भारतीय सांकेतिक विज्ञान संस्थ हैदराबाद
भारतीय प्रौद्योगिकी संस्थान हैदराबाद
Indian Institute of Technology Hyderabad

Biomolecular Simulation BT2123

Lecture 2 : Atomistic models of Biomolecules

Himanshu Joshi 05 January 2023

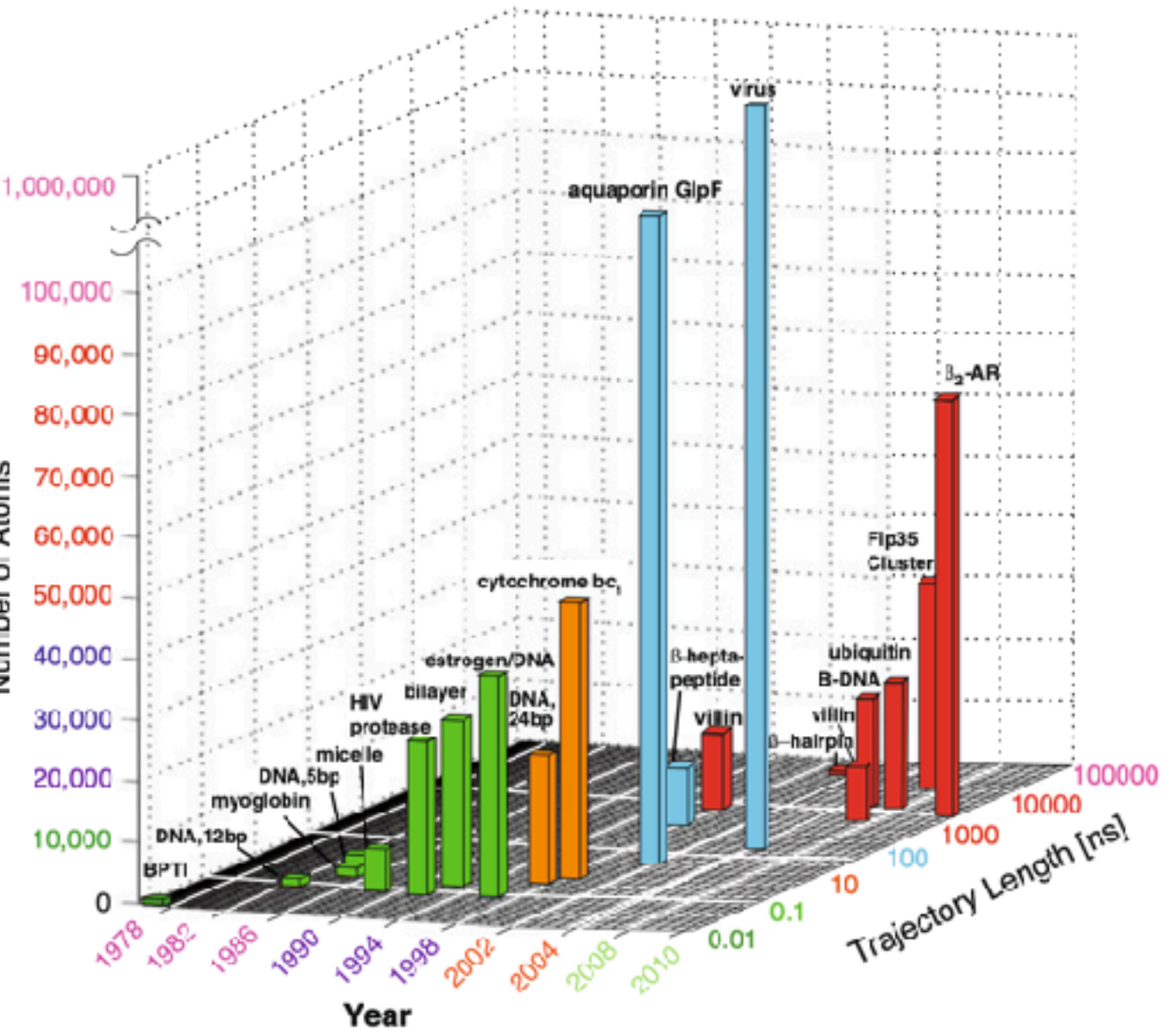
Dirac, 1929

The general theory of quantum mechanics is now almost complete. The underlying physical laws necessary for the mathematical theory of a large part of physics and the whole of chemistry are thus completely known, and the difficulty is only that the exact application of these laws leads to equations much too complicated to be soluble.”

