Deductive Multiscale Theory

and Computation

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Order Parameters (OPs)

OPs are variables that describe the overall structure and dynamics of the system. They are of various types:

- Structural parameters
- Scaled particle positions
- Density-like field variables
- Curvilinear coordinates

Multiscale Hypothesis on the *N*-atom Probability Density ρ

Newtonian Ansatz

$$\rho\left(\Gamma, \underline{\Phi}; t_0, \underline{t}; \varepsilon\right)$$

$$\underline{t} = \left\{t_1, t_2, \cdots\right\}$$

$$t_n = \varepsilon^n t$$

- ε is a time or space scale ratio. The specific choice of the $\Phi - \Gamma$ relation implies ε.

- The $t_n \left(n = 0, 1, \cdots\right)$ track processes on the ε^{-n} timescale.

Derived Langevin Equation for OP Dynamics

$$\frac{d\vec{\Phi}_k}{dt} = \sum_{k'} \vec{\vec{D}}_{kk'} \vec{f}_{k'} + \vec{\varepsilon}_k$$

Diffusion factors

$$\vec{\vec{D}}_{kk'} = \beta \int_{\infty}^{0} dt \left\langle \vec{\pi}_k(t) \vec{\pi}_{k'}(0) \right\rangle$$

$$\vec{\pi}_k = \sum_{i=1}^{N} U_{ki} \vec{P}_i$$

Thermal-average forces

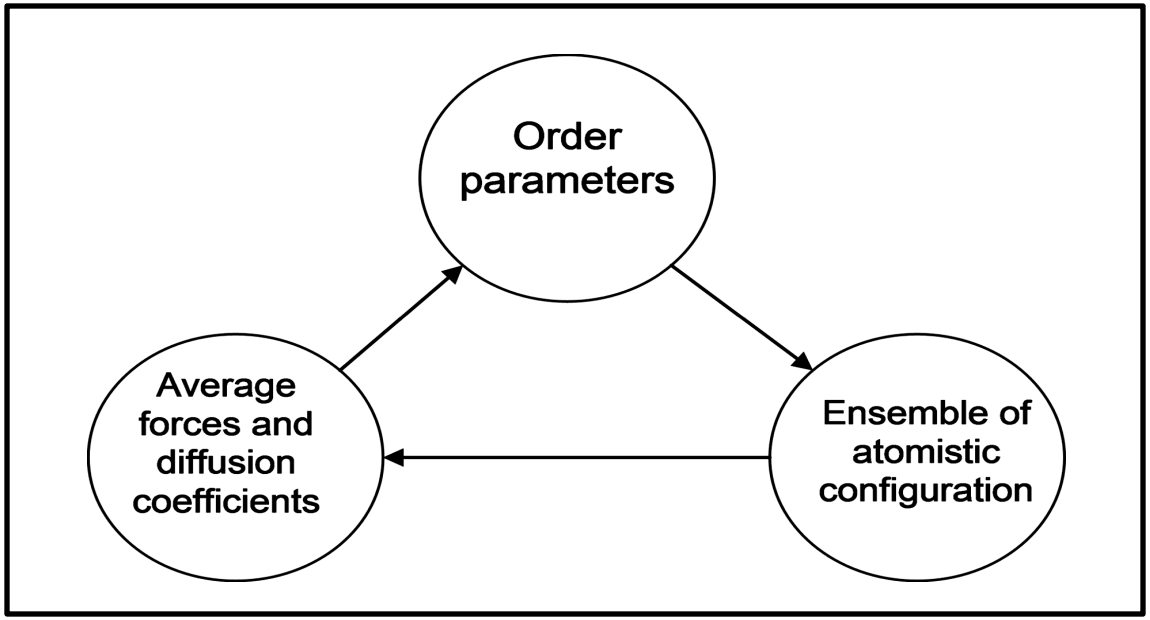
$$\vec{f}_k = -\frac{\partial F}{\partial \vec{\Phi}_k}$$

$$= \int d\Gamma^* \Delta\left(\underline{\Phi} - \underline{\Phi}^*\right) \vec{f}_k^{m*} e^{-\beta H^*}$$

