Fluctuating Hydrodynamics Approaches for Lipid Bilayer Membranes

Partial Order: Mathematics, Simulations and Applications.

Institute for Pure & Applied Mathematics (IPAM-UCLA)

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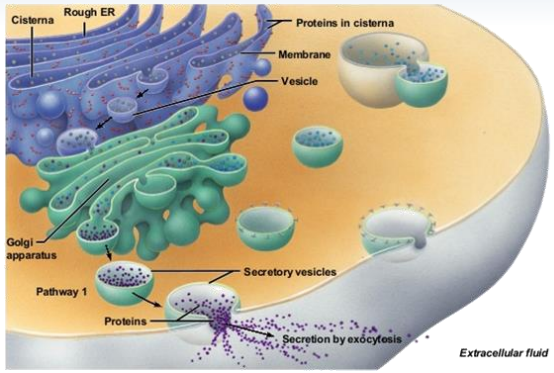
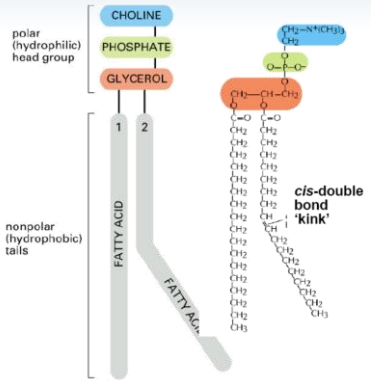
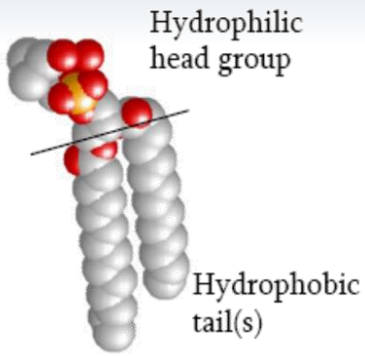
Lipid Bilayer Membranes : Amphiphilic Molecules

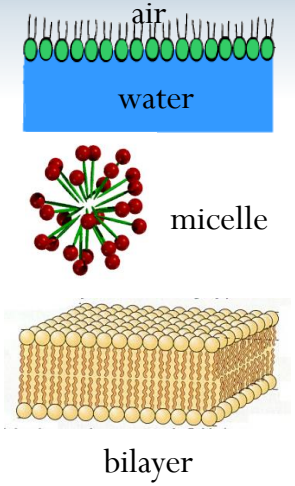
Cell Membranes



Phosphogylceride







Lipid Bilayer Membranes

- Cellular biology : membranes compartmentalize cell, dynamic structures, diverse functions.
- Fluid phase two layered structure (bilayer).
- Mechanics of a fluid-elastic sheet (in-plane flow, elastic response to bending).
- Phenomena span wide temporal-spatial scales.

Amphiphilic Molecules (Lipids)

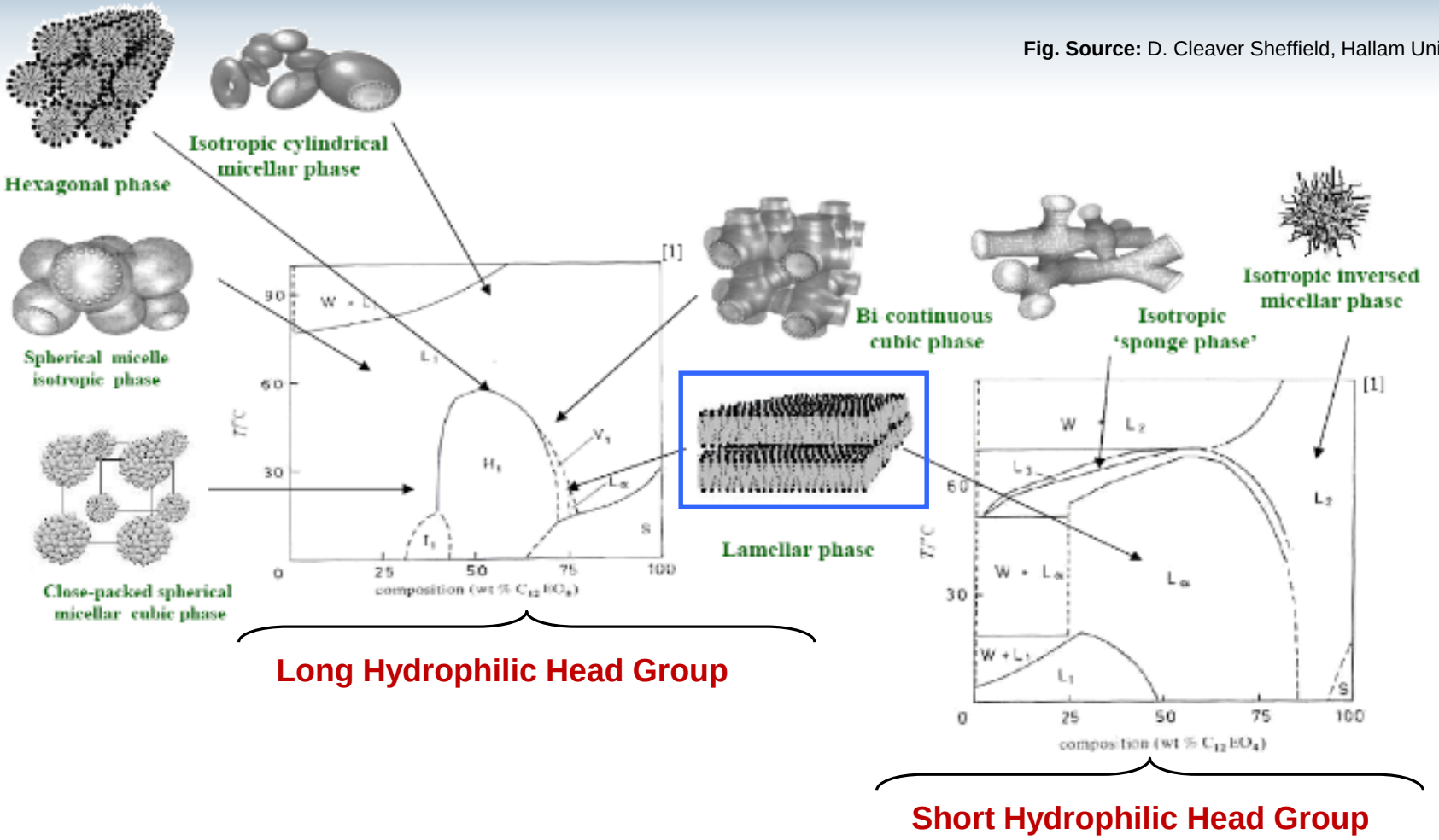
- Amphiphiles have a polar head (hydrophilic) and non-polar tail (hydrophobic).
- Solvent plays key role driving self-assembly (hydrophobic-hydrophilic effect).
- Phases fluid vs gel, micelle vs lamellar, size of polar vs non-polar part.

Partially Ordered Structures

- Lyotropic liquid crystals (temperature and concentration determines phase).
- Smectic A and C phases (translational order in layers, orientation orthogonal/tilt in layer).
- Lamellar sheets most relevant to biology, but many other phases possible.

Phases for Lipid Systems

Fig. Source: D. Cleaver Sheffield, Hallam University

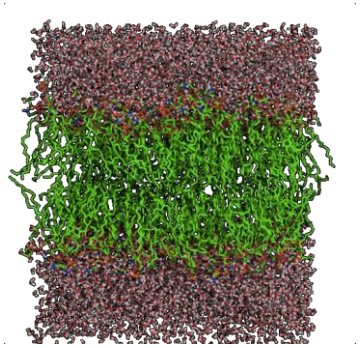


Lipid Phases

- Polar and non-polar lengths of molecule play role in phase.
- Many other applications of lipids i.e. in household products (hair gels, hand lotion, shampoo).
- Lamellar and micelle phases appear most relevant to biology.
- Lamellar phase appears more common with short hydrophilic head and longer hydrophobic tail.

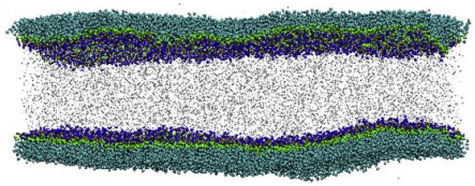
Modeling Approaches for Lipid Bilayer Membranes

Atomistic Molecular Dynamics



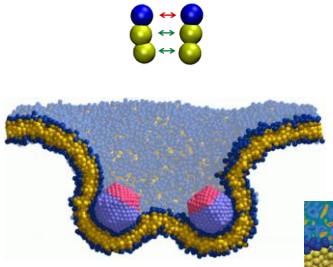
Grossfield 2013

Coarse-Grained Explicit-Solvent

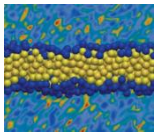


Duncan 2012

Coarse-Grained Implicit-Solvent

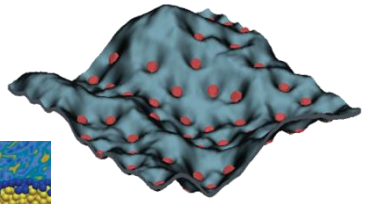


Deserno 2007



Atzberger 2013

Continuum Mechanics Hydrodynamics



Atzberger et al. 2009
Atzberger & Sigurdsson 2013

Atomistic Molecular Dynamics

- Representation of solvent fluid molecules and lipids.
- Atomic detail of molecules.
- Limited length and time-scales.

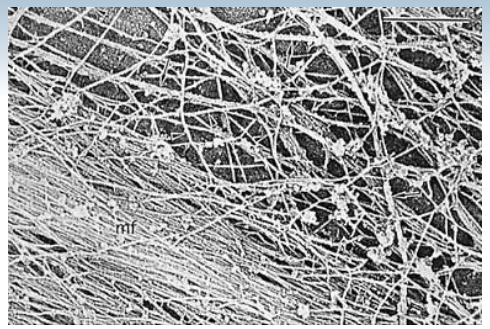
Explicit-Solvent Coarse-Grained (ES-CG)

- Atoms grouped/represented by coarse-grained units.
- Effective free-energy of interaction used on remaining degrees of freedom (DOF).
- Reduces entropy of the system (caution).
- Smooths energy landscape with often less stiff dynamics.
- Explicit-solvent is expensive, still requires resolving molecules of the bulk.

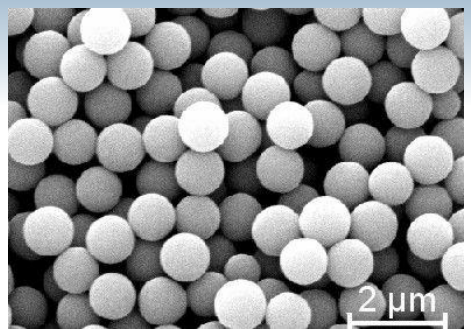
Implicit-Solvent Coarse-Grained (IS-CG)

- Atoms grouped/represented by coarse-grained units.
- Effective free-energy of interaction used on remaining degrees of freedom (DOF).
- Used widely for equilibrium studies, however, dynamics augmented by missing solvent effects.
- To extend for kinetic studies, need thermostats to account for correlation contributions of solvent in IS-CG.

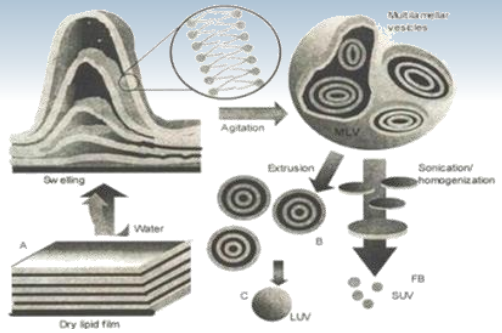
Soft Materials Simulation



Gels (Actin)



Colloids



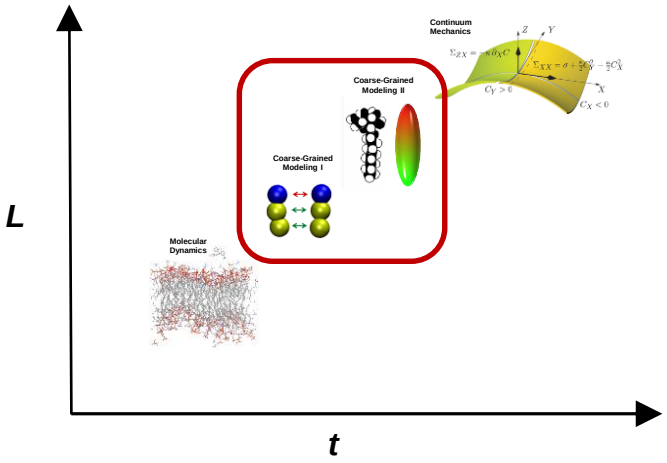
Membranes (lipids)

Soft Materials

- Interactions on order of K_BT.
- Properties arise from balance of entropy-enthalpy.
- Solvent plays important role (interactions / responses).
- Phenomena span wide temporal-spatial scales.

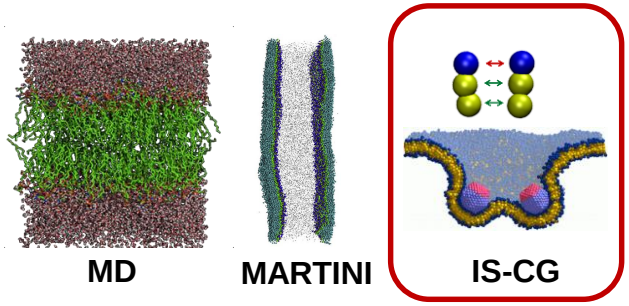
Approaches

- Atomistic Molecular Dynamics.
- Continuum Mechanics.
- Coarse-Grained Particle Models (solvated / implicit).

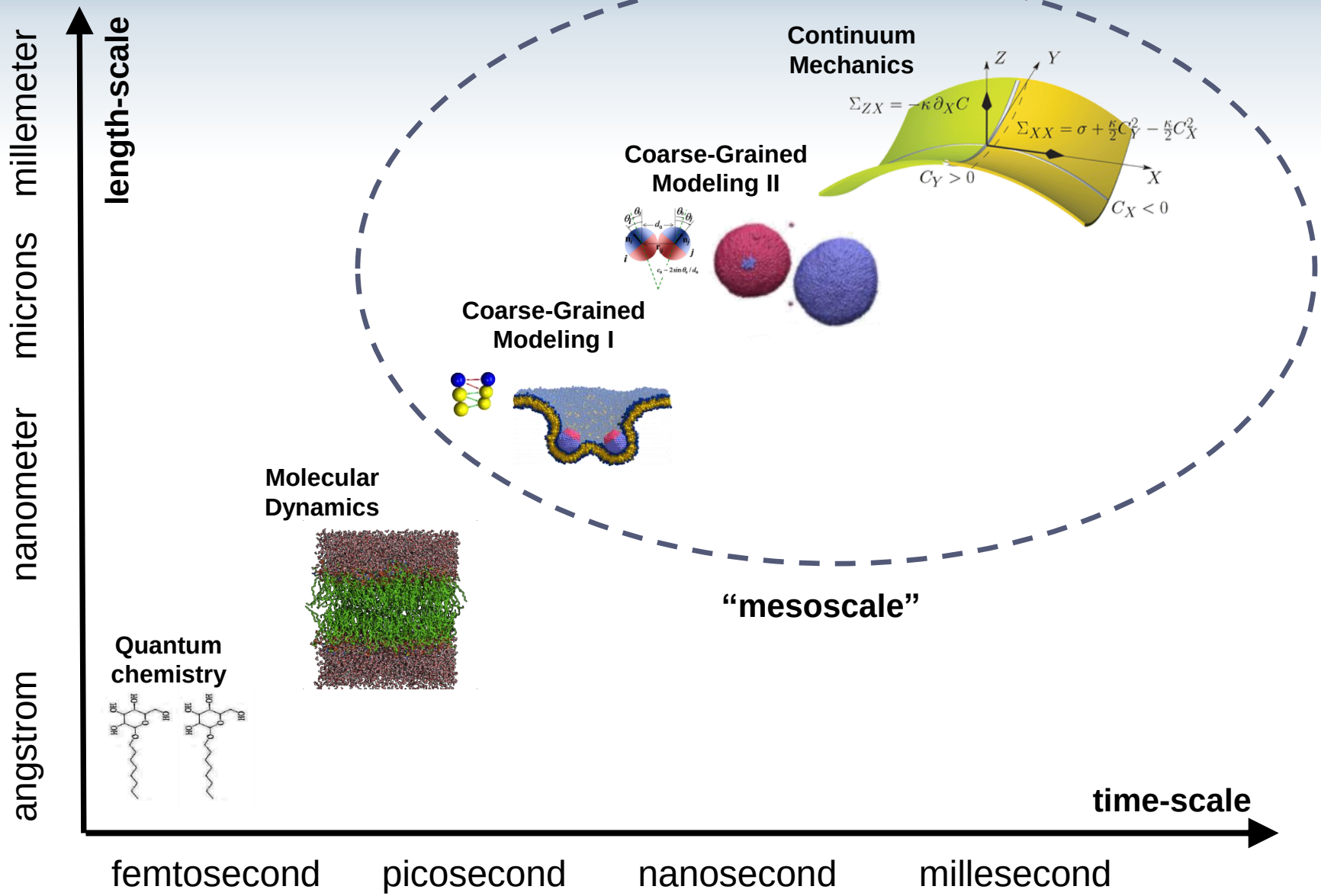


Simulation Methods / Thermostats

- NVE vs NVT ensembles.
- NVE → Velocity-Verlet (no thermostat).
- NVT → Berendsen, Nose-Hoover (artificial dynamics).
- NVT→ Langevin Dynamics (kinetics?).
- What about solvent mediated kinetics? What about other ensembles (NPT, $\dot{\gamma}$VT)?