Brief history of Molecular simulations

- Metropolis, Rosenbluth, Teller (1953) Monte Carlo Simulation of hard disks.
- Fermi, Pasta Ulam (1954) experiment on ergodicity
- Alder & Wainwright (1958) liquid-solid transition in hard spheres. “long time tails” (1970)
- Vineyard (1960) Radiation damage using MD
- Rahman (1964) liquid argon, water(1971)
- Verlet (1967) Correlation functions, ...
- Andersen, Rahman, Parrinello (1980) constant pressure MD
- Nose, Hoover, (1983) constant temperature thermostats.
- Car, Parrinello (1985) ab initio MD.

Evolution of molecular dynamics simulations with respect to system sizes and simulation lengths



Period	System and Size[a]	Trajectory Length[b] [ns]	CPU Time/Computer[c]
1973	Dinucleoside (GpC) in vacuum (8 flexible dihedral angles)	—	—
1977	BPTI, vacuum (58 residues, 885 atoms)	0.01	
1983	DNA, vacuum, 12/24 bp (754/1530 atoms)	0.09	several weeks each, Vax 780
1984	GnRH, vacuum (decapeptide, 161 atoms)	0.15	
1985	Myoglobin, vacuum (1423 atoms)	0.30	50 days, VAX 11/780
1985	DNA, 5 bp (2800 atoms)	0.50	20 hrs, Cray X-MP
1989	Phospholipid Micelle (≈ 7,000 atoms)	0.10	
1992	HIV protease (25,000 atoms)	0.10	100 hrs.,Cray Y-MP
1997	Estrogen/DNA (36,000 atoms, multipoles)	0.10	22 days, HP-735 (8)
1998	DNA, 24 bp (21,000 atoms, PME)	0.50	1 year, SGI Challenge
1998	β-heptapeptide in methanol (≈ 5000/9000 atoms)	200	8 months, SGI Challenge (3)
1998	Villin headpiece (36 residues, 12,000 atoms, cutoffs)	1000	4 months, 256-proc. Cray T3D/E
1999	bc_1 complex in phospholipid bilayer (91,061 atoms, cutoffs)	1	75 days, 64 450-MHz-proc. Cray T3E
2001	C-terminal β-hairpin of protein-G (177 atoms, implicit solvent)	38000[b]	~ 8 days, 5000 proc. Folding@home megacluster
2002	Channel protein in lipid membrane (106,189 atoms, PME)	5	30 hrs, 500 proc. LeMieux terascale system; 50 days, 32 proc. Linux (Athlon)
2006	Complete satellite tobacco mosaic virus (1 million atoms)	50	55 days (≈1ns/day), 256 Altix nodes, NCSA Athlon 2600+, NAMD program
2007	B-DNA dodecamer in solvent, PME, AMBER parm98 (15,774 atoms)	1200	130 days, 32 PowerPC BladeCenter proc., MareNostrum Supercomputer, Barcelona
2007	Villin headpiece (9,684 atoms) AMBER-2003	1000	6 months, Folding@home X86 megacluster, GROMACS/MPI
2008	Ubiquitin protein, explicit solvent OPLS-AA/SPC forcefield, (19,471 atoms)	1200	14 days (87ns/day), 32 processors Opteron cluster, Desmond program
2008	Fip35 protein, explicit solvent NAMD/CHARMM	10000	14 weeks, NCSA Abe cluster, NAMD program
2009	β_2AR protein mutants (50,000-99,000 atoms) CHARMM27 forcefield	2000	28 days, 32 (2.66 GHz) E5430 processors Desmond program

