

hybrid MD/hydrodynamics modelling

Hybrid MD/HD modelling

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The background

fields, atoms,
scales, etc...

fluctuating
hydrodynamics

Coupling the
scales

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laws

Constraining the
dynamics

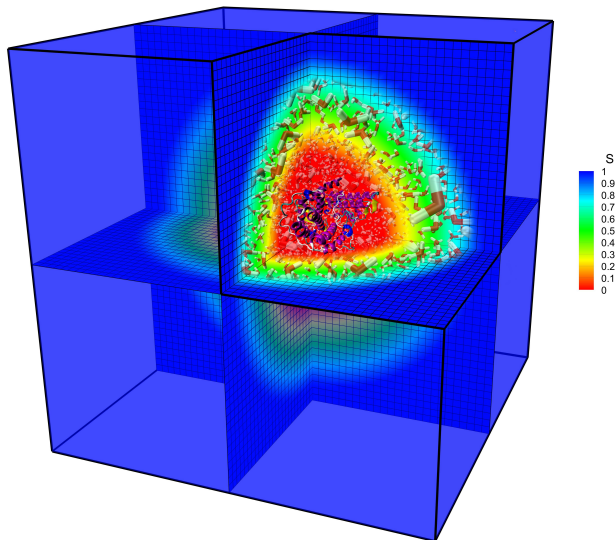
Results

Constant s

Variable s

Peptide

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Hybrid molecular dynamics - hydrodynamics approach for multiscale modelling of liquid molecular systems

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WATOC 2014

The project, acknowledgements

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Title: ‘Using next generation computers and algorithms for modelling the dynamics of large biomolecular systems’

Consortium: 5 groups (Japan, UK, Russia)

Funding: G8 Research Councils Initiative on Multilateral Research Funding - Exascale Computing

Hybrid MD/HD: motivation

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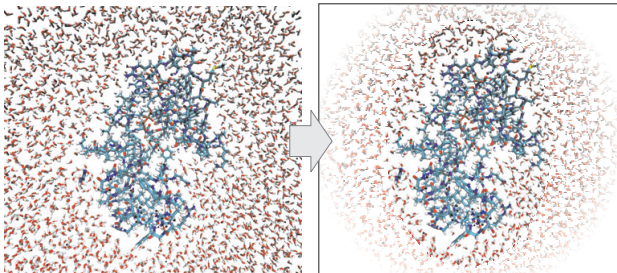
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- **Motivation:** multiphysics/multiscale (speed up and data reduction)
- **Examples:**
 - bridging atomistic times and microfluidic mixer times (9 orders of magnitude difference),
 - the effects of viscosity and hydrodynamic shear on protein folding.



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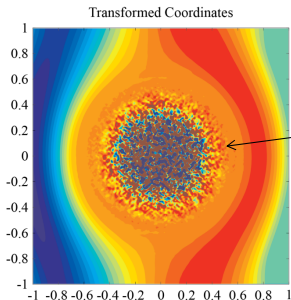
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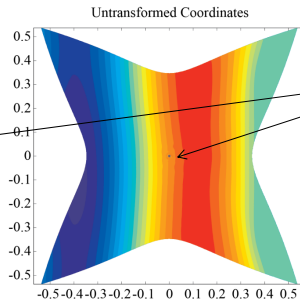
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Transformed (zoomed-in) space & time



Physical (uniform) space & time



The same region of molecular size

AP Markesteijn and SA Karabasov, *J. Comput. Phys.*, **258**, 137 (2014)

Fluctuations in biomolecular systems

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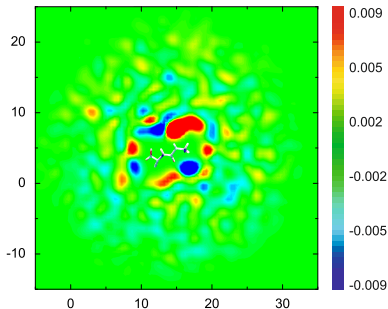
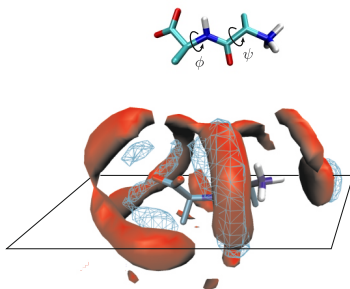
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Water density around dialanine zwitterion



Question: to what extent the dynamics of water density (fluctuations) is connected with the dynamics of the peptide (quantified by its dihedal angles ϕ and ψ)?