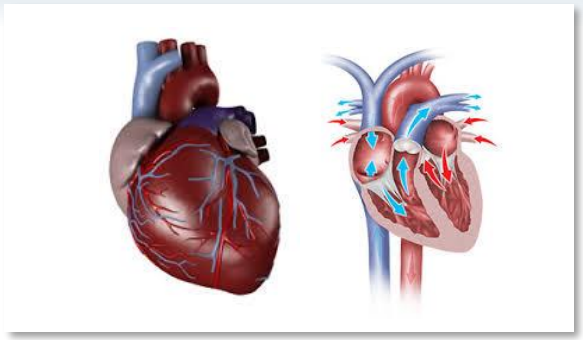


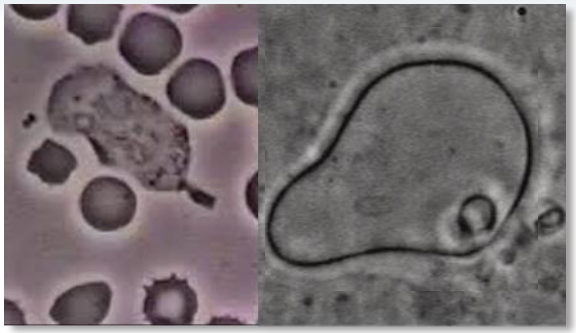
Model Resolution



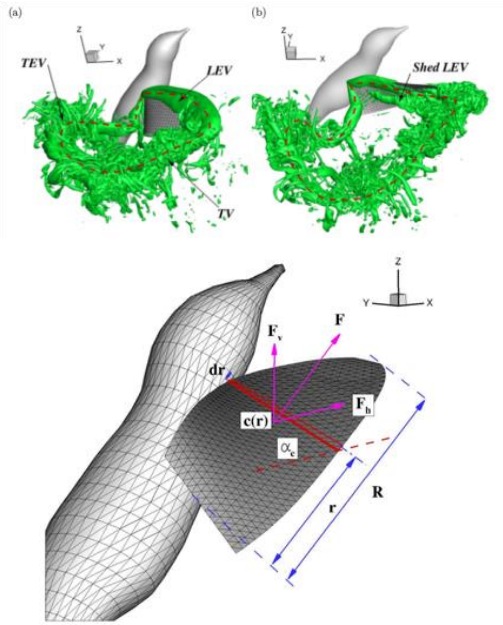
Solvent Hydrodynamics
CFD Fluid-Structure Interactions

Fluid-Structure Interactions

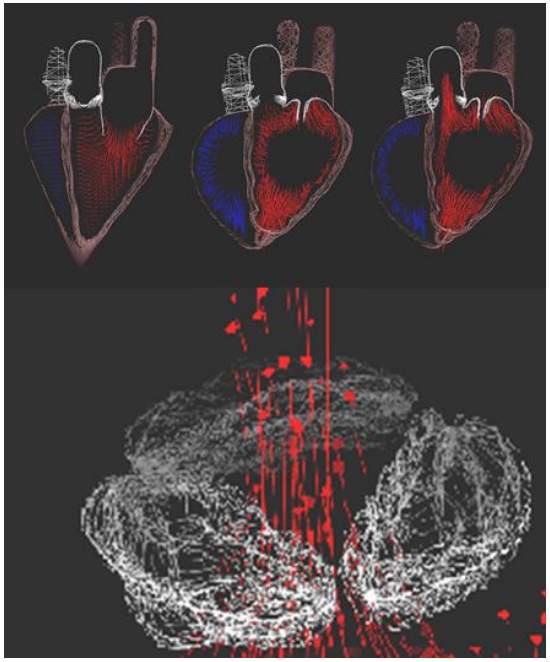




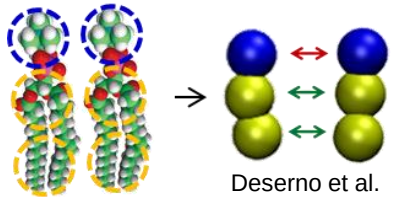
David Rogers



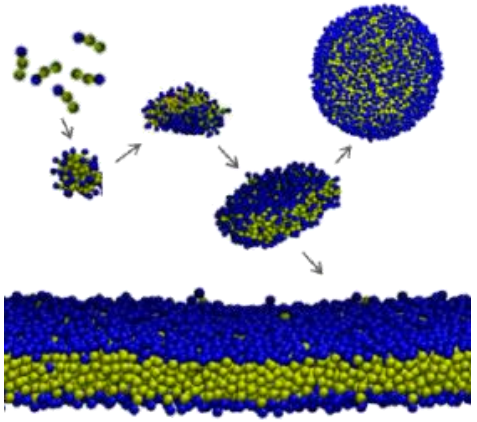
Song, J., Luo, H., Hedrick, T.L.



Peskin,C and McQueen, D. et al.

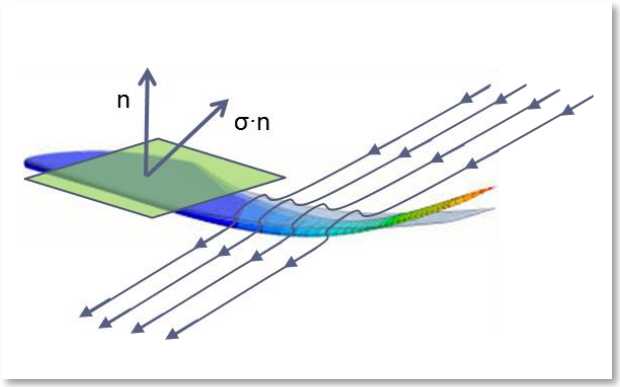


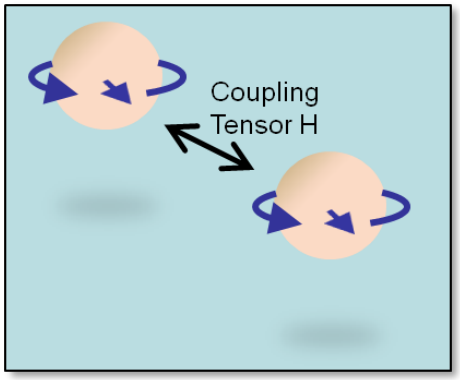
Deserno et al.

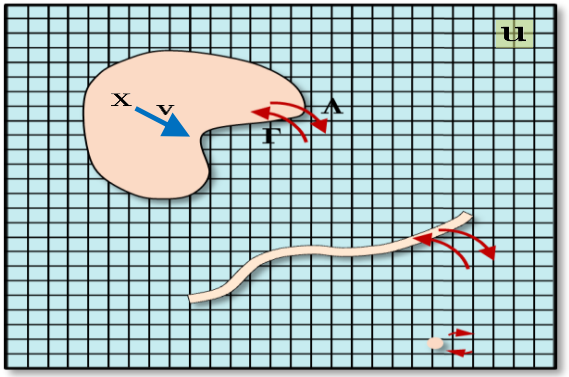


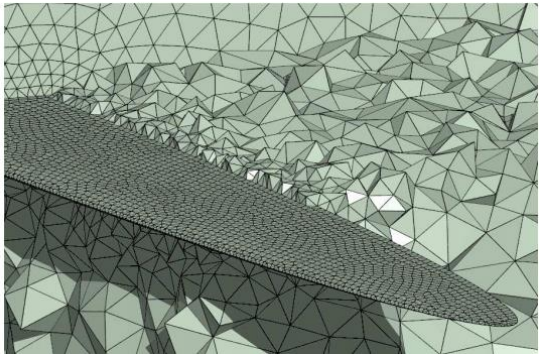
Atzberger, P.,Sigurdsson, J. et al.

CFD : Approaches



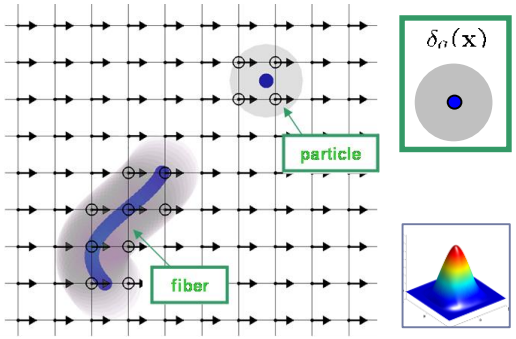






J. Peraire and P.-O. Persson

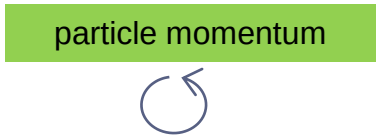
Brady et al., G. Gompper et al.

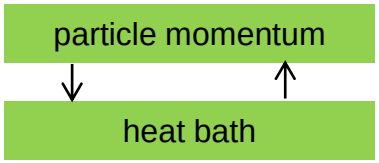


Atzberger, Peskin, Kramer

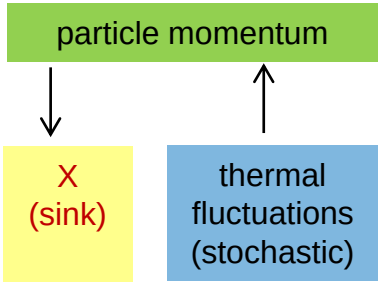
Thermostats

Berendson, Nose-Hoover





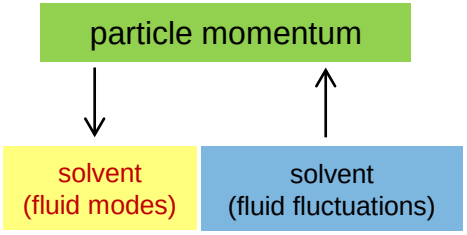
Langevin



$$m\frac{d\mathbf{V}}{dt} = -\gamma\mathbf{V} - \nabla\Phi(\mathbf{X}) + \sqrt{2k_BT\gamma}\frac{d\mathbf{B}_t}{dt}$$
$$\frac{d\mathbf{X}}{dt} = \mathbf{V}.$$

missing correlations through solvent!

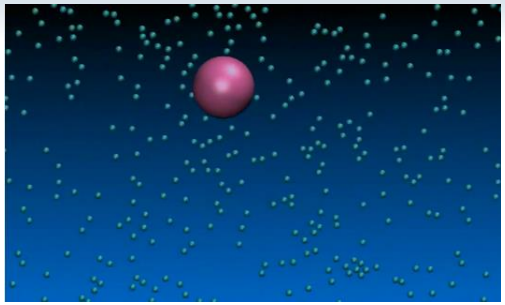
Fluctuating Hydrodynamics



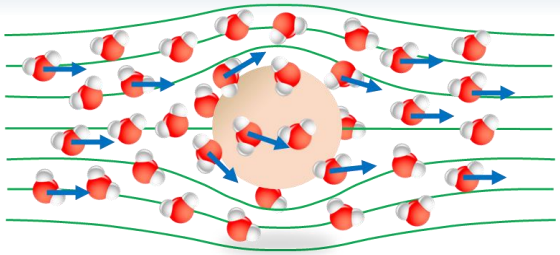
$$\frac{d\mathbf{X}}{dt} = \mathbf{v}$$
$$m\frac{d\mathbf{v}}{dt} = -\Upsilon\left(\mathbf{v} - \Gamma\mathbf{u}\right) - \nabla_{\mathbf{X}}\Phi[\mathbf{X}] + \zeta + \mathbf{F}_{\mathrm{thm}}$$

lateral momentum transfer : correlations

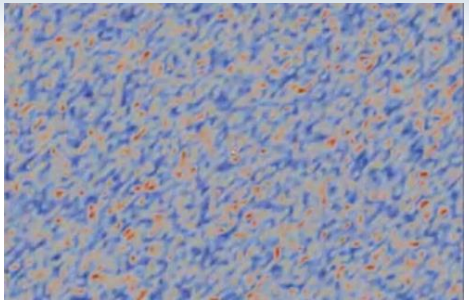
Fluctuating Hydrodynamics



Brownian Motion: Molecular Collisions



Hydrodynamics + Fluctuations



Continuum Gaussian Random Field

Landau-Lifschitz fluctuating hydrodynamics

$$\rho\left(\frac{\partial \mathbf{u}(\mathbf{x},t)}{\partial t} + \mathbf{u}(\mathbf{x},t)\cdot\nabla\mathbf{u}(\mathbf{x},t)\right) = \mu\Delta\mathbf{u}(\mathbf{x},t) - \nabla p(\mathbf{x},t) + \nabla\cdot\boldsymbol{\Sigma}(\mathbf{x},t).$$

$$\nabla\cdot\mathbf{u}(\mathbf{x},t) = 0.$$

$$\langle\Sigma_{ij}(\mathbf{x},t)\Sigma_{kl}(\mathbf{y},s)\rangle = 2\mu k_B T\left(\delta_{ik}\delta_{jl} + \delta_{il}\delta_{jk}\right)\delta(\mathbf{x}-\mathbf{y})\delta(t-s).$$

- Spontaneous momentum transfer from molecular-level interactions.
- Thermal fluctuations captured through random stress Σ.
- Mathematically, equations present challenges since δ-correlation in space-time.
- Fluid-structure interactions?

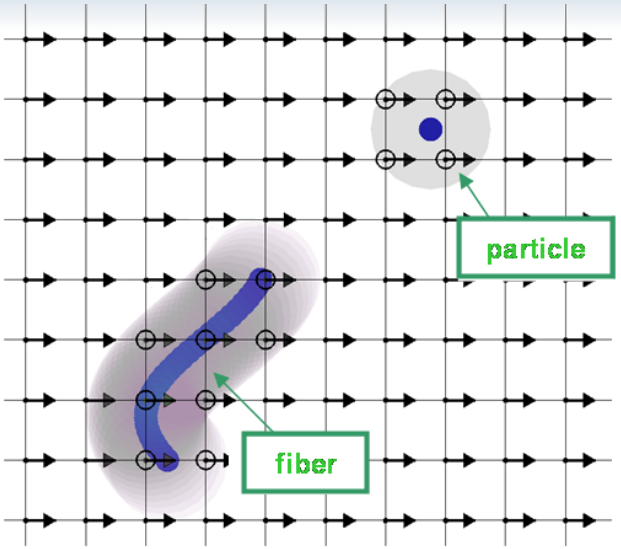
Immersed Boundary Method

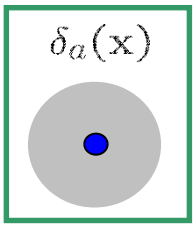
Fluid dynamics

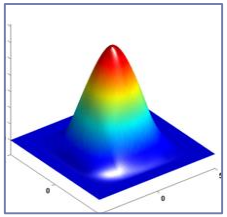
$$\rho \frac{D\mathbf{u}(\mathbf{x},t)}{Dt} = \mu \Delta \mathbf{u}(\mathbf{x},t) - \nabla p(\mathbf{x},t) + \mathbf{F}_{\text{prt}}(\mathbf{x},t) + \mathbf{F}_{\text{thm}}(\mathbf{x},t).$$
$$\nabla \cdot \mathbf{u}(\mathbf{x},t) = 0.$$

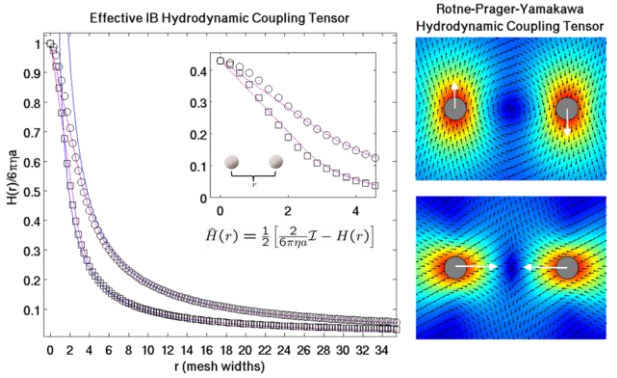
Structure dynamics

$$\frac{d\mathbf{X}^{[j]}(t)}{dt} = \int \delta_a(\mathbf{x} - \mathbf{X}^{[j]}(t))\mathbf{u}(\mathbf{x},t)d\mathbf{x}$$
$$\mathbf{F}_{\text{ptr}}(\mathbf{x},t) = \sum_{j=1}^{M} \mathbf{F}^{[j]} \delta_a \left(\mathbf{x} - \mathbf{X}^{[j]}(t)\right)$$









Atzberger, Peskin, Kramer 2007

Features:

- Allows conventional discretizations for fluid domain (FV, FFTs).
- Particles, fibers, membranes, and bodies possible.
- Thermal fluctuations: F_{thm} = ?

Stochastic Immersed Boundary Method

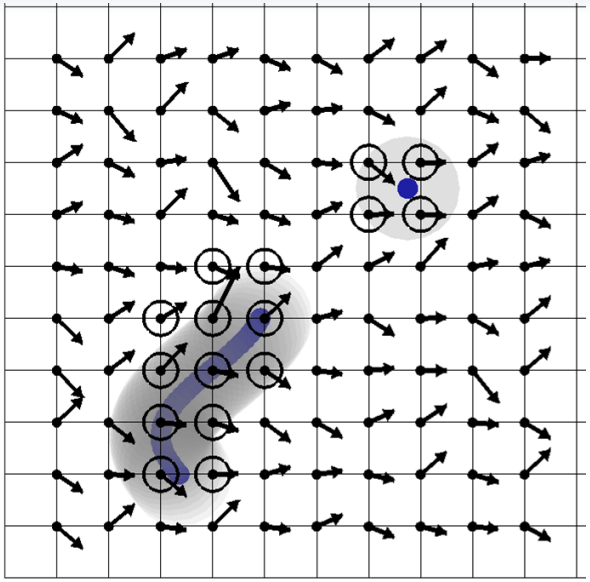
Fluid-structure equations

$$\rho \frac{D\mathbf{u}(\mathbf{x},t)}{Dt} = \mu \Delta \mathbf{u}(\mathbf{x},t) - \nabla p(\mathbf{x},t) + \mathbf{F}_{\text{prt}}(\mathbf{x},t) + \mathbf{F}_{\text{thm}}(\mathbf{x},t).$$

$$\nabla \cdot \mathbf{u}(\mathbf{x},t) = 0.$$

$$\frac{d\mathbf{X}^{[j]}(t)}{dt} = \int \delta_a(\mathbf{x} - \mathbf{X}^{[j]}(t))\mathbf{u}(\mathbf{x},t)d\mathbf{x}$$

$$\mathbf{F}_{\text{ptr}}(\mathbf{x},t) = \sum_{j=1}^{M} \mathbf{F}^{[j]} \delta_a \left(\mathbf{x} - \mathbf{X}^{[j]}(t)\right)$$

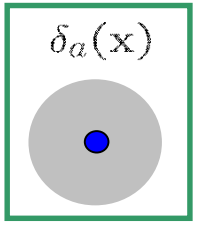


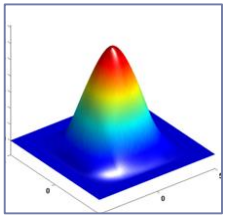
Thermal fluctuations

$$\mathbf{F}_{\text{thm}}(\mathbf{x},t) = \mathbf{F}_{\text{drift}}(\mathbf{x},t) + \mathbf{F}_{\text{stoch}}(\mathbf{x},t)$$

$$\mathbf{F}_{\text{drift}} = -k_B T \sum_{j=1}^{M} \nabla_{\mathbf{X}^{[j]}} \delta_a(\mathbf{x} - \mathbf{X}^{[j]}(t))$$