$$\vec{f}_k^{m} = \sum_{i=1}^{N} U_{ki} \vec{F}_i$$

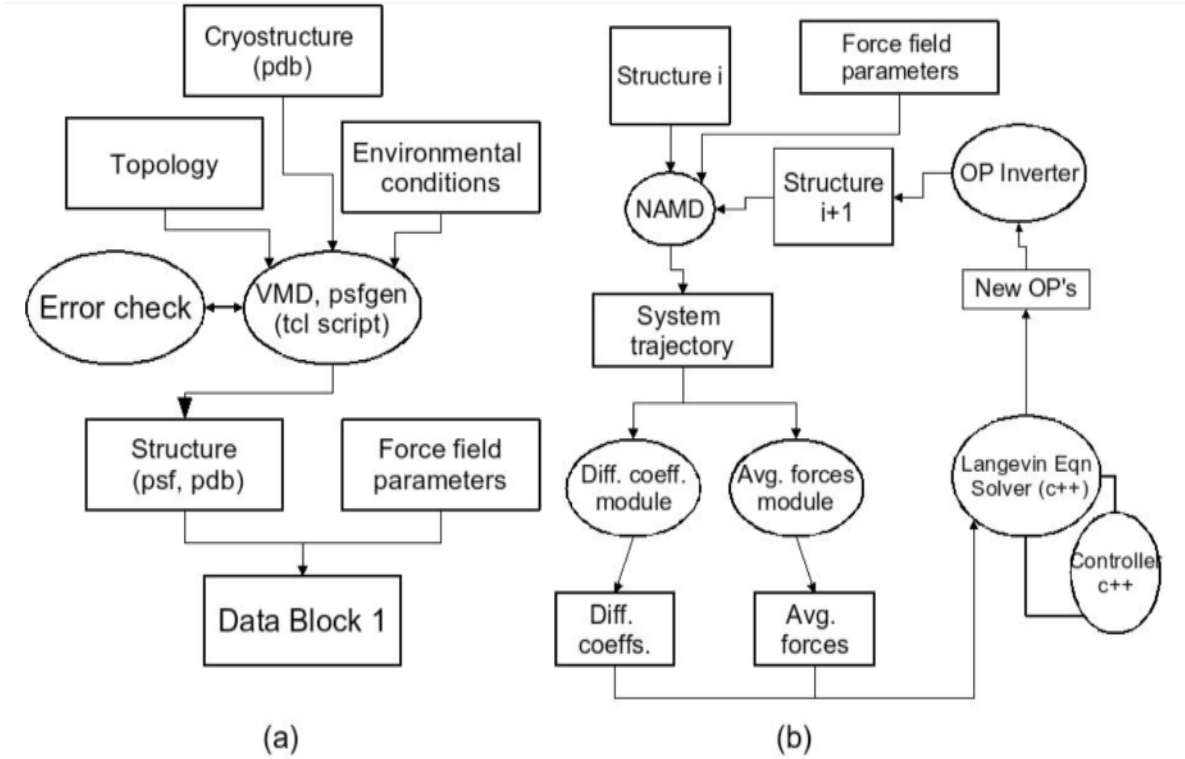
$\vec{F}_i$ = net force on atom i

Coupling of Processes Across Scales in Space and Time



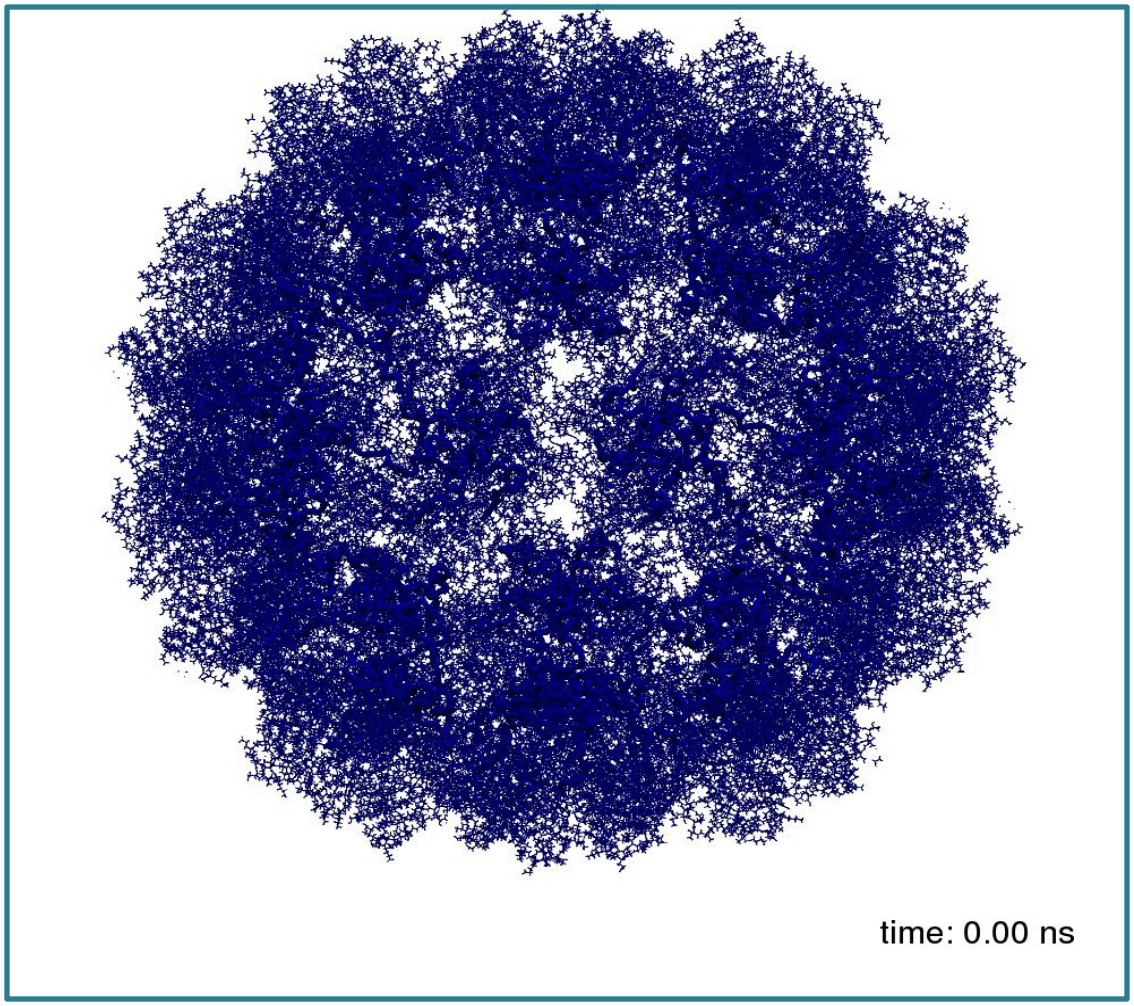
The order parameter-fixed ensemble of atomistic states