Water density correlation with the peptide motion

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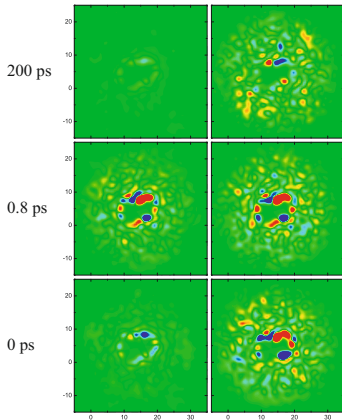
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Answer: strongly correlated but *only* at very specific short periods, when the conformational transitions occur

D Nerukh and S Karabasov, *J. Phys. Chem. Lett.*, **4**, 815 (2013)

The fundamentals: hydrodynamics and atomistic dynamics

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Continuous representation (hydrodynamics)

- All started with macroscopic thermodynamical quantities: the properties of the system **as a whole**, the largest possible scale.
- Describing the system at smaller scales: the properties become **fields** changing in **time**:

$$\rho(\mathbf{x}, t), \mathbf{u}(\mathbf{x}, t), T(\mathbf{x}, t).$$

Atomistic representation

- The variables are the positions and momenta of the point masses, the atoms:

$$\{\mathbf{q}_1, \dots, \mathbf{q}_N, \mathbf{p}_1, \dots, \mathbf{p}_N\}$$

Connecting the representations

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Calculating the continuous density:

$$\rho_q(\mathbf{q}; \mathbf{x}, t) = \sum_{j=1}^N m \delta(\mathbf{q}_j(t) - \mathbf{x})$$

It is a *function of the molecular coordinates* (phase space variable), which also parametrically depends on \mathbf{x} and t .

Connecting the representations: the scales

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How the measurement is done: a probe of volume Δx is placed at the point \mathbf{x} for a period of time Δt at time t .

The ‘true’ (measured) value of $\rho(\mathbf{x}, t)$ is obtained by overaging $\rho_q(\mathbf{q}; \mathbf{x}, t)$ over Δx and Δt .

$$\rho(\mathbf{x}, t) = \langle \rho_q(\mathbf{q}; \mathbf{x}, t) \rangle_{\Delta x, \Delta t}$$

Connecting the representations

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This is MD→HD transformation.

HD→MD - ???

Describing fluctuations of the continuum

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The Landau-Lifshitz Fluctuating Hydrodynamics (LL-FH) equations are a generalisation of the deterministic Navier-Stokes (NS) equations:

$$\frac{\partial \rho}{\partial t} + \nabla(\rho \mathbf{u}) = 0,$$

$$\frac{\partial \rho u_i}{\partial t} + \nabla(\rho u_i \mathbf{u}) = \nabla_j \left(\Pi_{ij} + \tilde{\Pi}_{ij} \right),$$

$$\frac{\partial \rho E}{\partial t} + \nabla(\rho E \mathbf{u}) = \nabla_j \left[\left(\Pi_{ij} + \tilde{\Pi}_{ij} \right) \cdot u_i \right] + \nabla(\mathbf{q} + \tilde{\mathbf{q}}).$$

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The stress tensor consists of a deterministic part

$$\Pi_{ij} = - (p - \eta_V \nabla \mathbf{u}) \delta_{ij} + \eta (\partial_i u_j + \partial_j u_i - 2D^{-1} \nabla \mathbf{u} \cdot \delta_{ij})$$

and a stochastic part, a random Gaussian matrix with zero mean and the covariance

$$\begin{aligned} \langle \tilde{\Pi}_{ij}(r_1, t_1) \cdot \tilde{\Pi}_{kl}(r_2, t_2) \rangle = \\ 2k_B T \left[\eta (\delta_{ij} \delta_{ik} + \delta_{ik} \delta_{jl}) + \left(\eta_V - \frac{2}{3} \eta \right) \delta_{ij} \delta_{jk} \right] \delta(r_1 - r_2) \delta(t_1 - t_2). \end{aligned}$$

This form of correlations follows from the fluctuation-dissipation theorem, which relates the thermal fluctuations to temperature.