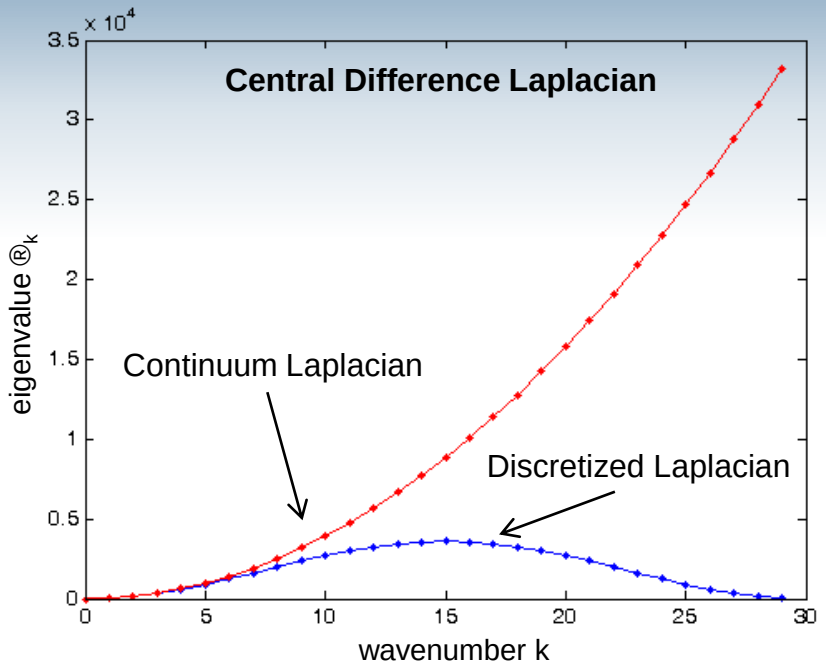
$$\left\langle \mathbf{F}_{\text{stoch}}(\mathbf{x},t)\mathbf{F}^{T}_{\text{stoch}}(\mathbf{y},s) \right\rangle = -2k_B T \mu \Delta \delta(\mathbf{x}-\mathbf{y})\delta(t-s)$$

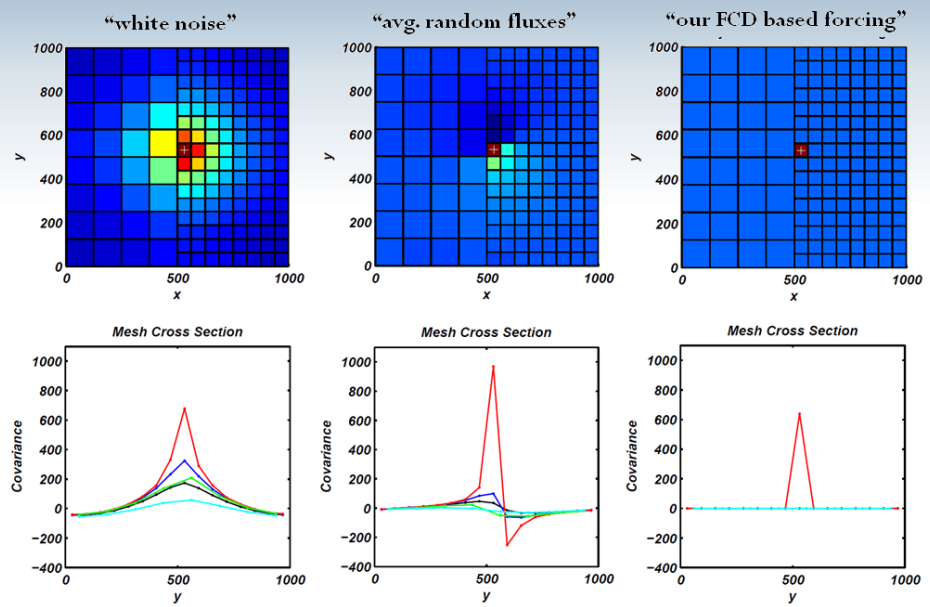




Atzberger, Peskin, Kramer 2007

Numerical Approximation





Dissipation rates are different for continuum and discrete system

- Must approximate differently thermal fluctuations in design of numerical methods.

- Mathematical formulation (Atzberger, Kramer, Peskin 2007, Atzberger 2011):
  - Fluctuation-dissipation balance (ito calculus, nyquist relations).
  - Invariance of Gibbs-Boltzmann (kolomogorov pde's, detailed balance)

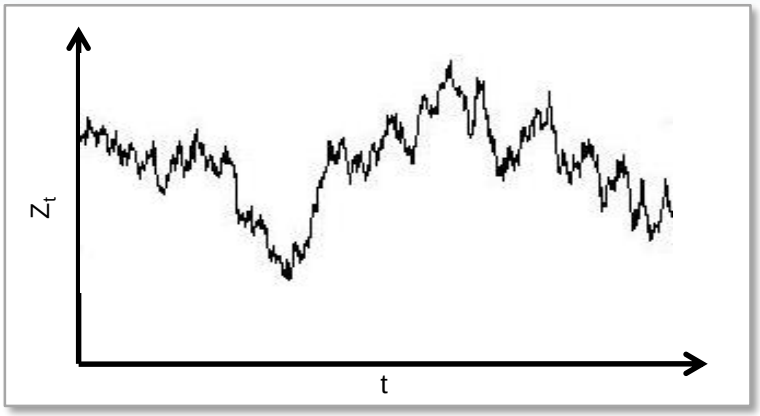
Fluctuation-dissipation balance condition

$$\langle \mathbf{f}_{\text{thm}}(s)\mathbf{f}_{\text{thm}}^T(t)\rangle = -\left(LC + CL^T\right)\delta(t-s)$$

$$L\mathbf{u} \leftarrow \mu\Delta\mathbf{u} \qquad C_{ij} \leftarrow \frac{k_B T}{\rho \Delta x^3}\delta_{ij}$$

Numerical Stiffness

Time-scales	
Fluid Modes	**Particle Diffusion**
$\tau_\lambda = \frac{\rho}{4\pi^2\mu}\lambda^2$	$\tau_{\text{diff}}(a) \approx \frac{a^2}{D_a}$
λ = 10nm : τ = 10^{-3}ns	$\tau_{\text{diff}}(1\text{nm}) \approx 10^0\text{ns}$
λ = 1000nm : τ = 10ns	$\tau_{\text{diff}}(10\text{nm}) \approx 10^3\text{ns}$



Sources of stiffness

- Fluid-structure have stochastic trajectories.
- Thermal fluctuations excite all fluid modes.
- Length-scales of microstructure involve fluid dynamics at small Re << 1.
- Equilibration relaxation time-scales of system.
- Elasticity of microstructures.

Two approaches

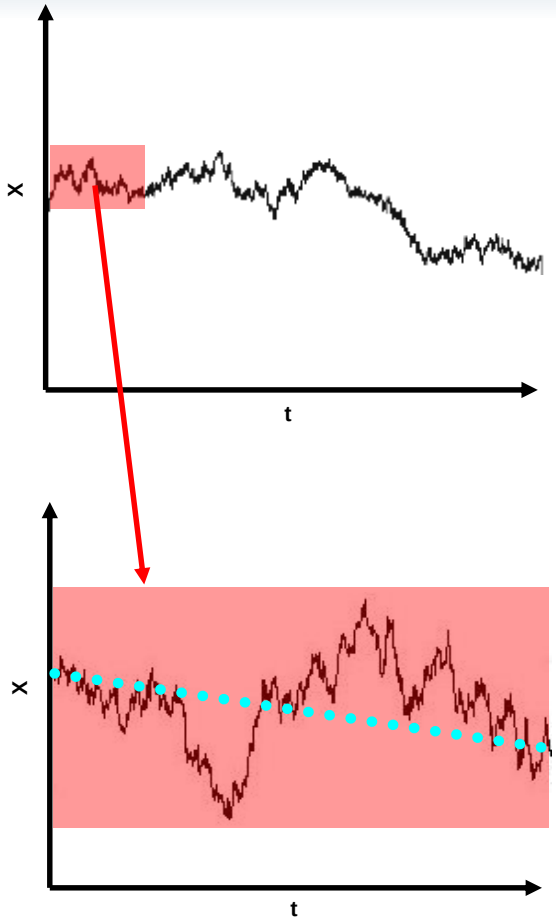
- Develop stiff stochastic time-step integrators.
- Perturbation analysis of SPDEs : reduced descriptions.

Stiff Time-step Integrator

Fluid equations

$$
\begin{aligned}
d\mathbf{u} &= \mathcal{L}\mathbf{u}dt && \text{(viscous damping)} \\
&+ \rho^{-1}\mathbf{F}_{\text{prt}}dt && \text{(particle force)} \\
&+ Qd\mathbf{B}_t && \text{(thermal force)}
\end{aligned}
$$

$$\nabla \cdot \mathbf{u} = 0 \qquad \text{(incompressibility)}$$



Structure equations

$$
\begin{aligned}
\frac{d\mathbf{X}^{[j]}(t)}{dt} &= \int \delta_a(\mathbf{x} - \mathbf{X}^{[j]}(t))\mathbf{u}(\mathbf{x},t)d\mathbf{x} \\
\mathbf{F}_{\text{prt}}(\mathbf{x},t) &= \sum_{j=1}^{M} -\nabla_{\mathbf{X}^{[j]}} V(\{\mathbf{X}(t)\})\delta_a(\mathbf{x} - \mathbf{X}^{[j]}(t))
\end{aligned}
$$

Integration by exponential factor (ito calculus)

$$= e^{t\mathcal{L}}\mathbf{u}(0) + \int_0^t e^{(t-s)\mathcal{L}}\rho^{-1}\mathbf{F}_{\text{prt}}(s)ds + \int_0^t e^{(t-s)\mathcal{L}}Qd\mathbf{B}_s = e^{t\mathcal{L}}\mathbf{u}(0) + \bar{\mathbf{I}}_{\text{prt}} + \bar{\mathbf{I}}_{\text{thm}}$$

Stiff Time-step Integrator

Integration by exponential factor (ito calculus)

$$\mathbf{u}(t) \;=\; e^{t\mathcal{L}}\mathbf{u}(0) + \int_0^t e^{(t-s)\mathcal{L}}\rho^{-1}\mathbf{F}_{\text{prt}}(s)ds + \int_0^t e^{(t-s)\mathcal{L}}Q d\mathbf{B}_s \;=\; e^{t\mathcal{L}}\mathbf{u}(0) + \bar{\mathbf{I}}_{\text{prt}} + \bar{\mathbf{I}}_{\text{thm}}$$

Particle force

$$\mathbf{I}_{\text{prt}}(t) := \int_0^t e^{(t-s)\mathcal{L}}\rho^{-1}\mathbf{F}_{\text{prt}}(s)ds$$

Approximate by constant force

$$\mathbf{I}_{\text{prt}}(t) \approx -\rho^{-1}\mathcal{L}^{-1}\left[\mathcal{I} - e^{t\mathcal{L}}\right]\mathbf{F}_{\text{prt}}(0)$$

Thermal fluctuations

$$\mathbf{I}_{\text{thm}}(t) := \int_0^t e^{(t-s)\mathcal{L}}Q d\mathbf{B}_s$$

Ito calculus yields Gaussian with

$$\langle \mathbf{I}_{\text{thm}}(t)\rangle \;=\; 0$$

$$\langle \mathbf{I}_{\text{thm}}(t)\mathbf{I}_{\text{thm}}(t)^T\rangle \;=\; \int_0^t e^{(t-s)\mathcal{L}}QQ^T e^{(t-s)\mathcal{L}^T}ds := \Lambda(t)$$

$$\Lambda_{\mathbf{k},\mathbf{k}}(t) = -\frac{1}{2\alpha_{\mathbf{k}}}\left[1 - e^{-2\alpha_{\mathbf{k}}\Delta t}\right]Q^2_{\mathbf{k},\mathbf{k}}$$

Stiff Time-step Integrator

Integration by exponential factor (ito calculus)

$$\mathbf{u}(t) = e^{t\mathcal{L}}\mathbf{u}(0) + \int_0^t e^{(t-s)\mathcal{L}}\rho^{-1}\mathbf{F}_{\text{prt}}(s)ds + \int_0^t e^{(t-s)\mathcal{L}}Qd\mathbf{B}_s = e^{t\mathcal{L}}\mathbf{u}(0) + \bar{\mathbf{I}}_{\text{prt}} + \bar{\mathbf{I}}_{\text{thm}}$$

$$\mathbf{I}_{\text{prt}}(t) \approx -\rho^{-1}\mathcal{L}^{-1}\left[\mathcal{I} - e^{t\mathcal{L}}\right]\mathbf{F}_{\text{prt}}(0)$$

$$\Lambda_{\mathbf{k},\mathbf{k}}(t) = -\frac{1}{2\alpha_{\mathbf{k}}}\left[1 - e^{-2\alpha_{\mathbf{k}}\Delta t}\right]Q^2_{\mathbf{k},\mathbf{k}}$$

Fluid Integrator

$$\mathbf{u}^{n+1} = e^{\Delta t\mathcal{L}}\mathbf{u}^n + \mathcal{L}^{-1}\left[\mathcal{I} - e^{\Delta t\mathcal{L}}\right]\rho^{-1}\mathbf{F}^n_{\text{prt}} + \Gamma\xi^n$$

ξ is Gaussian with

$$\langle\xi\rangle = 0\,,\ \langle\xi\xi^T\rangle = \mathcal{I}$$

$$\Lambda = \Gamma\Gamma^T$$

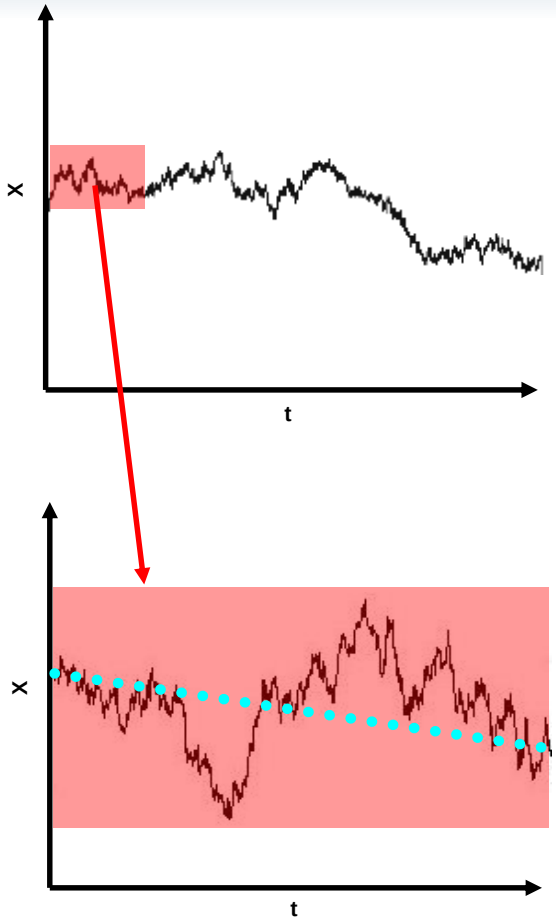
- unconditionally stable.
- accuracy depends only on structure force approximation (otherwise exact).
- requires prior knowledge of Γ.
- method viable only if efficient to compute $e^{\Delta t\mathcal{L}}$.
- viable for uniform meshes (FFTs).

Stiff Time-step Integrator

Fluid equations

$$
\begin{aligned}
d\mathbf{u} &= \mathcal{L}\mathbf{u}dt && \text{(viscous damping)} \\
&+ \rho^{-1}\mathbf{F}_{\text{prt}}dt && \text{(particle force)} \\
&+ Qd\mathbf{B}_t && \text{(thermal force)}
\end{aligned}
$$

$$\nabla \cdot \mathbf{u} = 0 \qquad \text{(incompressibility)}$$



Structure equations

$$\frac{d\mathbf{X}^{[j]}(t)}{dt} = \int \delta_a(\mathbf{x} - \mathbf{X}^{[j]}(t))\mathbf{u}(\mathbf{x}, t)d\mathbf{x}$$

$$\mathbf{F}_{\text{prt}}(\mathbf{x}, t) = \sum_{j=1}^{M} -\nabla_{\mathbf{X}^{[j]}} V(\{\mathbf{X}(t)\})\delta_a(\mathbf{x} - \mathbf{X}^{[j]}(t))$$

Integrate structure dynamics (ito calculus)

$$\mathbf{X}^{[j]}(t) = \mathbf{X}^{[j]}(0) + \int_0^t \int \delta_a(\mathbf{x} - \mathbf{X}^{[j]}(s))\mathbf{u}(\mathbf{x}, s)d\mathbf{x}ds \approx \mathbf{X}^{[j]}(0) + \int \delta_a(\mathbf{x} - \mathbf{X}^{[j]}(0)) \int_0^t \mathbf{u}(\mathbf{x}, s)dsd\mathbf{x}$$

Stiff Time-step Integrator

Integrate structure dynamics (ito calculus)

$$\mathbf{X}^{[j]}(t) \approx \mathbf{X}^{[j]}(0) + \int \delta_a(\mathbf{x} - \mathbf{X}^{[j]}(0)) \int_0^t \mathbf{u}(\mathbf{x}, s) ds d\mathbf{x}$$

$$\hookrightarrow \quad \mathbf{X}^{[j],n+1} = \mathbf{X}^{[j],n} + \int \delta_a(\mathbf{x} - \mathbf{X}^{[j],n}) \mathbf{I}_{\text{vel}}(\mathbf{x}, \Delta t) d\mathbf{x}$$

$$\mathbf{I}_{\text{vel}}(t) := \int_0^t \mathbf{u}(s) ds$$

Integrated fluctuating fluid velocity

$\mathbf{I}_{\text{vel}}(t)$ is a Gaussian with

$$\bar{\mathbf{I}}_{\text{vel}} := \langle \mathbf{I}_{\text{vel}}(t) \rangle = \int_0^t \langle \mathbf{u}(s) \rangle ds = -\mathcal{L}^{-1} \left[\mathcal{I} - e^{t\mathcal{L}} \right] \mathbf{u}(0) + -\mathcal{L}^{-1} \left[t + \mathcal{L}^{-1} \left[\mathcal{I} - e^{t\mathcal{L}} \right] \right] \mathbf{F}_{\text{prt}}(0)$$

$$\Phi := \langle \left(\mathbf{I}_{\text{vel}}(t) - \bar{\mathbf{I}}_{\text{vel}}(t) \right) \left(\mathbf{I}_{\text{vel}}^T(t) - \bar{\mathbf{I}}_{\text{vel}}^T(t) \right) \rangle = \int_0^t \int_0^t e^{r\mathcal{L}} C e^{s\mathcal{L}^T} dr ds + \int_0^t \int_0^t \int_0^{s \wedge r} e^{(r-w)\mathcal{L}} Q Q^T e^{(s-w)\mathcal{L}^T} dw dr ds$$

$\mathbf{I}_{\text{vel}}(t)$ is correlated with $\mathbf{I}_{\text{thm}}(t)$

$$W := \langle \left(\mathbf{I}_{\text{vel}}(t) - \bar{\mathbf{I}}_{\text{vel}}(t) \right) \mathbf{I}_{\text{thm}}^T(t) \rangle = \mathcal{L}^{-1} \int_0^t e^{(t-w)\mathcal{L}} Q Q^T e^{(t-w)\mathcal{L}^T} dw + \mathcal{L}^{-1} Q Q^T \mathcal{L}^{-T} \left[\mathcal{I} - e^{t\mathcal{L}^T} \right]$$

Structure Integrator

$$\mathbf{X}^{[j],n+1} = \mathbf{X}^{[j],n} + \int \delta_a(\mathbf{x} - \mathbf{X}^{[j],n}) \mathbf{I}_{\text{vel}}(\mathbf{x}, \Delta t) d\mathbf{x}$$

- stability depends now on structure forces.
- accuracy depends on
  - fluid sampling approximation X(t) ~ X(0) and structure force approximation.
- method viable only if efficient to compute exponentials.
- viable for uniform meshes (FFTs).