Γ determines factors in the Langevin equations yielding Φ

Implementation as *SimNanoWorld™*



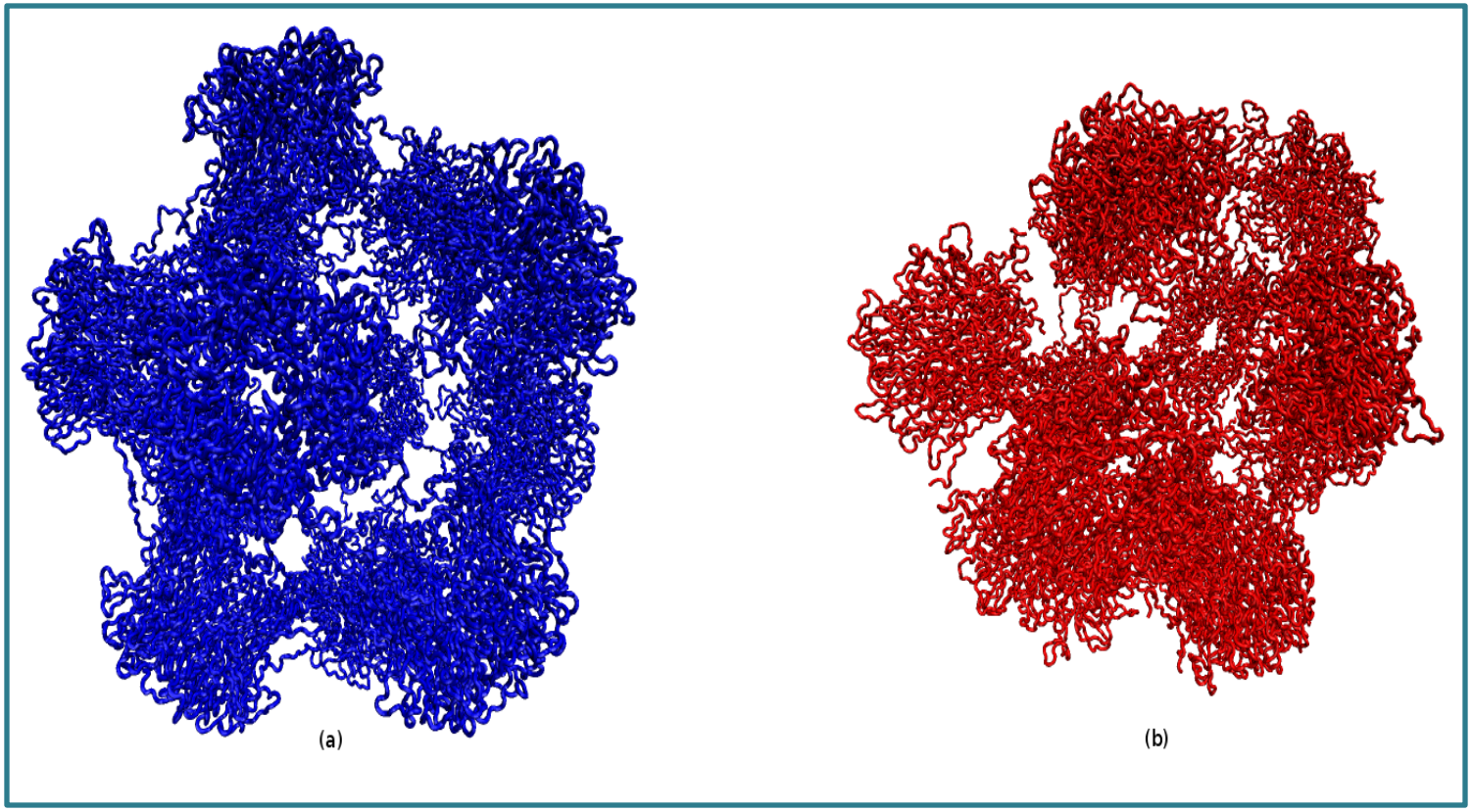
We use VMD for constructing and analyzing systems, and NAMD for atomic forces needed to calculate thermal average forces, and diffusion factors

