Psi(x, t) = \left[ -\frac{\hbar^2}{2m} \frac{\partial^2}{\partial x^2} + V(x, t) \right] \Psi(x, t).$$

de-Brogli wavelength

$$\lambda_{DB} = \frac{h}{p}$$

# Home work and reading material

nature nanotechnology

Letter

<https://doi.org/10.1038/s41565-022-01285-z>

## DNA double helix, a tiny electromotor

Received: 15 March 2022

Christopher Maffeo<sup>1,2</sup>, Lauren Quednau<sup>2</sup>, James Wilson<sup>1</sup> & Aleksei Aksimentiev<sup>1,2,3</sup> 

Accepted: 4 November 2022

Published online: 23 December 2022

 Check for updates

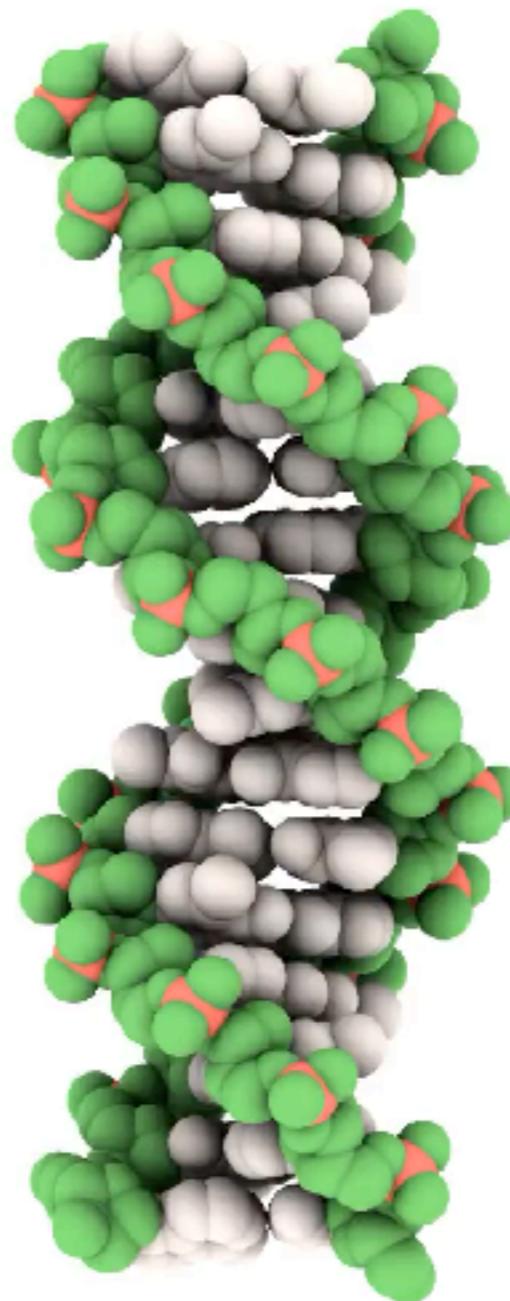
Flowing fluid past chiral objects has been used for centuries to power rotary motion in man-made machines. By contrast, rotary motion in nanoscale biological or chemical systems is produced by biasing Brownian motion through cyclic chemical reactions. Here we show that a chiral biological molecule, a DNA or RNA duplex rotates unidirectionally at billions of revolutions per minute when an electric field is applied along the duplex, with the rotation direction being determined by the chirality of the duplex. The rotation is found to be powered by the drag force of the electro-osmotic flow, realizing the operating principle of a macroscopic turbine at the nanoscale. The resulting torques are sufficient to power rotation of nanoscale beads and rods, offering an engineering principle for constructing nanoscale systems powered by electric field.

Although incremental miniaturization of man-made machines is possible by simply reducing the size of its parts, radical miniaturization typically requires re-evaluation of the physical principles that govern the machine's operation<sup>1</sup>. For example, in a conventional electromotor, an electric field is transformed into rotary motion by means of electromagnetic induction. However, rotary motion is already best produced at the submillimetre scale using electrostatic actuation<sup>2</sup>. At the nanoscale, biological molecular motors operate with high precision and efficiency<sup>3</sup> using a chemical reaction to bias direction of random displacement<sup>4</sup>. Some molecular motors, such as F<sub>0</sub>F<sub>1</sub>ATP synthase<sup>5</sup> and the bacterial flagellum motor<sup>6</sup>, are true electromotors, transforming the energy of a transmembrane electric potential into rotation<sup>7</sup>. Although the biased diffusion mechanism has been realized in purely

concentric DNA origami structures were synthesized to undergo rotary diffusion, driven by stochastic forces<sup>8–10</sup>. Unidirectional rotation of a self-assembled DNA arms was realized by coupling the arm's orientation to the direction of the fluid flow and alternating the flow direction in a cyclic pattern<sup>10</sup>. Yet it has not escaped our notice that the screwshape of a DNA molecule could allow it to function as the simplest possible electromotor.

### DNA duplex rotation in electric field

To investigate whether a single DNA duplex will rotate unidirectionally in an external electric field, we constructed an all-atom model of a 16 base pair (bp) DNA duplex submerged in 1 M KCl electrolyte solution (Fig. 1a). Using the all-atom molecular dynamics method, we simulated



<https://www.nature.com/articles/s41565-022-01285-z>

<https://www.nature.com/articles/s41565-022-01288-w>

## Question of the class

What is chirality and

how does it matter in the structure of DNA molecule ??

Read the paper by Rahman



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भारतीय प्रौद्योगिकी संस्थान हैदराबाद  
Indian Institute of Technology Hyderabad

## Next Class

**4 PM Thursday, 5 January 2024**