Describing fluctuations of the continuum

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The heat flow is also a sum of the averaged flow

$$q_i = \kappa \cdot \partial_i T$$

and a stochastic component with zero mean and the covariance

$$\langle \tilde{q}_i(r_1, t_1) \cdot \tilde{q}_j(r_2, t_2) \rangle = 2k_B \kappa T^2 \delta_{ij} \delta(r_1 - r_2) \delta(t_1 - t_2)$$

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The connection of the scales $\Delta x, \Delta t$ with the hydrodynamic fluctuations:

$$\tilde{\Pi}_{ij} = \sqrt{\frac{2k_B T}{\Delta x \Delta t}} \left(\sqrt{2\eta} \cdot \mathbf{G}_{ij}^s + \sqrt{D\eta V} \frac{\text{tr}[\mathbf{G}]}{D} \mathbf{E}_{ij} \right)$$

$$\tilde{q}_i = \sqrt{\frac{2k_B \kappa T^2}{\Delta x \Delta t}} \mathbf{G}_i$$

Biomolecular scales

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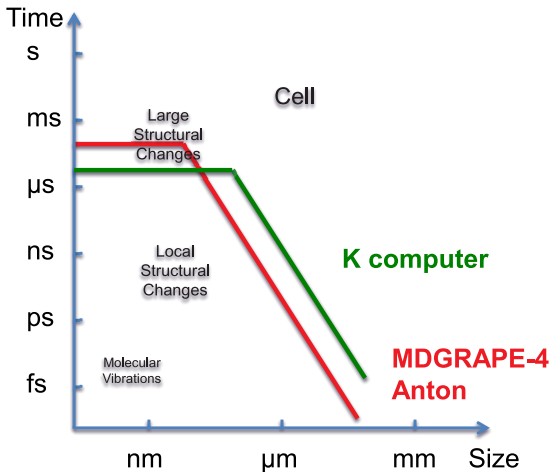
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Scales coupling: one-way (acyclic) 'bottom-up'

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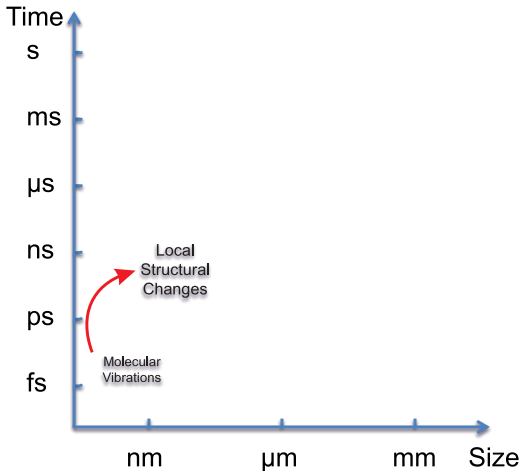
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Scales coupling: one-way (acyclic) 'top-down'

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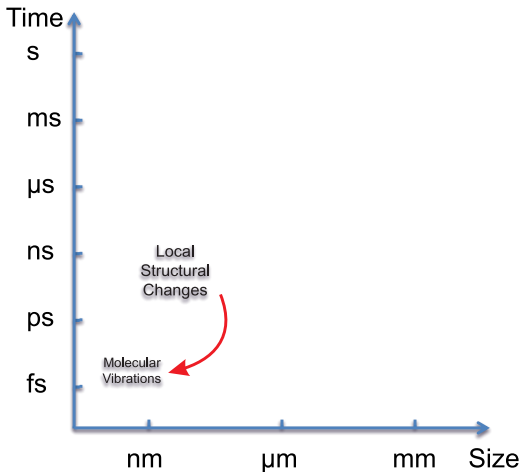
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Scales coupling: two-way (cyclic)

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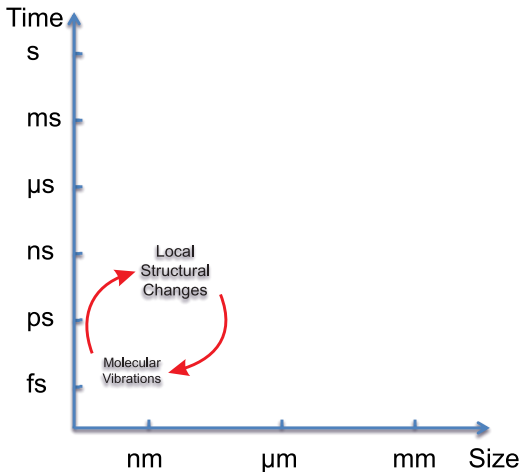
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Our framework

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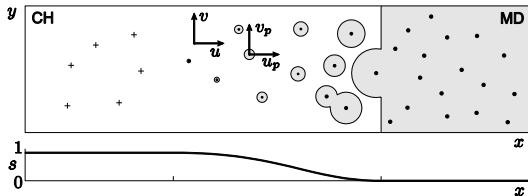
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- The end domains HD and MD are described by purely hydrodynamic and purely Newtonian equations of motion respectively.
- In the hybrid domain the fluid consists of two “phases”:
 - HD phase is a continuum water with volume fraction $s = \frac{V_1}{V}$,
 - MD phase is a phase that incorporates atoms, its volume fraction is $(1 - s)$.
- The parameter $s = s(x)$ is the function of space coordinates, such that $s = 1$ in the HD domain, $s = 0$ in the MD domain.