Summary : Stiff Integrator

Fluid Integrator

$$\mathbf{u}^{n+1} = e^{\Delta t \mathcal{L}}\mathbf{u}^n + \mathcal{L}^{-1}\left[\mathcal{I} - e^{\Delta t \mathcal{L}}\right]\rho^{-1}\mathbf{F}^n_{\text{prt}} + \Gamma\xi^n$$

ξ is Gaussian with

$$\langle\xi\rangle = 0\,,\ \langle\xi\xi^T\rangle = \mathcal{I}$$

$$\Lambda = \Gamma\Gamma^T$$

Structure Integrator

$$\mathbf{X}^{[j],n+1} = \mathbf{X}^{[j],n} + \int \delta_a(\mathbf{x} - \mathbf{X}^{[j],n})\mathbf{I}_{\text{vel}}(\mathbf{x}, \Delta t)d\mathbf{x}$$

$\mathbf{I}_{\text{vel}}(t)$ is a Gaussian with

$$\bar{\mathbf{I}}_{\text{vel}} := \langle\mathbf{I}_{\text{vel}}(t)\rangle = \int_0^t \langle\mathbf{u}(s)\rangle ds = -\mathcal{L}^{-1}\left[\mathcal{I} - e^{t\mathcal{L}}\right]\mathbf{u}(0) + -\mathcal{L}^{-1}\left[t + \mathcal{L}^{-1}\left[\mathcal{I} - e^{t\mathcal{L}}\right]\right]\mathbf{F}_{\text{prt}}(0)$$

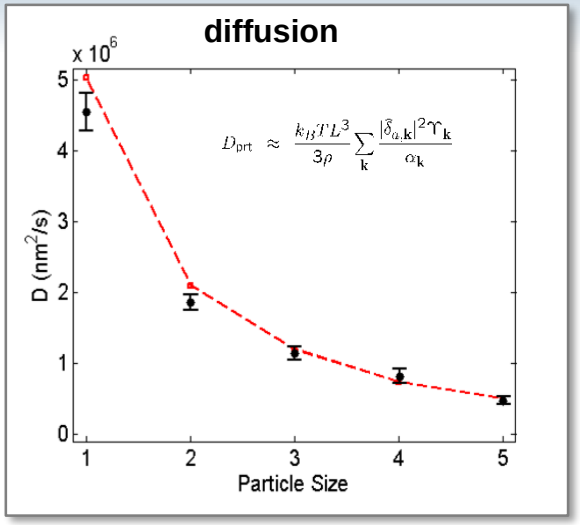
$$\Phi := \langle\left(\mathbf{I}_{\text{vel}}(t) - \bar{\mathbf{I}}_{\text{vel}}(t)\right)\left(\mathbf{I}^T_{\text{vel}}(t) - \bar{\mathbf{I}}^T_{\text{vel}}(t)\right)\rangle = \int_0^t\int_0^t e^{r\mathcal{L}}Ce^{s\mathcal{L}^T}drds + \int_0^t\int_0^t\int_0^{s\wedge r} e^{(r-w)\mathcal{L}}QQ^Te^{(s-w)\mathcal{L}^T}dwdrds$$

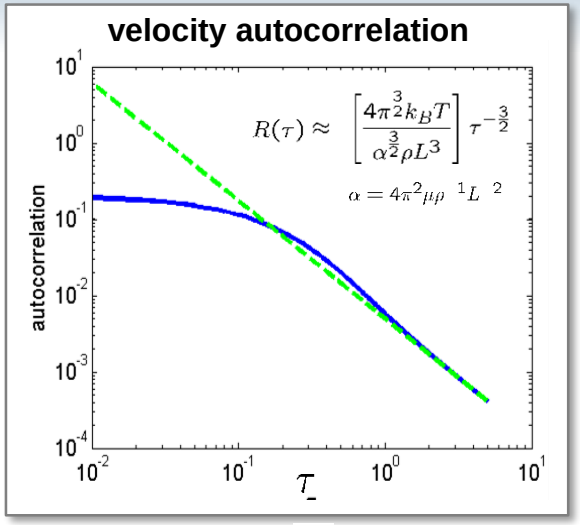
$\mathbf{I}_{\text{vel}}(t)$ is correlated with $\mathbf{I}_{\text{thm}}(t)$

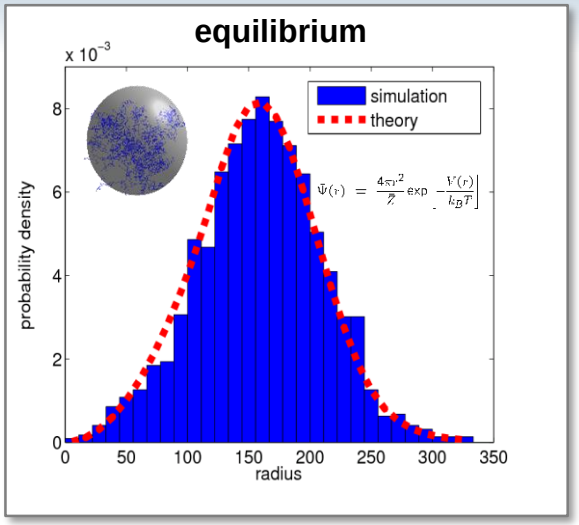
$$W := \langle\left(\mathbf{I}_{\text{vel}}(t) - \bar{\mathbf{I}}_{\text{vel}}(t)\right)\mathbf{I}^T_{\text{thm}}(t)\rangle = \mathcal{L}^{-1}\int_0^t e^{(t-w)\mathcal{L}}QQ^Te^{(t-w)\mathcal{L}^T}dw + \mathcal{L}^{-1}QQ^T\mathcal{L}^{-T}\left[\mathcal{I} - e^{t\mathcal{L}^T}\right]$$

- method viable only if efficient to compute exponentials.
- viable for uniform meshes (FFTs).
- under-resolves fluid mode dynamics and fluctuations.
- time-step limited by structure's motions.

Validation of Numerical Methods

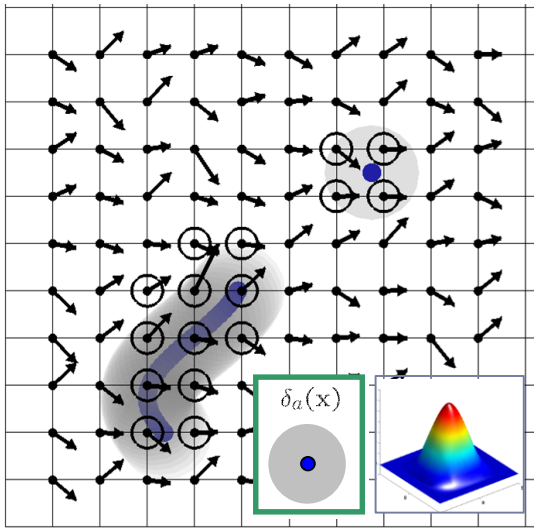






Validation

- Diffusivity of under-resolved particles correct.
- Velocity auto-correlation has $t^{-3/2}$ tail (Adler & Wainright 1950),
- Auto-correlation persists from hydrodynamic “memory.”
- Equilibrium configurations have Gibbs-Boltzmann statistics.
- Can ideas be extended to other coupling types and regimes?



Generalization : Stochastic Eulerian Lagrangian Methods

Fluid

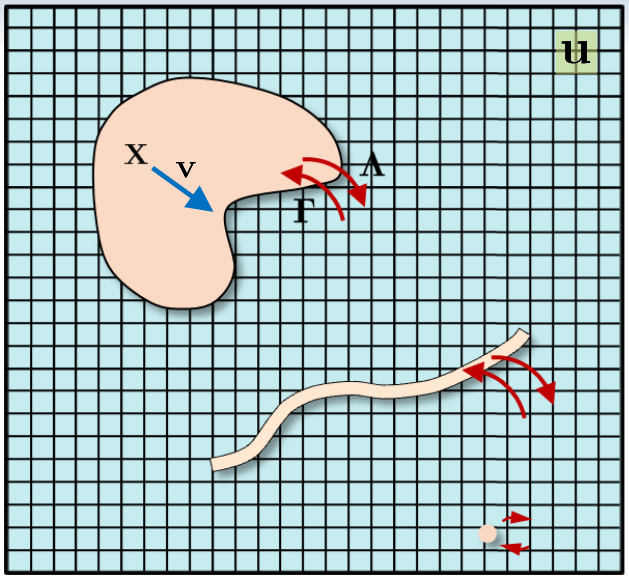
$$\rho \frac{\partial \mathbf{u}}{\partial t} = \mathcal{L}\mathbf{u} + \Lambda[\Upsilon(\mathbf{v} - \Gamma\mathbf{u})] + \lambda + \mathbf{f}_{\text{thm}}$$
$$\nabla \cdot \mathbf{u} = 0$$

Structure

$$\frac{d\mathbf{X}}{dt} = \mathbf{v}$$
$$m\frac{d\mathbf{v}}{dt} = -\Upsilon\left(\mathbf{v} - \Gamma\mathbf{u}\right) - \nabla_{\mathbf{X}}\Phi[\mathbf{X}] + \zeta + \mathbf{F}_{\text{thm}}$$

Thermal fluctuations

$$\langle \mathbf{f}_{\text{thm}}(s)\mathbf{f}^T_{\text{thm}}(t)\rangle = -\left(2k_BT\right)\left(\mathcal{L} - \Lambda\Upsilon\Gamma\right)\delta(t-s)$$
$$\langle \mathbf{F}_{\text{thm}}(s)\mathbf{F}^T_{\text{thm}}(t)\rangle = \left(2k_BT\right)\Upsilon\,\delta(t-s)$$
$$\langle \mathbf{f}_{\text{thm}}(s)\mathbf{F}^T_{\text{thm}}(t)\rangle = -\left(2k_BT\right)\Lambda\Upsilon\,\delta(t-s).$$



Operators:

- $\mathcal{L}$ ⟶ Fluid dissipation (viscosity).
- Υ ⟶ Structure "slip" relative to local flow field.
- Γ ⟶ Kinematic particle velocity for given flow.
- Λ ⟶ Induced fluid force density from particle.

Notation:

- $\mathbf{u} = \mathbf{u}(\mathbf{x}, t)$ ⟶ Fluid velocity.
- $\mathbf{X} = \mathbf{X}(\mathbf{q}, t)$ ⟶ Structure configuration
- $\mathbf{v} = \mathbf{v}(\mathbf{q}, t)$ ⟶ Structure velocity.

Atzberger 2011

Coupling Operators

Conservation of momentum

$$\int_\Omega (\Lambda \mathbf{F})(\mathbf{x}) d\mathbf{x} = \int_\mathcal{S} \mathbf{F}(\mathbf{q}) d\mathbf{q}$$

$\longrightarrow$ "integrates to one."

Conservation of energy

(overdamped limit)

$$E[\mathbf{u}, \mathbf{X}] = \tfrac{1}{2} \int \rho |\mathbf{u}(\mathbf{y})|^2 d\mathbf{y} + \Phi(\mathbf{X})$$

Adjoint condition

$$\int_\mathcal{S} (\Gamma \mathbf{u})(\mathbf{q}) \cdot \mathbf{F}(\mathbf{q}) d\mathbf{q} = \int_\Omega \mathbf{u}(\mathbf{x}) \cdot (\Lambda \mathbf{F})(\mathbf{x}) d\mathbf{x}$$

$$\longrightarrow \langle \Gamma \mathbf{u}, \mathbf{F} \rangle = \langle \mathbf{u}, \Lambda \mathbf{F} \rangle \longrightarrow \text{“}\Gamma = \Lambda^T\text{”}$$

- Energy conserved → coupling operators are adjoints!
- Useful for deriving coupling operators.

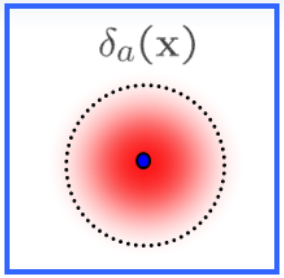
Immersed Boundary Method

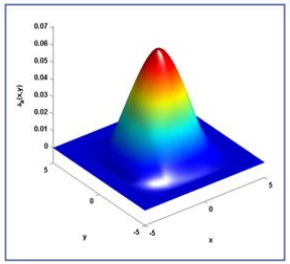
Coupling operators

$$\Gamma[u] = \int \delta_a(\mathbf{x} - \mathbf{X}^{[j]}(t))\mathbf{u}(\mathbf{x},t)d\mathbf{x}$$

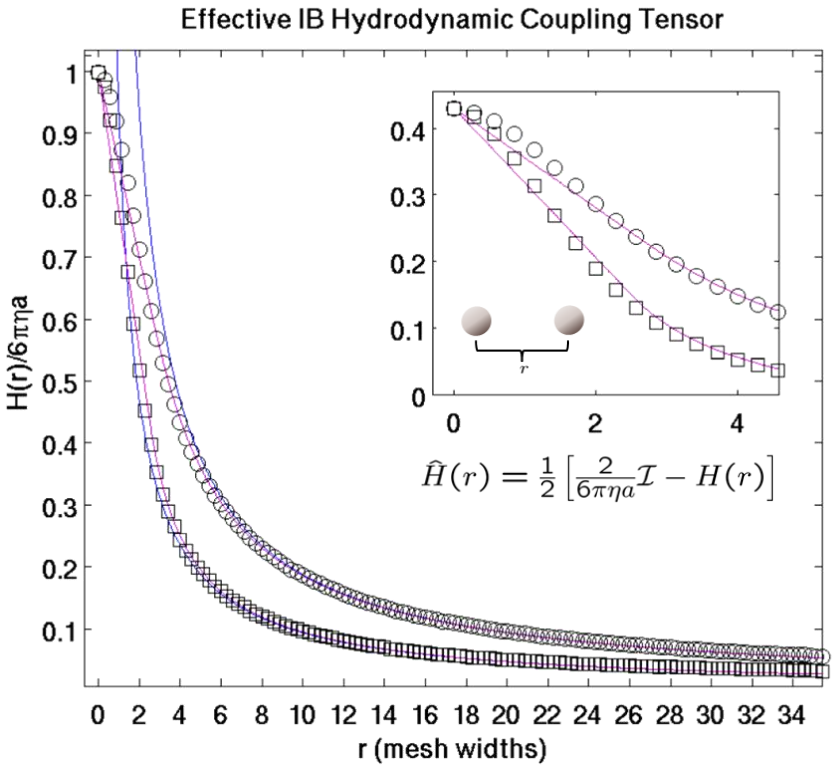
$$\Lambda[F] = \delta_a(\mathbf{x} - \mathbf{X}^{[j]}(t))\mathbf{F}$$

$$\text{“}\Gamma = \Lambda^T\text{”}$$

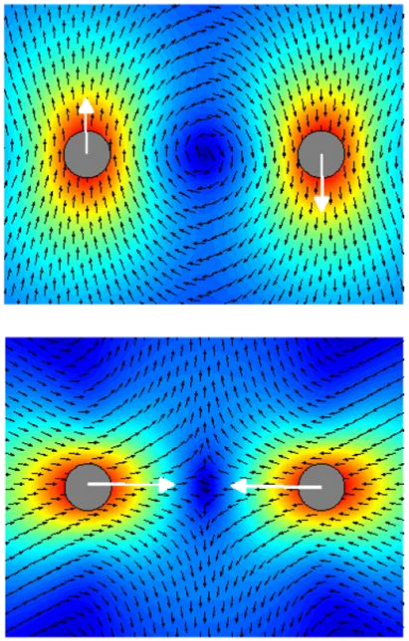




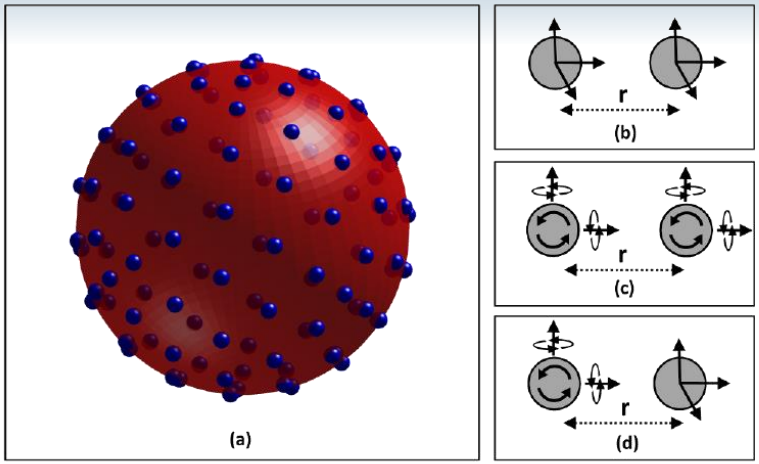
Peskin delta-function

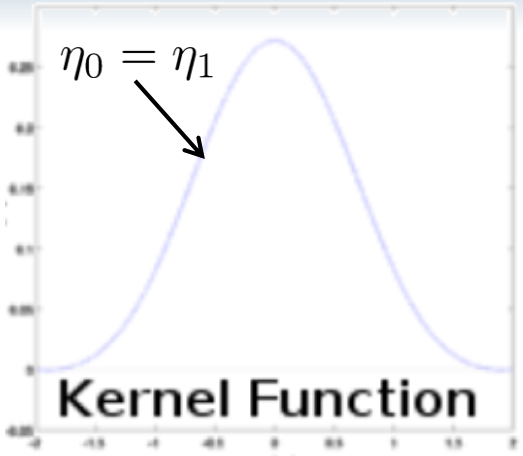


Rotne-Prager-Yamakawa
Hydrodynamic Coupling Tensor



Coupling Operators based on Faxen Relations





Faxen Kinematic Relations→ Γ :

$$\Gamma_0 \mathbf{u} = \sum_{\mathbf{m}} \left\langle \, \eta_0(\mathbf{y_m} - (\mathbf{X_{cm}} + \mathbf{z}))\ \mathbf{u_m} \, \right\rangle_{\tilde{\mathcal{S}},|\mathbf{z}|=R} \Delta x_{\mathbf{m}}^3$$