CCMV Capsid Swelling: the Nucleation/propagation Pathway (in host electrolyte)



Simulation showing the N-terminal arms of capsid proteins undergo large deviations from the initial configurations. The capsid swelling rate is 0.25 nm/ns (npn) during the early stage of the simulation, and propagation of the structural transition across the capsid is roughly 0.6 npn.

HPV 16 L1 VLP Disassembly Pathway



Simulation via ***SimNanoWorld***™ of the *T*=1 HPV16 L1 protein VLP with helices h2, h3 and h4 removed at (a) 0ns and (b) 125ns showing disassembly. Single pentamer ejection nucleated disassembly.

Multiscale Electrostatics

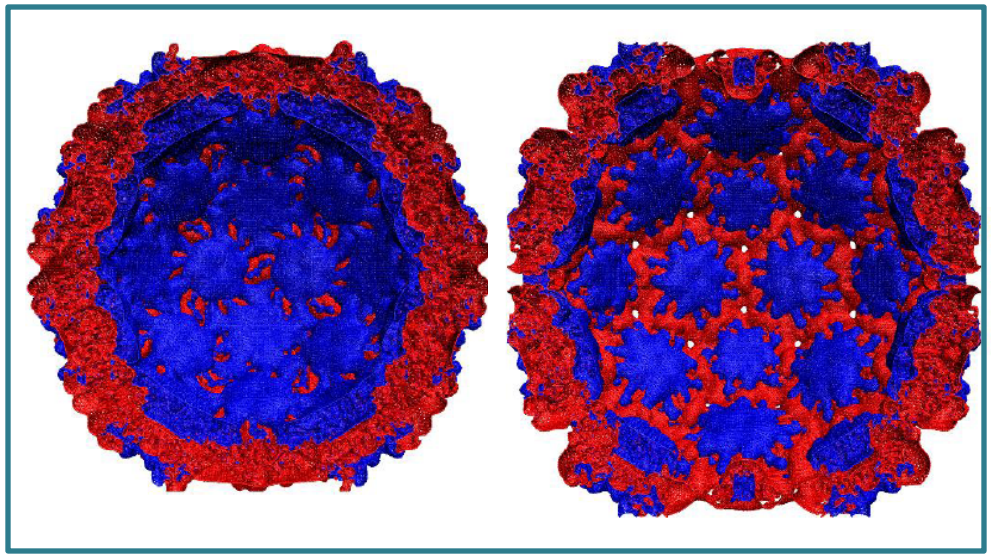
Poisson Boltzmann equation: $\vec{\nabla}\bullet(\varepsilon\vec{\nabla}\Phi)+f=0$

PB Ansatz $\Phi\equiv\Phi(\vec{r},\vec{R});\sigma=\left|\vec{r}\right|/\left|\vec{R}\right|\ll 1$