Mass conservation (similar for momentum)

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For HD phase:

$$\frac{\partial}{\partial t} (s\rho) + \frac{\partial}{\partial x_i} (u_i s\rho) = J,$$

For MD phase:

$$\frac{\partial}{\partial t} \left((1-s) \sum_{p=1, N(t)} \rho_p \right) + \frac{\partial}{\partial x_i} \left((1-s) \sum_{p=1, N(t)} \rho_p u_{ip} \right) = -J,$$

where $\rho_p = m_p/V$ is the density of MD particles and J is the birth/death rate due to the coupling between the phases.

$$\tilde{\rho} = s\rho + (1-s) \sum_{p=1, N(t)} \rho_p$$

Restricted dynamics

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The deviations of $\tilde{\rho}$ are driven towards the correct value $\sum_{p=1, N(t)} \rho_p$:

$$\frac{D}{Dt_0} \left(\tilde{\rho} - \sum_{p=1, N(t)} \rho_p \right) = L^{(\rho)} \cdot \left(\tilde{\rho} - \sum_{p=1, N(t)} \rho_p \right),$$

where $\frac{D}{Dt_0} \cdot = \frac{\partial}{\partial t} \cdot + \nabla(\mathbf{u} \cdot)$,

and similarly for $\tilde{u}_j \tilde{\rho}$

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$\tilde{\rho}$ is diffused towards $\sum_{p=1, N(t)} \rho_p$:

$$L^{(\rho)} \cdot \left(\tilde{\rho} - \sum_{p=1, N(t)} \rho_p \right) = \frac{\partial}{\partial x_i} \left(s(1-s) \alpha \frac{\partial}{\partial x_i} \left(\tilde{\rho} - \sum_{p=1, N(t)} \rho_p \right) \right).$$

and similarly for $\tilde{u}_j \tilde{\rho}$

The sources J and J_2

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From these constraints the sources J and J_2 can be found:

$$J = s \frac{\partial}{\partial t} \sum_{p=1, N(t)} \rho_p + \frac{\partial}{\partial x_i} \left(s u_i \sum_{p=1, N(t)} \rho_p \right) + \frac{\partial}{\partial x_i} \left(s(1-s) \alpha \frac{\partial}{\partial x_i} \left(\tilde{\rho} - \sum_{p=1, N(t)} \rho_p \right) \right),$$

and similarly for the momentum source J_2

Modified MD equations

Hybrid MD/HD
modelling

For known J and J_2 MD equations are modified to preserve macroscopic conservation laws:

$$\frac{dx_{ip}}{dt} = u_{ip} + s(u_i - u_{ip}) + s(1-s)\alpha \frac{\partial}{\partial x_i} \left(\tilde{\rho} - \sum_{p=1, N(t)} \rho_p \right) \frac{1}{\rho_p N(t)},$$

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$$\begin{aligned} \frac{du_{jp}}{dt} &= (1-s)F_{jp}/\rho_p + sF_j/\rho_p/N(t) \\ &+ \frac{\partial}{\partial x_i} \left(s(1-s)\alpha \sum_{p=1, N(t)} u_{jp}/N(t) \frac{\partial}{\partial x_i} \left(\tilde{\rho} - \sum_{p=1, N(t)} \rho_p \right) \right) \frac{1}{\rho_p N(t)} \\ &- \frac{\partial}{\partial x_i} \left(s(1-s)\beta \frac{\partial}{\partial x_i} \left(\tilde{u}_j \tilde{\rho} - \sum_{p=1, N(t)} u_{jp} \rho_p \right) \right) \frac{1}{\rho_p N(t)}, \end{aligned}$$

Results: pure water

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Constant coupling across the domain
Movies for $s = 0$ and $s = 0.99$

Results: pure water

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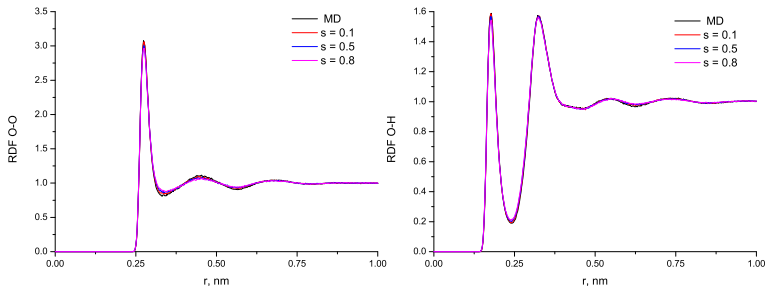
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Radial distribution functions of SPC/E water model