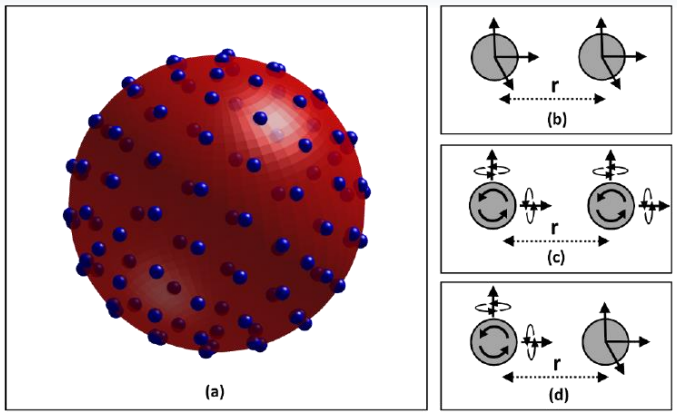
$$\Gamma_1 \mathbf{u} = \frac{3}{2R^2} \sum_{\mathbf{m}} \left\langle \, \eta_1(\mathbf{y_m} - (\mathbf{X_{cm}} + \mathbf{z}))\, (\mathbf{z} \times \mathbf{u_m}) \, \right\rangle_{\tilde{\mathcal{S}},|\mathbf{z}|=R} \Delta x_{\mathbf{m}}^3.$$

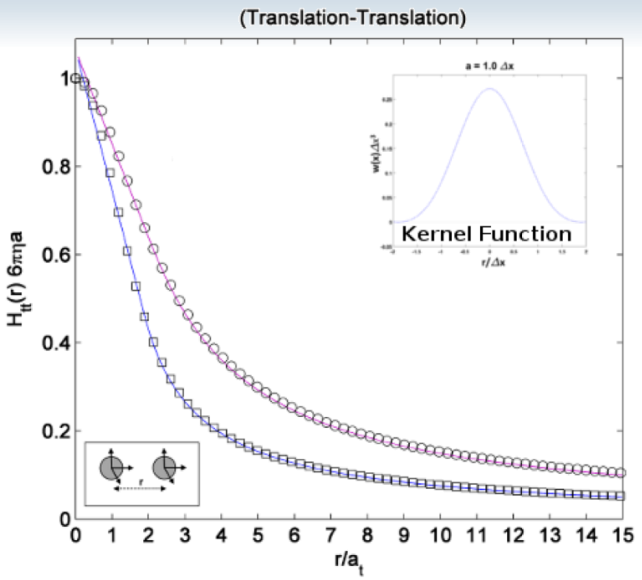
Adjoint Condition → Λ :

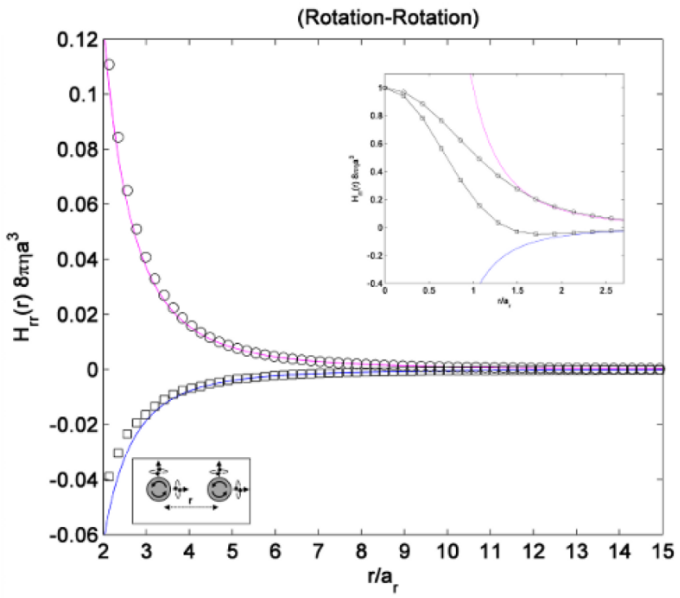
$$\Lambda_0(\mathbf{x_m}) = \left(\left\langle \, \eta_0(\mathbf{x_m} - (\mathbf{X_{cm}} + \mathbf{z})) \, \right\rangle_{\tilde{\mathcal{S}},|\mathbf{z}|=R} \right) \mathbf{F}$$

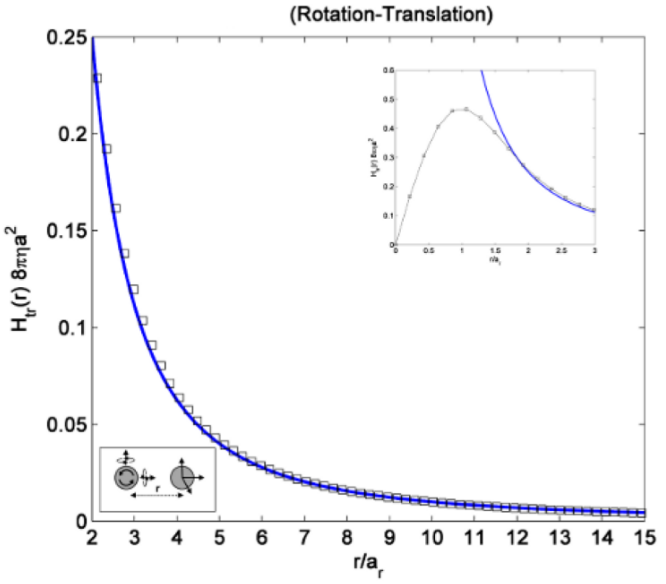
$$\Lambda_1(\mathbf{x_m}) = -\frac{3}{2R^2} \left(\left\langle \, \mathbf{z}\eta_1(\mathbf{x_m} - (\mathbf{X_{cm}} + \mathbf{z})) \, \right\rangle_{\tilde{\mathcal{S}},|\mathbf{z}|=R} \right) \times \mathbf{T}.$$

Coupling Operators based on Faxen Relations





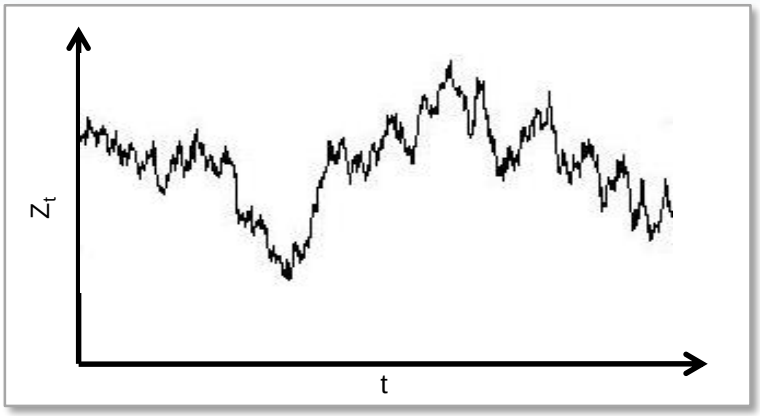




Excellent agreement for r > 2a !

Numerical Stiffness

Time-scales	
Fluid Modes	**Particle Diffusion**
$\tau_\lambda = \frac{\rho}{4\pi^2\mu}\lambda^2$	$\tau_{\text{diff}}(a) \approx \frac{a^2}{D_a}$
λ = 10nm : τ = 10^{-3}ns	$\tau_{\text{diff}}(1\text{nm}) \approx 10^0$ns
λ = 1000nm : τ = 10ns	$\tau_{\text{diff}}(10\text{nm}) \approx 10^3$ns



Sources of stiffness

- In SELM additional sources of stiffness from
  - microstructure inertia
  - fluid-structure slip $-\Upsilon\left(\mathbf{v}-\Gamma\mathbf{u}\right)$
- Thermal fluctuations also excite coupling modes and all fluid modes.
- Elasticity of microstructures.
- Equilibration time-scales of system vary over wide range.

Two approaches

- Develop stiff stochastic time-step integrators (as for SIBM).
- Perturbation analysis of SPDEs : reduced descriptions.

Stochastic Reduction

Stochastic differential equation:

$$d\mathbf{Z}(t) = \mathbf{a}(\mathbf{Z}(t))dt + \mathbf{b}(\mathbf{Z}(t))d\mathbf{W}_t \longrightarrow L_\epsilon = \mathbf{a}\cdot\frac{\partial}{\partial \mathbf{z}} + \frac{1}{2}\mathbf{b}\mathbf{b}^T : \frac{\partial^2}{\partial \mathbf{z}^2}$$

Backward-Kolomogorov PDE:

$$\begin{aligned}\frac{\partial u}{\partial t} &= L_\epsilon u \\ u(x,0) &= f(x)\end{aligned} \longrightarrow u(x,t) = E^{x,0}\left[f(X_t)\right]$$

Perturbation Analysis:

$$u(\mathbf{z},t) = u_0(\mathbf{z},t) + u_1(\mathbf{z},t)\epsilon + u_2(\mathbf{z},t)\epsilon^2 \cdots + u_n(\mathbf{z},t)\epsilon^n + \cdots$$

Split operator into "slow" and "fast" parts:

$$L_\epsilon = \epsilon^{-1}L_1 + \epsilon^{-2}L_{fast}$$

↓ **ε → 0 : compare orders**

$$L_0 = -\left[\int_{\mathbb{R}^N} \psi L_1 L_{fast}^{-1} L_1 d\mathbf{v}\right]$$ **leading order dynamics.**

Reduced dynamics:

$$L_0 = \tilde{\mathbf{a}}\cdot\frac{\partial}{\partial \mathbf{z}} + \frac{1}{2}\tilde{\mathbf{b}}\tilde{\mathbf{b}}^T : \frac{\partial^2}{\partial \mathbf{z}^2} \longrightarrow d\tilde{\mathbf{Z}}_t = \tilde{\mathbf{a}}(\tilde{\mathbf{Z}}_t)dt + \tilde{\mathbf{b}}(\tilde{\mathbf{Z}}_t)d\tilde{\mathbf{W}}_t$$

Atzberger & Tabak 2015

Summary of regimes

Stochastic Eulerian Lagrangian Method (SELM)

Fluid dynamics:

$$\begin{aligned}\rho\frac{\partial \mathbf{u}}{\partial t} &= \mu\Delta\mathbf{u} - \nabla p + \Lambda[\Upsilon(\mathbf{v}-\Gamma\mathbf{u})] + \mathbf{f}_{\text{thm}}\\ \nabla\cdot\mathbf{u} &= 0\end{aligned}$$

Structure dynamics:

$$\begin{aligned}\frac{d\mathbf{X}}{dt} &= \mathbf{v}\\ m\frac{d\mathbf{v}}{dt} &= -\Upsilon\left(\mathbf{v}-\Gamma\mathbf{u}\right) - \nabla_{\mathbf{X}}\Phi[\mathbf{X}] + \zeta + \mathbf{F}_{\text{thm}}\end{aligned}$$

Thermal Fluctuations

$$\begin{aligned}\langle \mathbf{f}_{\text{thm}}(s)\mathbf{f}^T_{\text{thm}}(t)\rangle &= -\left(2k_BT\right)\left(\mu\Delta - \Lambda\Upsilon\Gamma\right)\delta(t-s)\\ \langle \mathbf{F}_{\text{thm}}(s)\mathbf{F}^T_{\text{thm}}(t)\rangle &= \left(2k_BT\right)\Upsilon\,\delta(t-s)\\ \langle \mathbf{f}_{\text{thm}}(s)\mathbf{F}^T_{\text{thm}}(t)\rangle &= -\left(2k_BT\right)\Lambda\Upsilon\,\delta(t-s).\end{aligned}$$

Microstructure density matched with fluid

$m \ll \rho\ell^3$

Fluid-structure dynamics:

$$\begin{aligned}\frac{d\mathbf{p}}{dt} &= \rho^{-1}\mathcal{L}\mathbf{p} + \Lambda[-\nabla_{\mathbf{X}}\Phi(\mathbf{X})] + \left(\nabla_{\mathbf{X}}\cdot\Lambda\right)k_BT + \lambda + \mathbf{g}_{\text{thm}}\\ \frac{d\mathbf{X}}{dt} &= \rho^{-1}\Gamma\mathbf{p} + \Upsilon^{-1}[-\nabla_{\mathbf{X}}\Phi(\mathbf{X})] + \zeta + \mathbf{G}_{\text{thm}}.\\ \nabla_{\mathbf{X}}\cdot\Lambda &= \text{Tr}[\nabla_{\mathbf{X}}\Lambda]\end{aligned}$$

Phase space compressibility (p,X).

Thermal Fluctuations:

$$\begin{aligned}\langle \mathbf{g}_{\text{thm}}(s)\mathbf{g}^T_{\text{thm}}(t)\rangle &= -\left(2k_BT\right)\mathcal{L}\,\delta(t-s)\\ \langle \mathbf{G}_{\text{thm}}(s)\mathbf{G}^T_{\text{thm}}(t)\rangle &= \left(2k_BT\right)\Upsilon^{-1}\,\delta(t-s)\\ \langle \mathbf{g}_{\text{thm}}(s)\mathbf{G}^T_{\text{thm}}(t)\rangle &= 0.\end{aligned}$$

- Structure momentum no longer tracked.
- Removes a source of stiffness.
- Non-conjugate Hamiltonian formulation yields metric-factor in phase-space.

Microstructure-fluid no-slip coupling (S-Immersed-Boundary)

$\Upsilon \to \infty$

Fluid-Structure Equations:

$$\begin{aligned}\frac{d\mathbf{p}}{dt} &= \rho^{-1}\mathcal{L}\mathbf{p} + \Lambda[-\nabla_{\mathbf{X}}\Phi(\mathbf{X})] + \left(\nabla_{\mathbf{X}}\cdot\Lambda\right)k_BT + \lambda + \mathbf{g}_{\text{thm}}\\ \frac{d\mathbf{X}}{dt} &= \rho^{-1}\Gamma\mathbf{p}\end{aligned}$$

Thermal Fluctuations:

$$\langle \mathbf{g}_{\text{thm}}(s)\mathbf{g}^T_{\text{thm}}(t)\rangle = -\left(2k_BT\right)\mathcal{L}\,\delta(t-s).$$

- Structure dynamics no-longer inertial.
- Removes additional sources of stiffness.
- Regime of the Stochastic Immersed Boundary Method.
- Phase-space metric reflected in the drift term.

Microstructure-fluid stress balance

$\mu \to \infty$

Fluid-Structure Equations:

$$\begin{aligned}\frac{d\mathbf{X}}{dt} &= H_{\text{SELM}}[-\nabla_{\mathbf{X}}\Phi(\mathbf{X})] + \left(\nabla_{\mathbf{X}}\cdot H_{\text{SELM}}\right)k_BT + \mathbf{h}_{\text{thm}}\\ H_{\text{SELM}} &= \Gamma(-\wp\mathcal{L})^{-1}\Lambda\end{aligned}$$

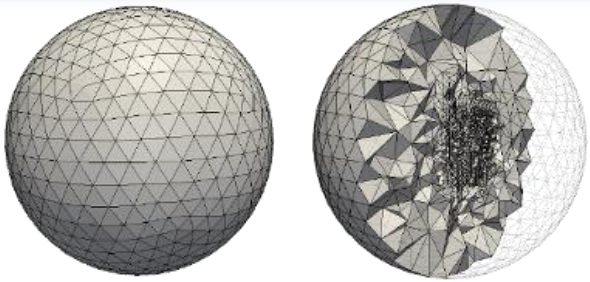
Thermal Fluctuations:

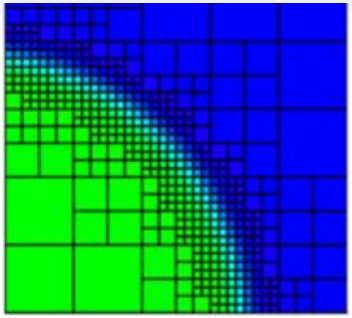
$$\langle \mathbf{h}_{\text{thm}}(s)\mathbf{h}^T_{\text{thm}}(t)\rangle = \left(2k_BT\right)H_{\text{SELM}}\,\delta(t-s).$$

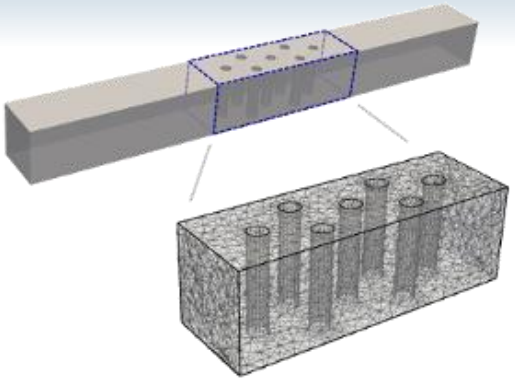
- Fluid momentum no longer tracked.
- Balance of hydrodynamic stresses with elastic stresses.
- Removes additional sources of stiffness.
- Regime of the Stokesian-Brownian Dynamics (Brady 1980, McCammond 1980's).
- Phase-space metric reflected in the drift term.

Atzberger & Tabak 2015

Adaptive Meshes







Fluid dynamics

$$\rho \frac{\partial \mathbf{u}}{\partial t} = \mathcal{L}\mathbf{u} + \Lambda[\Upsilon(\mathbf{v} - \Gamma\mathbf{u})] + \lambda + \mathbf{f}_{\text{thm}}$$
$$\nabla \cdot \mathbf{u} = 0$$

Structure dynamics

$$\frac{d\mathbf{X}}{dt} = \mathbf{v}$$
$$m\frac{d\mathbf{v}}{dt} = -\Upsilon\left(\mathbf{v} - \Gamma\mathbf{u}\right) - \nabla_{\mathbf{X}}\Phi[\mathbf{X}] + \zeta + \mathbf{F}_{\text{thm}}$$

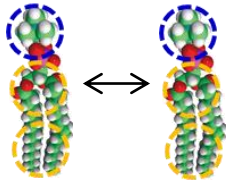
- Thermal fluctuation propagation pose challenges for non-uniform discretizations.
- Dissipative numerical operators need to be compatible stochastic driving fields.
- Additional time-scales arise from the microstructure – fluid momentum coupling.
- We developed Finite Element Methods + Stochastic Iterative Methods for SELM.

Atzberger, Plunkett, Hu, Siefert 2014

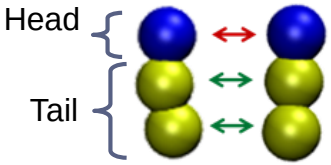
Implicit-Solvent Coarse-Grained Models
Lipid Bilayer Membranes

Coarse-Grained Lipid Model

Lipid Interactions



Coarse-Grained Model



Deserno 2005.