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Newton's laws of motion

Naturalis Principia Mathematica, 1687

$$\mathbf{r}(t) = \mathbf{r}(0) + \mathbf{v}t$$

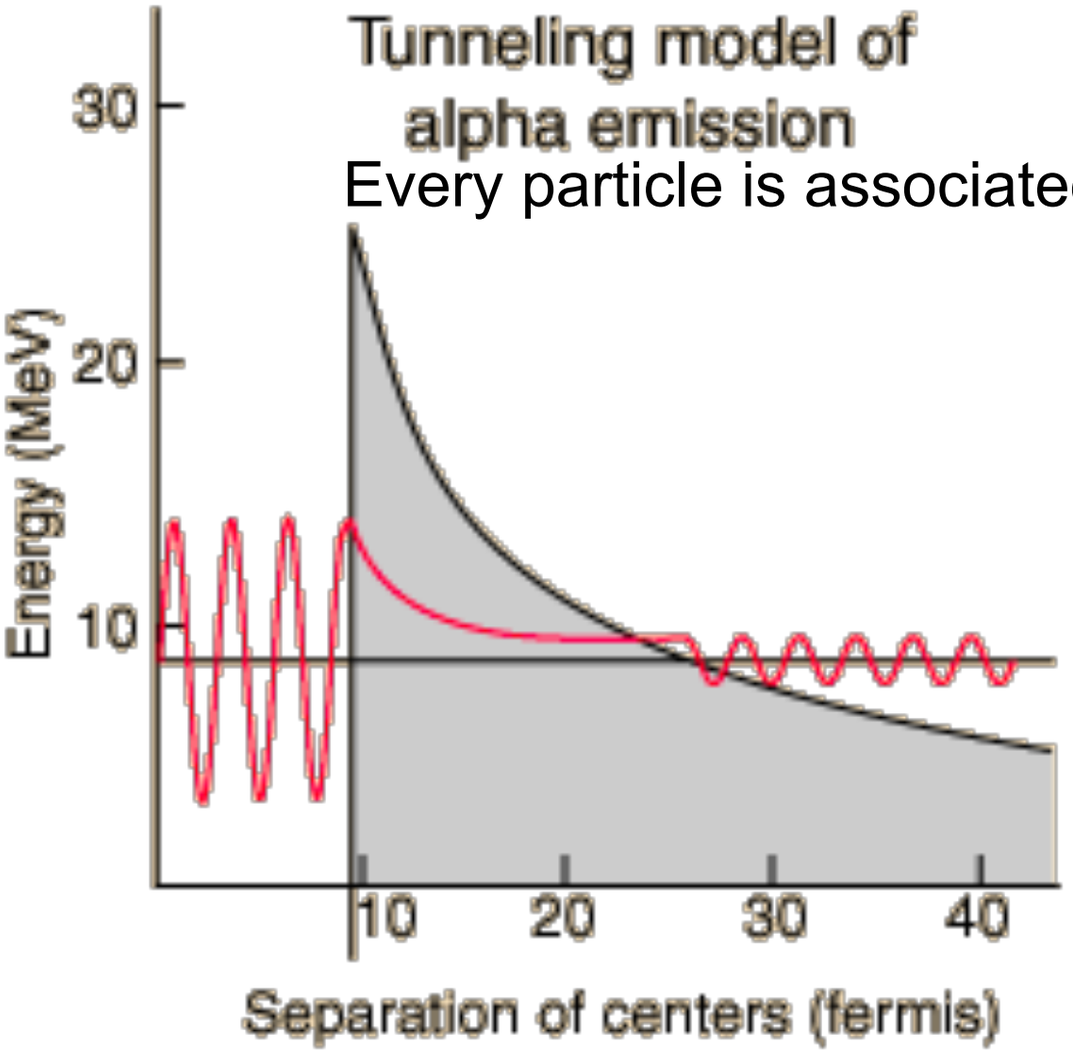
$$m\frac{d^2\mathbf{r}}{dt^2} = \mathbf{F}$$

$$F_{BA.} = -F_{AB}$$

Although, newton's equation of motion are proposed for celestial bodies they work well 300 years ago, we will see that with some approximation they works pretty well at molecular level

$$W = \int_A^B \mathbf{F}.d\mathbf{l}$$

Quantum Mechanics



Wave particle duality principle

Every particle is associated with a wavefunction Ψ ; the wavelength is give by

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

Uncertainity principles

△E*△t ≥ = h/4∏

△P*△x ≥ = h/4∏

Classical mechanics fail to explain the decay alpha particles from Polonium-212

http://hyperphysics.phy-astr.gsu.edu/hbase/Nuclear/alptun.html#c2

Operators in Quantum Mechanics

Every quantity is associated with a

$f(x)$	Any function of position, such as x, or potential V(x)	$f(x)$
p_x	x component of momentum (y and z same form)	$\frac{\hbar}{i}\frac{\partial}{\partial x}$
E	Hamiltonian (time independent)	$\frac{p_{op}^2}{2m} + V(x)$
E	Hamiltonian (time dependent)	$i\hbar\frac{\partial}{\partial t}$
KE	Kinetic energy	$\frac{-\hbar^2}{2m}\frac{\partial^2}{\partial x^2}$
L_z	z component of angular momentum	$-i\hbar\frac{\partial}{\partial \phi}$

Many body problem

$$F_i(r_1, r_2, ..., r_N, \dot{r}_i) = \sum_{j \neq i} f_{ij}(r_i - r_j) + f^{ext}(r_i, \dot{r}_i)$$

$$m\ddot{r}_i = F_i(r_1, r_2, ..., r_N, \dot{r}_i)$$

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Laws of Thermodynamics

Thermodynamics is a phenomenological theory of macroscopic

Macroscopic vs microscopic quantities/approaches

Temperature, Pressure, Volume, quantify/visualize by normal senses or regular instruments

Extensive vs intensive quantities

Pressure, Temperature, density, color, melting point, Mass, Energy, Volume, Entropy

Statistical mechanics vs Thermodynamics

Statistical mechanisms tries to justify the laws of thermodynamics by finding underlying microscopical models