Multiscale PB equation: $(\vec{\nabla}_0+\sigma\vec{\nabla}_1)\bullet[\varepsilon(\vec{\nabla}_0+\sigma\vec{\nabla}_1)\Phi)]+f_c(\vec{R},\vec{r},\Phi)+f_d(\vec{R},\vec{r})=0$

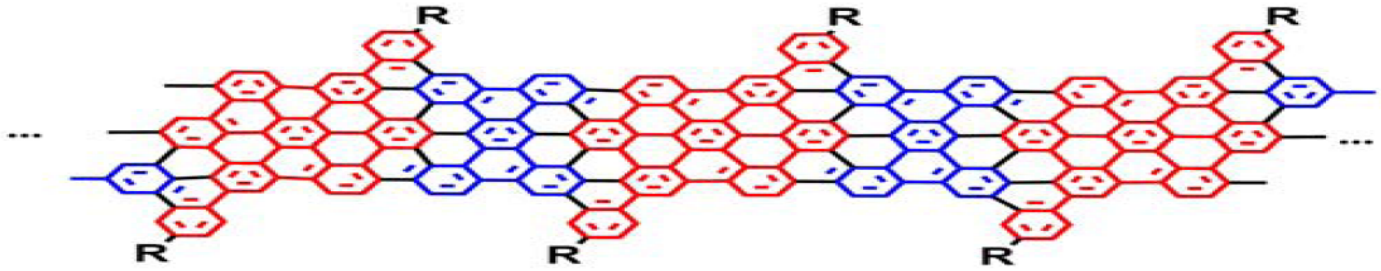
Coarse-grained PB equation: $\vec{\nabla}_1\bullet[\bar{\bar{\varepsilon}}*\vec{\nabla}_1\Phi^*]+\left\langle\vec{\nabla}_1\bullet(\varepsilon\vec{\nabla}_0\psi)\right\rangle+\left\langle\vec{\nabla}_1\bullet(\varepsilon\vec{\nabla}_1\theta)\right\rangle+f^*_{c(1)}(\vec{R},\Phi_0,\Phi_1)=0$

Average charge density



Coarse-grained potential is calculated with on-the-fly fine scale corrections that account for local Details. This is demonstrated via a cut-away view of +1KT/e and -1KT/e iso-surfaces in CCMV.

Quantum Nanosystems



Depiction of a graphene nanoribbon

Semiconductor quantum dots sorted by size emitting light of different colors.

We seek long space-time behavior displayed by quantum nanosystems

Multiscale Theory of Quantum Nanosystems

Quantum Ansatz

$$\Psi\left(\underline{r},\underline{R};t_0,\underline{t};\varepsilon\right)$$

$$\varepsilon = \frac{\text{avg. nearest-neighbor distance}}{\text{nanoscale characterestic length}}$$

$$i\hbar\sum_{n=0}^{\infty}\varepsilon^n t\frac{\partial\Psi}{\partial t_n} = \left(H_0 + \varepsilon H_1 + \varepsilon^2 H_2\right)\Psi$$

$$\Psi = \sum_{n=0}^{\infty}\Psi_n\varepsilon^n$$

Coarse-grained Wave Equation

$$\varepsilon \to 0 \Rightarrow \Psi \to \hat{\Psi}\left(\underline{r}\right) W\left(\underline{R}, \underline{t}\right)$$

$$i\hbar \frac{\partial W}{\partial t_2} = \underbrace{\sum_{\ell\ell'\alpha\alpha'} \mu_{\ell\ell'\alpha\alpha'} \frac{\partial W}{\partial R_{\ell\alpha} \partial R_{\ell'\alpha'}}}_{\text{Coarse-grained Kinetic Energy}} + \underbrace{V^{CG} W}_{\text{Coarse-grained Potential Energy}}$$

Both $\mu_{\ell\ell'\alpha\alpha'}$ and V^{CG} are obtained from lowest order Hamiltonian.

This is one of the several classes of CG Wave Equations which differ according to the scaling of space, time and inter-particle forces.

Conclusions

- The OP-deductive multiscale approach captures coupling of processes across many scales space and time.

- Test for self-consistency and completeness of the set of OPs enable the creation of stable algorithm.

- The methodology enables the creation of software (*SimNanoWorld*^{TM}) with great computational efficiency that we have demonstrated for:
  (1) secondary and tertiary structural changes in RNA
  (2) nucleation and front propagation accompanying viral structural transition
  (3) VLP disassembly induced by helix truncation
  (4) Epitopes display anomalous fluctuations

- Analogous idea hold for multiscale electrostatics and quantum nanosystems.