Interaction Potentials

Steric Repulsion: Weeks-Chandler Anderson

$$V_{\text{steric}}(r) = \begin{cases} 4\epsilon\left[(b/r)^{12} - (b/r)^6 + 1/4\right], & r \le r_c, \\ 0, & r > r_c. \end{cases} \qquad r_c = 2^{1/6} b$$

Bonds: FENE

$$V_{\text{bond}}(r) = -\frac{1}{2} k_{\text{bond}} r_\infty^2 \ln\left(1 - \left(r/r_\infty^2\right)\right)$$

Bending

$$V_{\text{bend}}(r) = \frac{1}{2} k_{\text{bend}} (r - 4\sigma)^2$$

Tail-Tail Attraction: Hydrophobic-Hydrophilic Effect

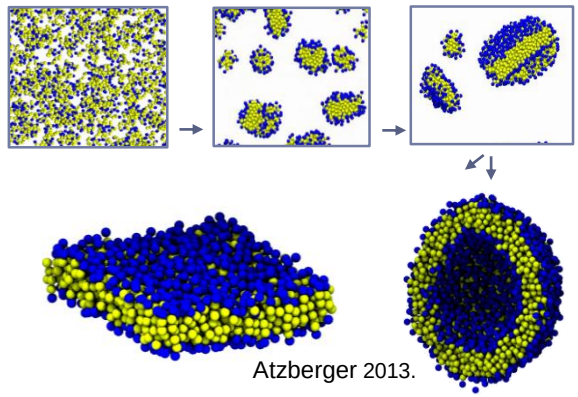
$$V_{\text{tail-tail}}(r) = \begin{cases} -\epsilon, & r < r_c, \\ -\epsilon \cos^2(\pi(r - r_c)/2w_c), & r_c \le r \le r_c + w_c, \\ 0, & r > r_c. \end{cases}$$

Deserno 2005.

Lipid Bilayer Membranes

Self Assembles

Self-Assembled Bilayers

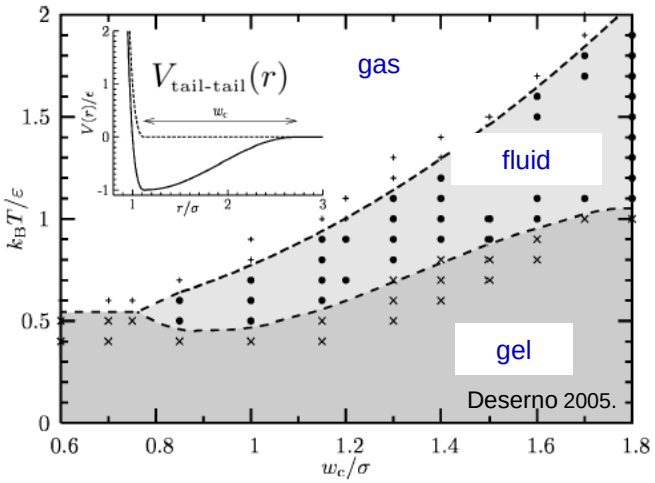


Atzberger 2013.

Key Features

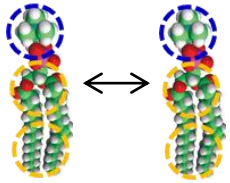
- Atomic details coarse-grained to obtain simplified model.
- Lipids represented by a few “beads.”
- Hydrophobic-hydrophilic effect drives bilayer formation.
- Solvent treated implicitly through free energy of interactions.
- Long-range tail-tail interaction drives self-assembly (important to obtain fluid phase).
- IS-CG models widely used for equilibrium. What about kinetics?

Phases

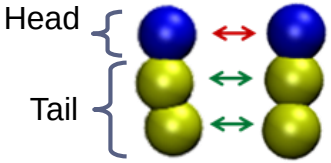


Extending IS-CG Models with Fluctuating Hydrodynamics

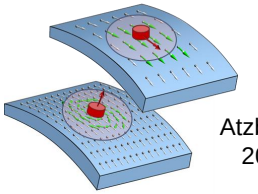
Lipid Interactions



Coarse-Grained Model



Deserno 2005.



Atzberger 2016.

Fluctuating Hydrodynamics

Particle Dynamics:

$$\frac{d\mathbf{X}}{dt} = \mathbf{v}$$
$$m\frac{d\mathbf{v}}{dt} = -\Upsilon(\mathbf{v}-\Gamma\mathbf{u}) - \nabla_X \Phi[X] + \mathbf{F}_{thm}$$

Fluctuating Hydrodynamics (SELM):

$$\rho\frac{\partial \mathbf{u}}{\partial t} = \mu\Delta\mathbf{u} - \nabla p + \Lambda[\Upsilon(\mathbf{v}-\Gamma\mathbf{u})] + \mathbf{f}_{thm}$$
$$\nabla\cdot\mathbf{u} = 0.$$

Thermal Fluctuations

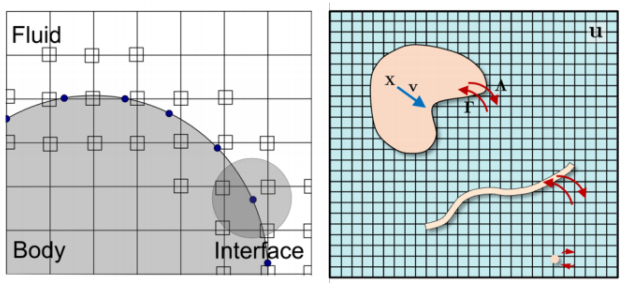
$$\left\langle \mathbf{f}_{\rm thm}(s)\mathbf{f}_{\rm thm}(t)^T\right\rangle = -2k_BT\left(\mu\Delta - \Lambda\Upsilon\Gamma\right)\delta(t-s)$$
$$\left\langle \mathbf{F}_{\rm thm}(s)\mathbf{F}_{\rm thm}(t)^T\right\rangle = 2k_BT\Upsilon\,\delta(t-s)$$
$$\left\langle \mathbf{f}_{\rm thm}(s)\mathbf{F}_{\rm thm}(t)^T\right\rangle = -2k_BT\Lambda\Upsilon\,\delta(t-s).$$

Coupling by Immersed Boundary Method

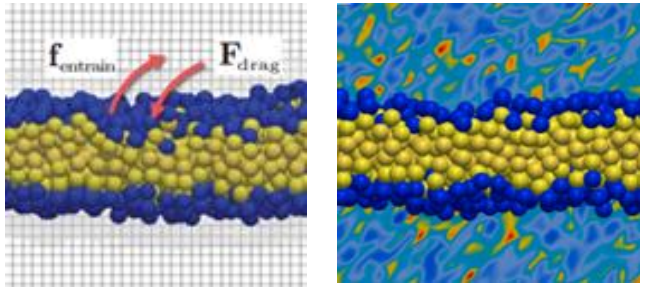
$$\Gamma\mathbf{u} = \int_\Omega \eta\left(\mathbf{y}-\mathbf{X}(t)\right)\mathbf{u}(\mathbf{y},t)d\mathbf{y}$$
$$\Lambda\mathbf{F} = \eta\left(\mathbf{x}-\mathbf{X}(t)\right)\mathbf{F}.$$

Atzberger 2007

Stochastic Eulerian-Lagrangian Method



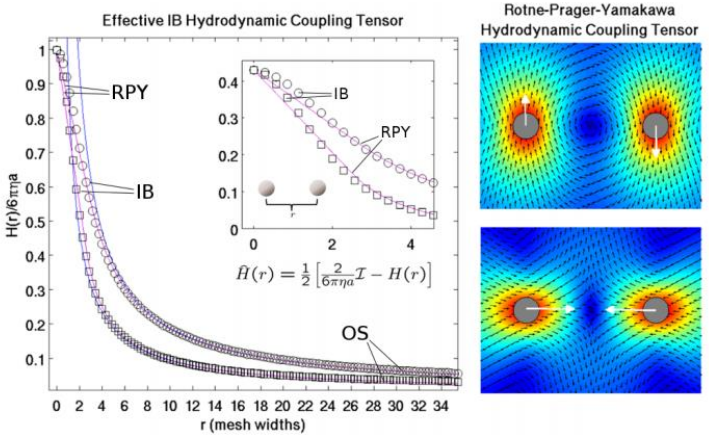
SELM-CG Bilayer Model



Extending Implicit Solvent Models for Kinetics

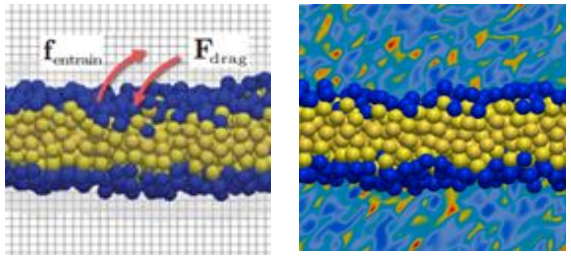
- Solvent treated implicitly (free energy contributions).
- Missing momentum transport through solvent.
- Saffman-Delbruck diffusion shows solvent important!
- We introduce fluctuating hydrodynamics to thermostat system.
- Extends IS-CG models for kinetic studies (SELM-CG).

Hydrodynamic Coupling

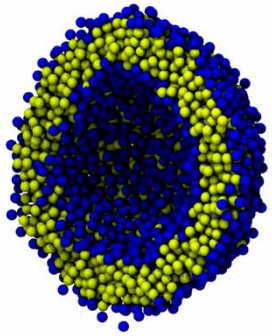


SELM-CG Bilayer Model

SELM-CG Bilayer Model

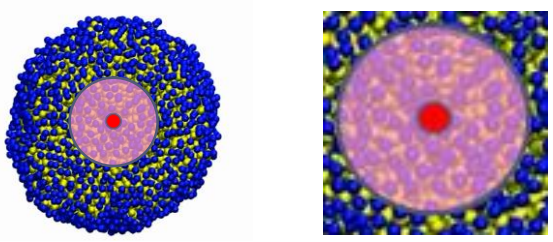


Lipid Vesicles

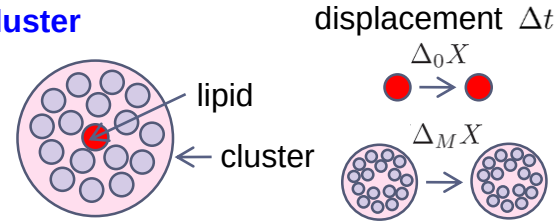


Correlation Analysis

Lipid Vesicle



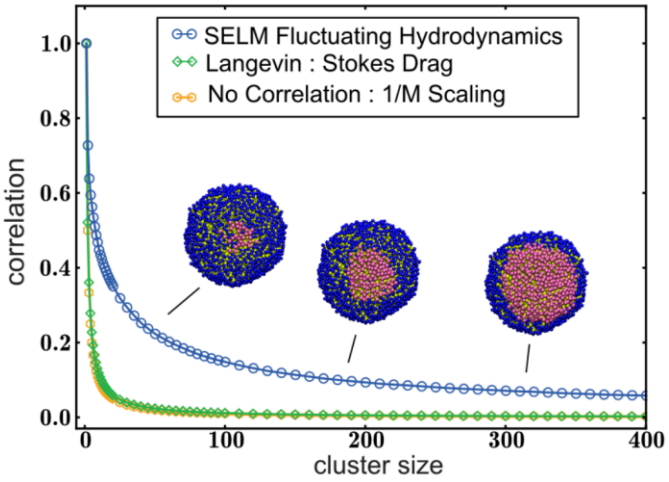
Cluster



Cluster Correlation: Dynamics

$$c_M = \langle \Delta_0 X \Delta_M X \rangle \,/\, \langle \Delta_0 X^2 \rangle$$

Results: SELM vs Langevin Stokes



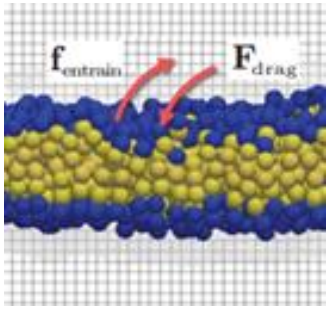
Lipid Dynamics within Vesicle Bilayers

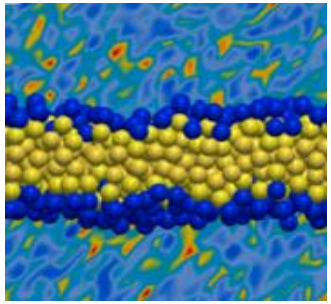
- Saffman-Delbruck diffusion shows solvent is important!
- Lipid motions correlated through direct contacts and solvent flow.
- Langevin dynamics models momentum transfer as local.
- Lipid dynamics: consider correlations within a cluster.
- SELM-CG vs Langevin dynamics (Stokes drag).
- Langevin drag suppresses lateral correlations.
- SELM exhibits long-range correlations.

Atzberger 2013

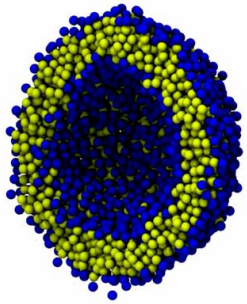
SELM-CG Bilayer Model

SELM-CG Bilayer Model



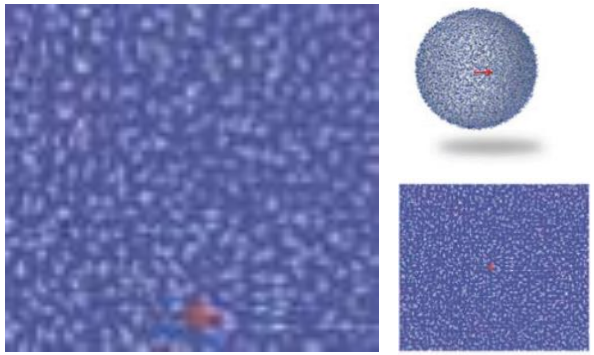


Lipid Vesicles



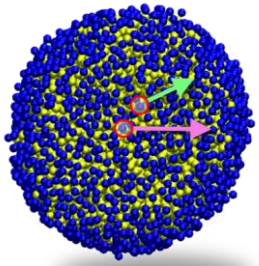
Results

Langevin:Stokes Drag

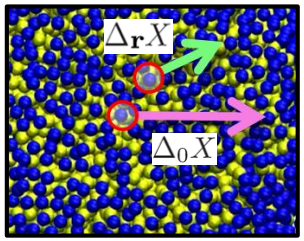


Correlation Analysis

Two-point correlation

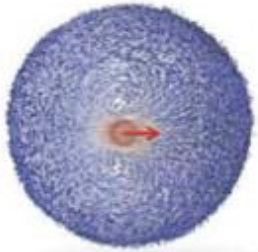


Displacement Δt

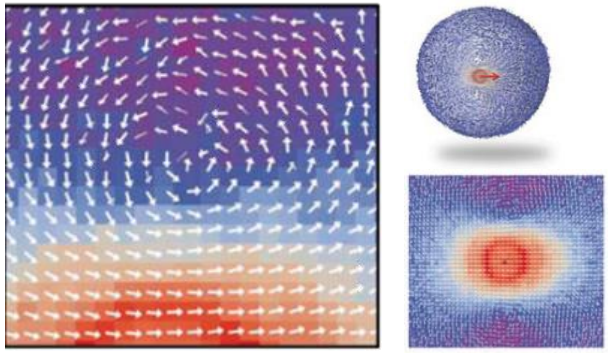


$$\Psi(\mathbf{r}) = \langle \Delta_{\mathbf{r}} X \Delta_0 X^T \rangle$$

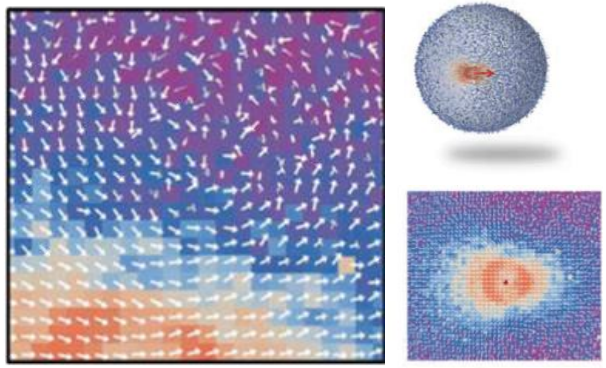
Spatial Correlation



SELM: Fluctuating Hydrodynamics



Langevin: Small Drag

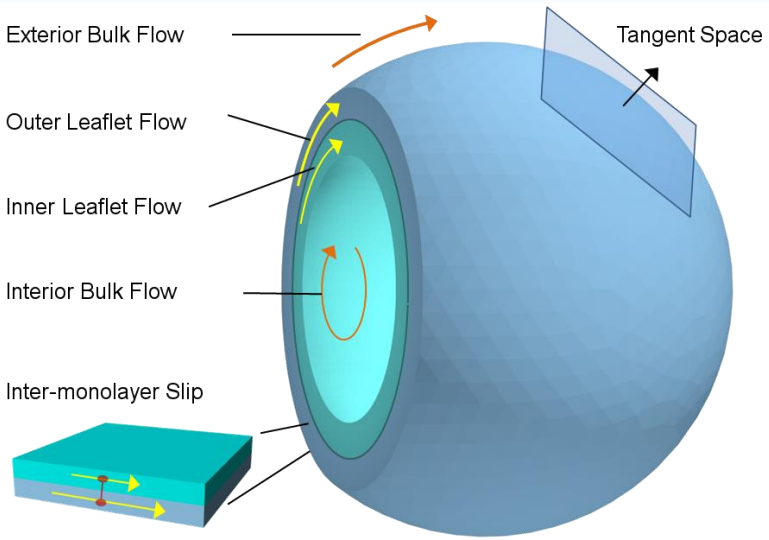


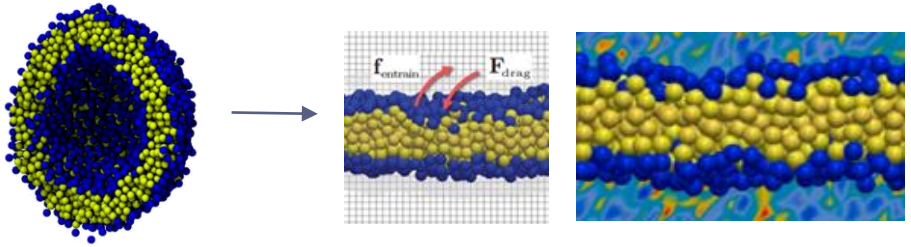
Lipid Dynamics within Vesicle Bilayers

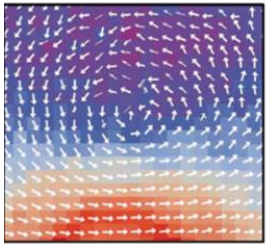
- Spatial analysis of lipid motions (passive fluctuations).
- Two point correlations (linear response to point force).
- SELM vs Langevin Dynamics.