Results: pure water

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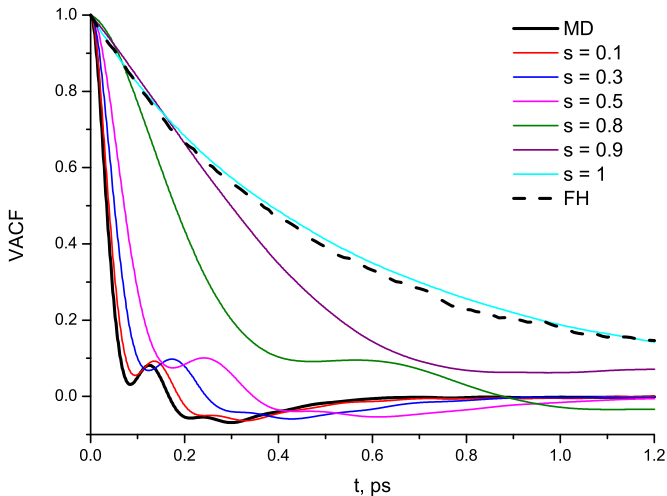
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Velocity autocorrelation function of the SPC/E water

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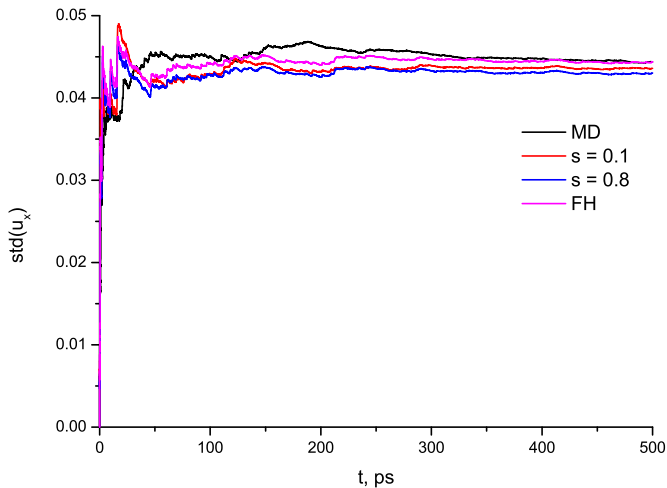
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Standard deviations of the velocity x component for SPC/E water

Results: pure water

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Variable coupling: atomistic core and continuum bulk
Movies for variable s

Results: peptide in water

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The atomistic core can move with the peptide
Movies for dialanine

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- Atomistic and continuum representations of liquid can be connected without artificial barriers or ad hoc correction forces in space and time.
- The domains of each representation can be defined arbitrarily in space and time.
- Challenges: *multiphysics* (non-stationary MD + hydrodynamics), multiscale *computing* (efficient multi space-time algorithms in parallel environment).

Outlook: porcine circovirus single protein

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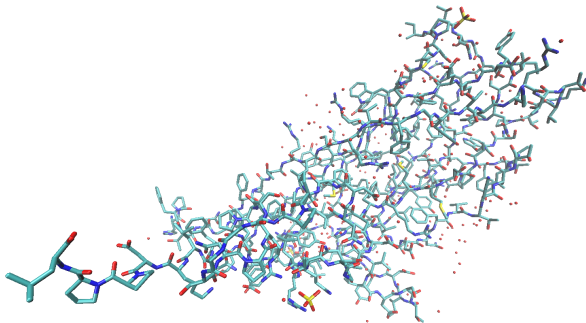
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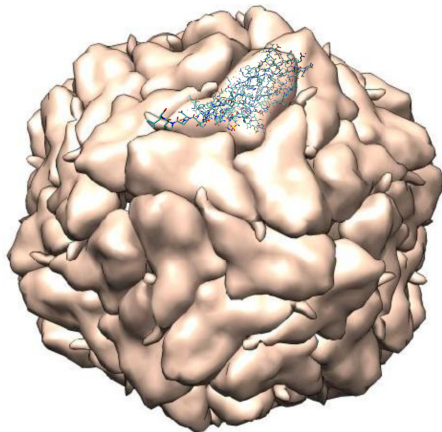
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Thank you.