Atzberger 2013

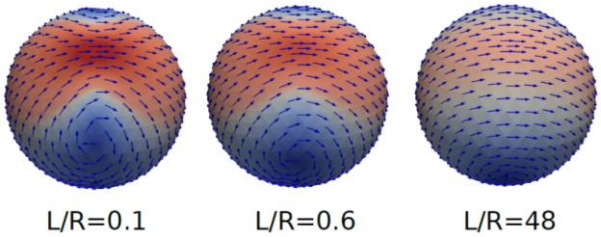
Hydrodynamics of Spherical Vesicles







Two-point correlation



L: Saffman-Delbruck length $L_{SD} = \mu_m/2\mu_f$

Hydrodynamics Covariant Formulation

Fluid Equations (Stokes Flow)

$$\begin{cases} \mu_m\left(-\boldsymbol{\delta}\mathbf{d}\mathbf{v}^\flat + 2K\mathbf{v}^\flat\right) - \mathbf{d}p + \mathbf{b}^\flat &= 0 \\ -\boldsymbol{\delta}\mathbf{v}^\flat &= 0. \end{cases}$$

Lipid Bilayer Membrane Hydrodynamics

$$\begin{cases} \mu_m\left[-\boldsymbol{\delta}\mathbf{d}\mathbf{v}_+^\flat + 2K_+\mathbf{v}_+^\flat\right] + \mathbf{t}_+^\flat - \gamma\left(\mathbf{v}_+^\flat - \mathbf{v}_-^\flat\right) \\ \quad = \mathbf{d}p_+ - \mathbf{b}_+^\flat = -\mathbf{c}_+^\flat, & \mathbf{x}\in\Gamma_+ \\ \boldsymbol{\delta}\mathbf{v}_+^\flat = 0, & \mathbf{x}\in\Gamma_+, \\ \\ \mu_m\left[-\boldsymbol{\delta}\mathbf{d}\mathbf{v}_-^\flat + 2K_-\mathbf{v}_-^\flat\right] + \mathbf{t}_-^\flat - \gamma\left(\mathbf{v}_-^\flat - \mathbf{v}_+^\flat\right) \\ \quad = \mathbf{d}p_- - \mathbf{b}_-^\flat = -\mathbf{c}_-^\flat, & \mathbf{x}\in\Gamma_- \\ \boldsymbol{\delta}\mathbf{v}_-^\flat = 0, & \mathbf{x}\in\Gamma_-. \end{cases}$$

Responses (spherical harmonics)

$$\mathbf{v}_\pm^\flat = -\star\,\mathbf{d}\sum_s a_s^\pm \Phi_s$$

$$\begin{bmatrix} a_s^+ \\ a_s^- \end{bmatrix} = \mathcal{A}_s^{-1}\begin{bmatrix} -c_s^+ \\ -c_s^- \end{bmatrix}$$

$$\mathcal{A}_s = \begin{bmatrix} A_1^\ell - \gamma & \gamma \\ \gamma & A_2^\ell - \gamma \end{bmatrix}$$

$$A_1^\ell = \frac{\mu_m}{R_+^2}\left(2 - \ell(\ell+1) - \frac{R_+}{L^+}(\ell+1)\right)$$

$$A_2^\ell = \frac{\mu_m}{R_-^2}\left(2 - \ell(\ell+1) - \frac{R_-}{L^-}(\ell-1)\right)$$

Exterior Calculus

$$g^{ac}g^{bd}v_{c|d|b} = (\Delta^R\mathbf{v})^a + Kv^a$$

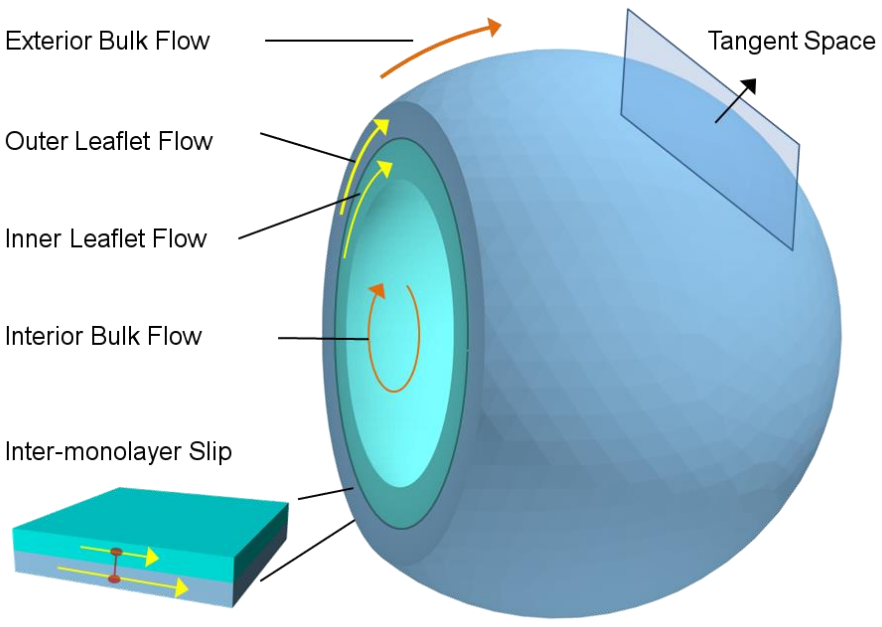
$$\begin{aligned} g^{ac}g^{bd}v_{d|c|b} &= \text{grad}\,(\text{div}\,(\mathbf{v})) + Kv^a \\ &= Kv^a. \end{aligned}$$

$$\begin{aligned} \text{grad}(f) &= [\mathbf{d}f]^\sharp \\ \text{div}(\mathbf{F}) &= -(\star\mathbf{d}\star\mathbf{F}^\flat) = -\boldsymbol{\delta}\mathbf{F}^\flat \\ \text{curl}(\mathbf{F}) &= \left[\star(\mathbf{d}\mathbf{F}^\flat)\right]^\sharp. \end{aligned}$$

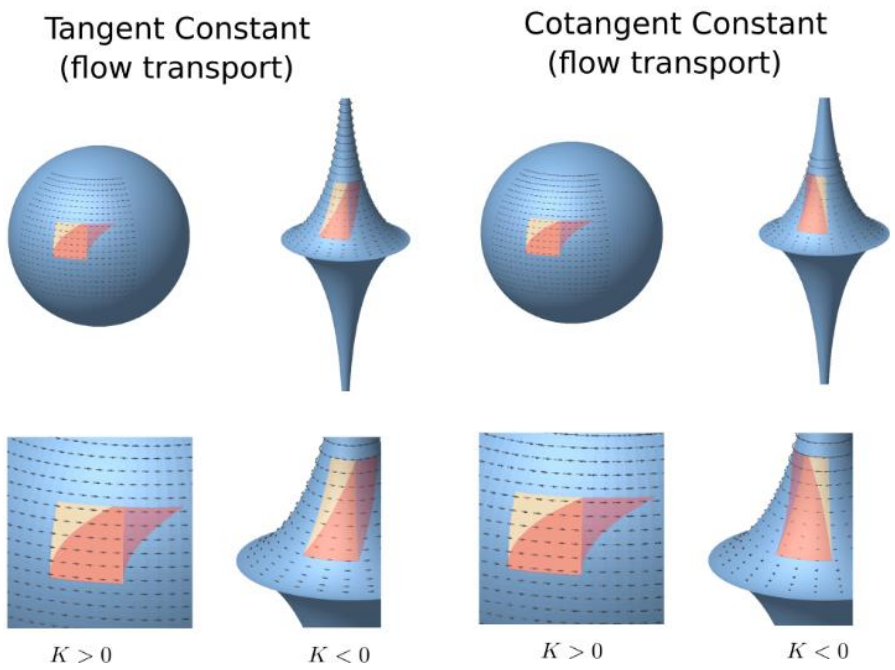
$$\Delta^R f = -(\star\mathbf{d}\star)\mathbf{d}f = -\boldsymbol{\delta}\mathbf{d}f.$$

$$\text{div}(\mathbf{D}) = -\boldsymbol{\delta}\mathbf{d}\mathbf{v}^\flat + 2K\mathbf{v}^\flat$$

Hydrodynamics of Spherical Vesicles



Flow on Sphere and Pseudosphere



Hydrodynamics on Surfaces : Curvature Induced Shear

- Curvature plays role in Newtonian stresses on surface.
- Intrinsic curvature → Gaussian curvature appears.
- Shear induced even by “constant” velocity fields!
- Two types of “constant” fields of interest on surface
  - tangent vector is constant (covariant deriv. zero).
  - co-tangent vector is constant (exterior deriv. zero).

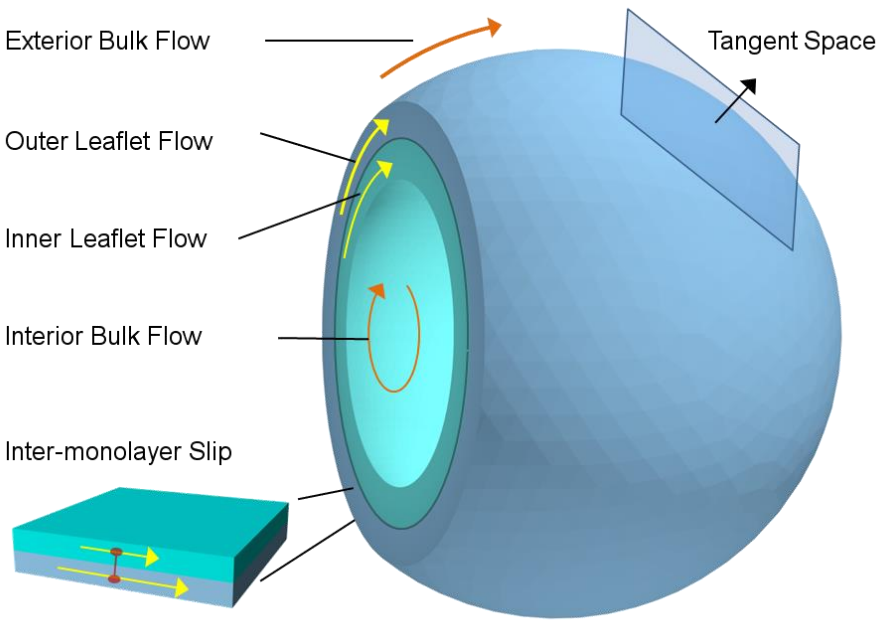
Stokes Flow

$$\begin{cases} \mu_m \left(-\boldsymbol{\delta} \mathbf{d} \mathbf{v}^\flat + 2K \mathbf{v}^\flat\right) - \mathbf{d}p + \mathbf{b}^\flat &= 0 \\ -\boldsymbol{\delta} \mathbf{v}^\flat &= 0. \end{cases}$$

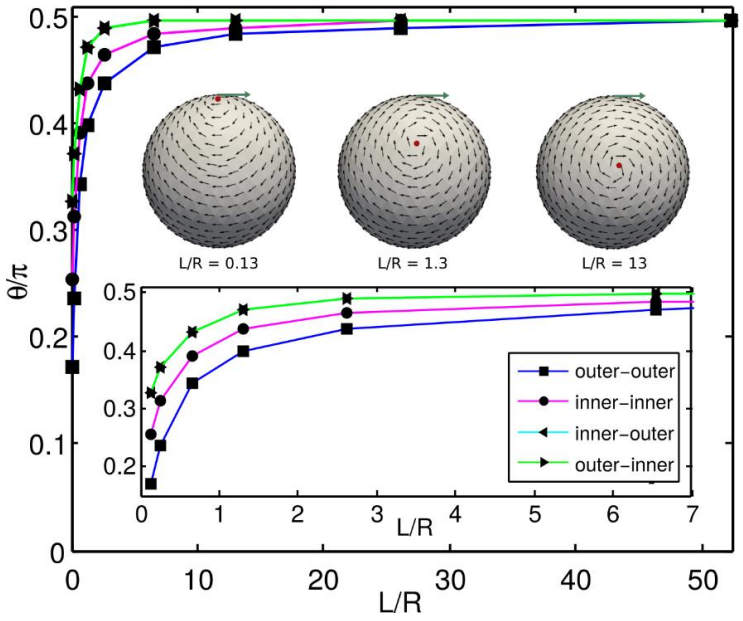
Lipid Bilayer Membrane Hydrodynamics

$$\begin{cases} \mu_m \left[-\boldsymbol{\delta} \mathbf{d} \mathbf{v}_+^\flat + 2K_+ \mathbf{v}_+^\flat\right] + \mathbf{t}_+^\flat - \gamma \left(\mathbf{v}_+^\flat - \mathbf{v}_-^\flat\right) \\ \quad = \mathbf{d}p_+ - \mathbf{b}_+^\flat = -\mathbf{c}_+^\flat, \quad \mathbf{x} \in \Gamma_+ \\ \boldsymbol{\delta} \mathbf{v}_+^\flat = 0, \qquad\qquad\qquad \mathbf{x} \in \Gamma_+, \\ \\ \mu_m \left[-\boldsymbol{\delta} \mathbf{d} \mathbf{v}_-^\flat + 2K_- \mathbf{v}_-^\flat\right] + \mathbf{t}_-^\flat - \gamma \left(\mathbf{v}_-^\flat - \mathbf{v}_+^\flat\right) \\ \quad = \mathbf{d}p_- - \mathbf{b}_-^\flat = -\mathbf{c}_-^\flat, \quad \mathbf{x} \in \Gamma_- \\ \boldsymbol{\delta} \mathbf{v}_-^\flat = 0, \qquad\qquad\qquad \mathbf{x} \in \Gamma_-. \end{cases}$$

Hydrodynamics of Spherical Vesicles



Viscosity and Vortex Position



Hydrodynamics on Surfaces : Viscosity and Vortices

- Spherical topology requires in-plane flow to have vortex.
- Consider flow induced by point force at north-pole.
- Membrane viscosity closely related to the steady-state vortex location.
- Inner and outer vortex locations are offset when there is inter-monolayer slip.

Stokes Flow

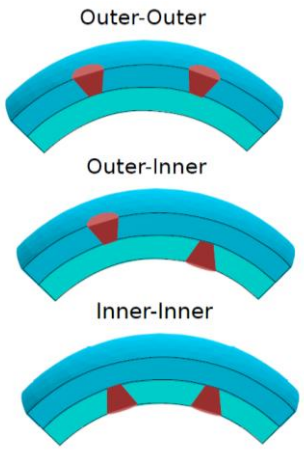
$$\begin{cases} \mu_m\left(-\boldsymbol{\delta}\mathbf{d}\mathbf{v}^\flat + 2K\mathbf{v}^\flat\right) - \mathbf{d}p + \mathbf{b}^\flat &= 0 \\ -\boldsymbol{\delta}\mathbf{v}^\flat &= 0. \end{cases}$$

Lipid Bilayer Membrane Hydrodynamics

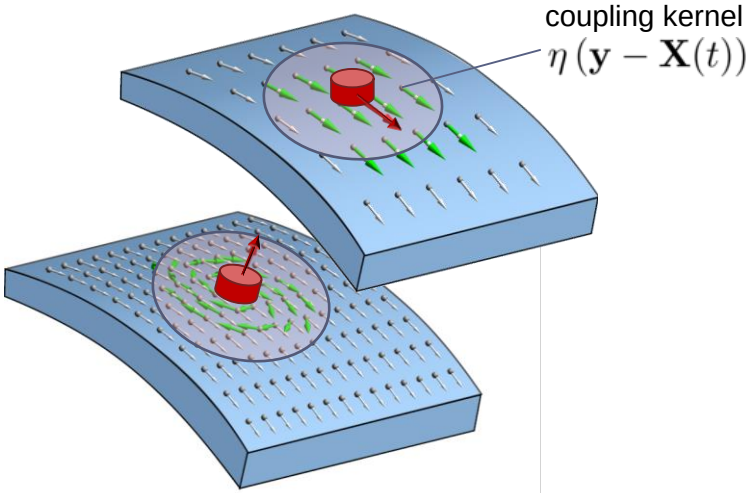
$$\begin{cases} \mu_m\left[-\boldsymbol{\delta}\mathbf{d}\mathbf{v}_+^\flat + 2K_+\mathbf{v}_+^\flat\right] + \mathbf{t}_+^\flat - \gamma\left(\mathbf{v}_+^\flat - \mathbf{v}_-^\flat\right) \\ \quad = \mathbf{d}p_+ - \mathbf{b}_+^\flat = -\mathbf{c}_+^\flat, & \mathbf{x}\in\Gamma_+ \\ \boldsymbol{\delta}\mathbf{v}_+^\flat = 0, & \mathbf{x}\in\Gamma_+, \\ \\ \mu_m\left[-\boldsymbol{\delta}\mathbf{d}\mathbf{v}_-^\flat + 2K_-\mathbf{v}_-^\flat\right] + \mathbf{t}_-^\flat - \gamma\left(\mathbf{v}_-^\flat - \mathbf{v}_+^\flat\right) \\ \quad = \mathbf{d}p_- - \mathbf{b}_-^\flat = -\mathbf{c}_-^\flat, & \mathbf{x}\in\Gamma_- \\ \boldsymbol{\delta}\mathbf{v}_-^\flat = 0, & \mathbf{x}\in\Gamma_-. \end{cases}$$

Mobility of Protein Inclusions within Surface

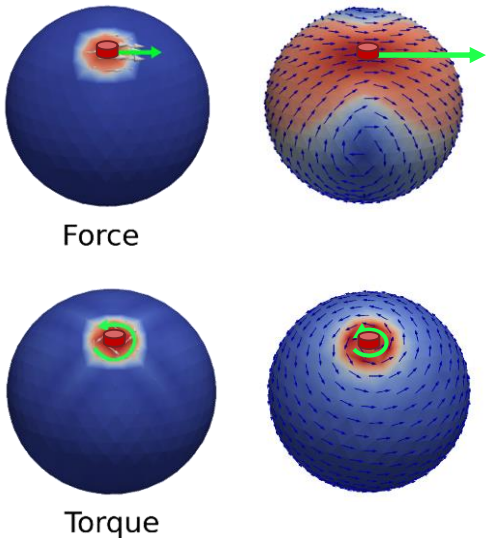
Protein Inclusion in Leaflet



Immersed Boundary Coupling



Mobility Response (Force / Torque)



Mobility of Inclusions

- Protein-Lipid Coupling → Immersed Boundary Coupling (manifold operators)
- Proteins embedded within inner or outer leaflet of bilayer.
- Mobility tensor between particle i and particle j

$$M_{ij} = \Gamma_i \mathcal{S} \Lambda_j$$

$$\Gamma \mathbf{u} = \int_\Omega \eta(\mathbf{y}-\mathbf{X}(t))\,\mathbf{u}(\mathbf{y},t)d\mathbf{y}$$

$$\Lambda \mathbf{F} = \eta(\mathbf{x}-\mathbf{X}(t))\,\mathbf{F}.$$

solution flow $\mathcal{S}$

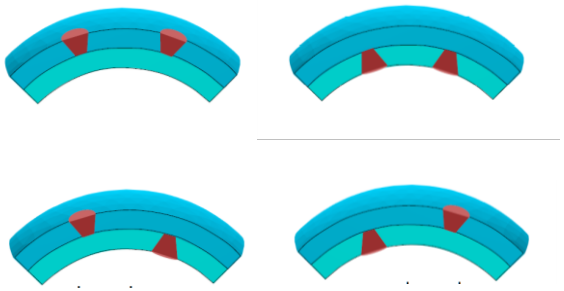
- Adjoint condition $\Gamma^T = \Lambda$
- Translational and rotational mobilities.

Lipid Bilayer Hydrodynamics

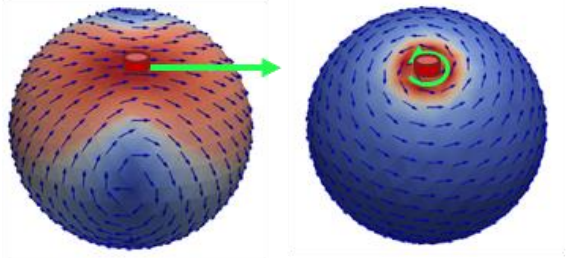
$$\begin{cases} \mu_m\left[-\delta_d \mathbf{v}_+^\flat + 2K_+\mathbf{v}_+^\flat\right] + \mathbf{t}_+^\flat - \gamma\left(\mathbf{v}_+^\flat - \mathbf{v}_-^\flat\right) \\ \quad = \mathbf{d}p_+ - \mathbf{b}_+^\flat = -\mathbf{c}_+^\flat, & \mathbf{x}\in\Gamma_+ \\ \delta_d \mathbf{v}_+^\flat = 0, & \mathbf{x}\in\Gamma_+, \\ \\ \mu_m\left[-\delta_d \mathbf{v}_-^\flat + 2K_-\mathbf{v}_-^\flat\right] + \mathbf{t}_-^\flat - \gamma\left(\mathbf{v}_-^\flat - \mathbf{v}_+^\flat\right) \\ \quad = \mathbf{d}p_- - \mathbf{b}_-^\flat = -\mathbf{c}_-^\flat, & \mathbf{x}\in\Gamma_- \\ \delta_d \mathbf{v}_-^\flat = 0, & \mathbf{x}\in\Gamma_-. \end{cases}$$

Hydrodynamic Flow within Bilayer

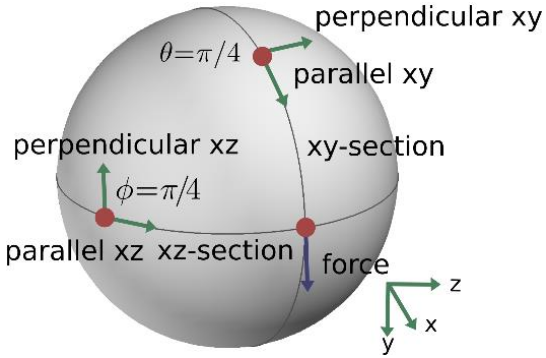
Leaflet Cases (Inner/Outer)



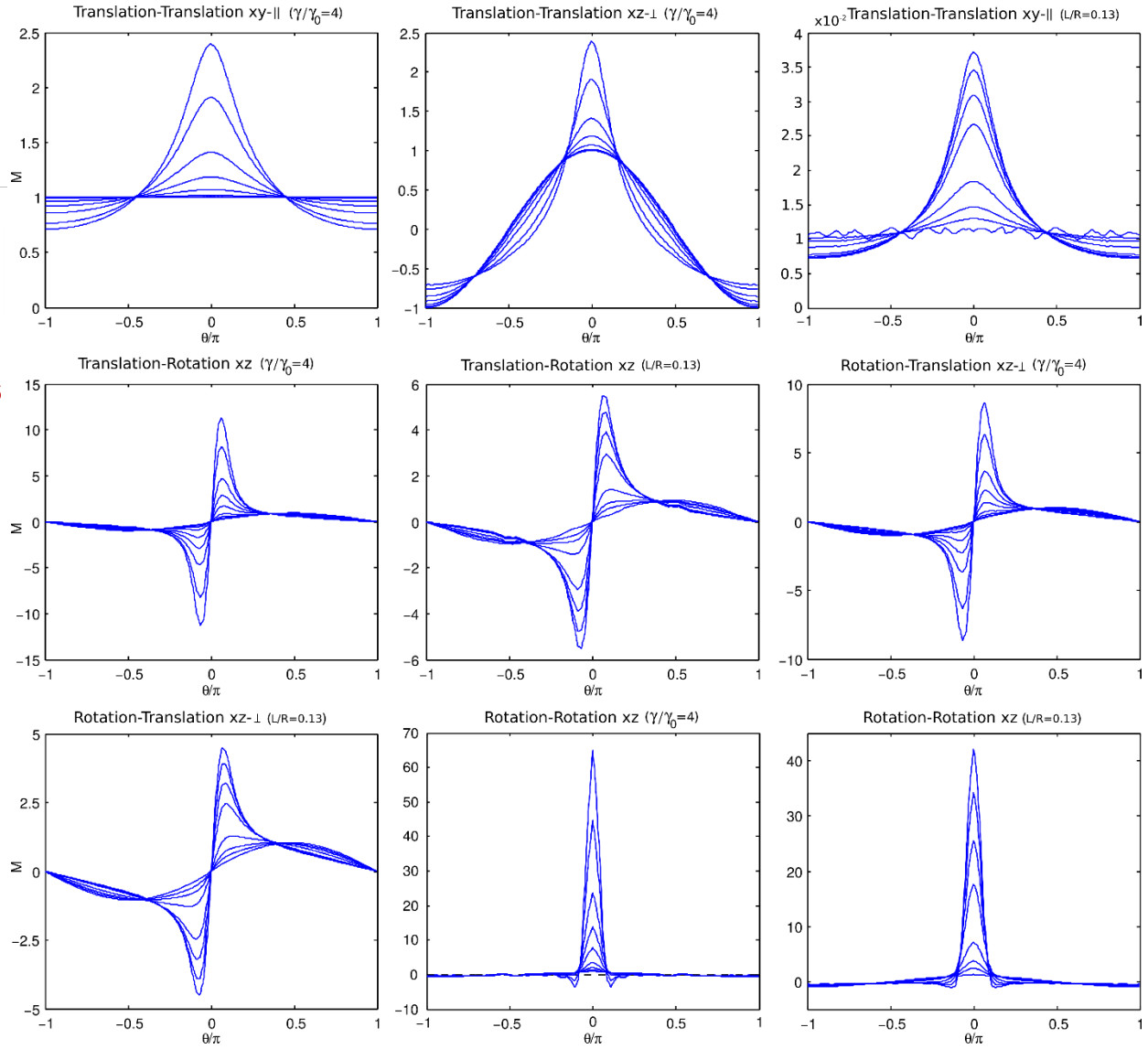
Translation and Rotation Cases



Mobility Cross-Sections



Mobility vs Position : (viscosity or slip varied)



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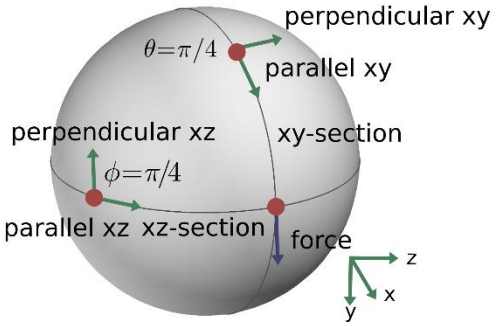
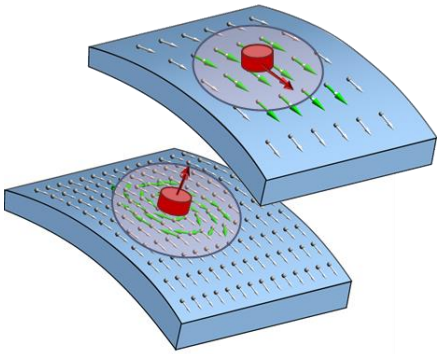
Mobility vs Membrane Viscosity

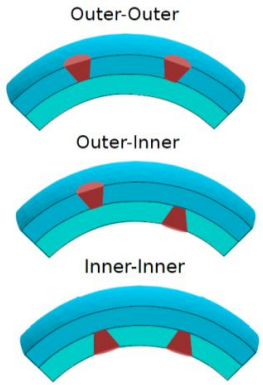
Mobility Cross-Sections



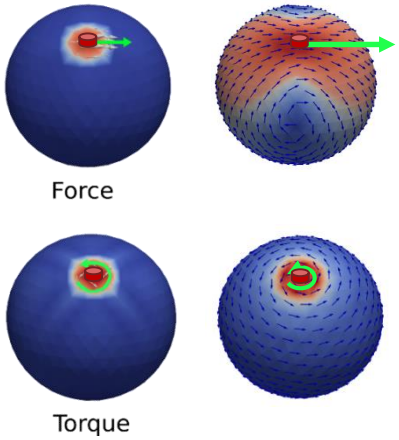
IB-Coupling



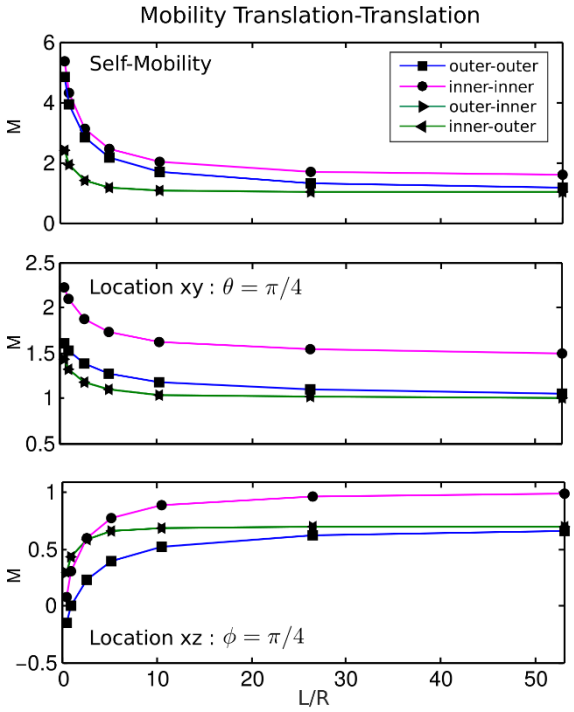
Leaflet Cases

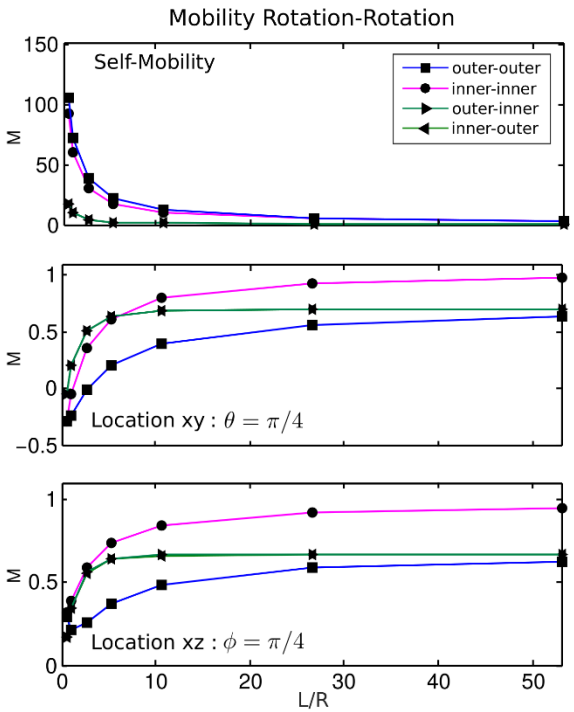


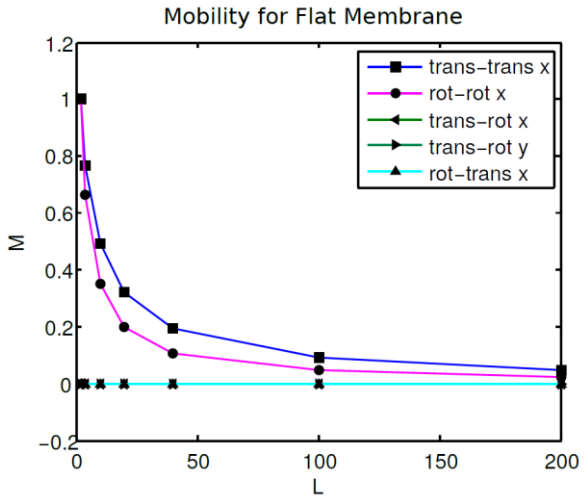
Response to Force/Torque



Mobility : (viscosity varied)

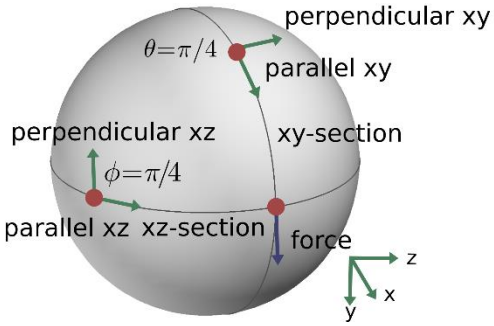




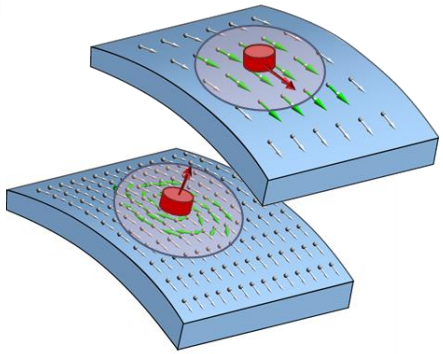


Mobility vs Intermonolayer Slip

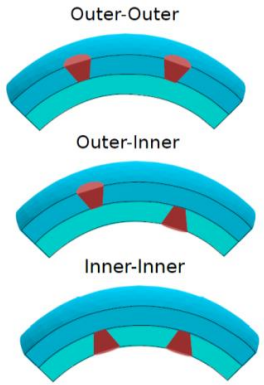
Mobility Cross-Sections



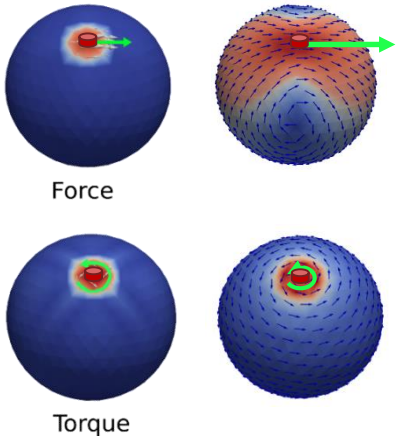
IB-Coupling



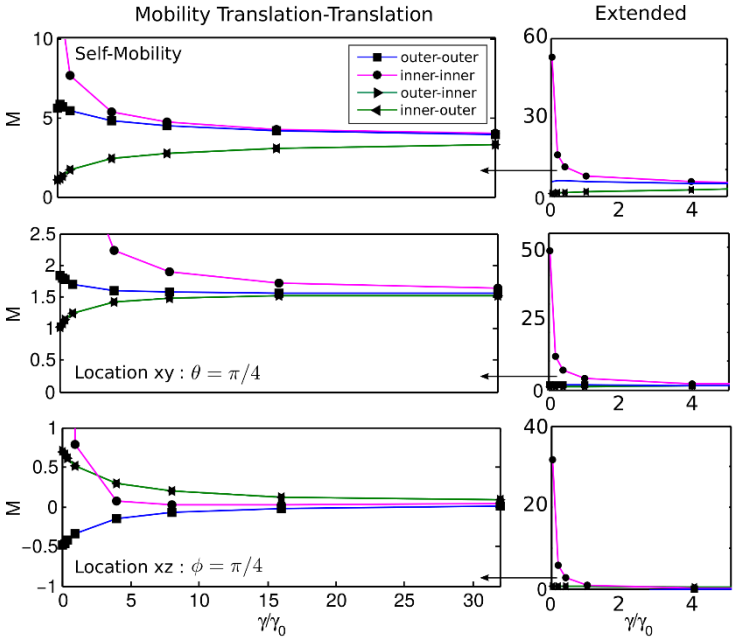
Leaflet Cases

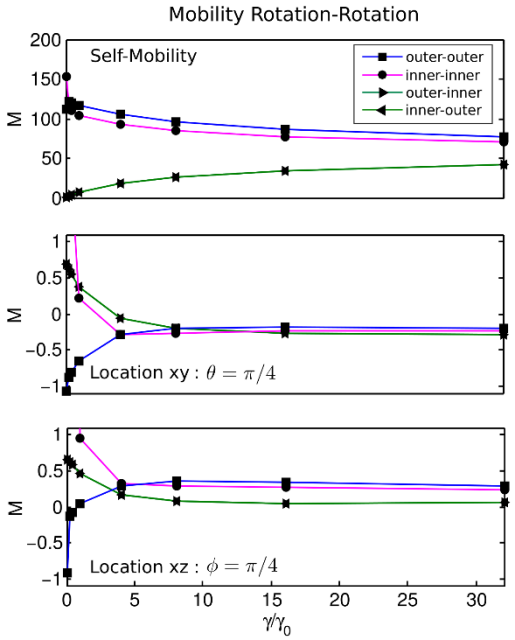


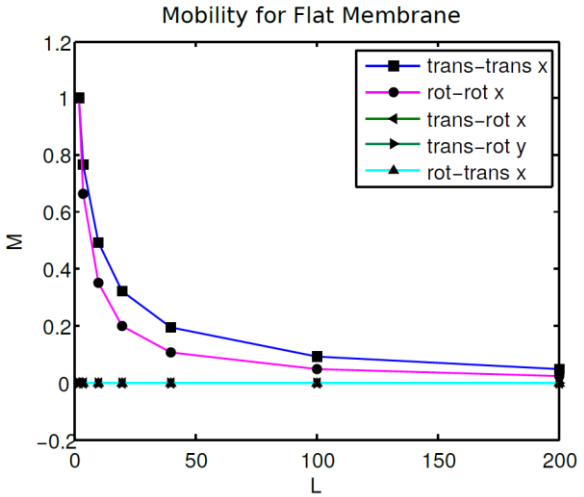
Response to Force/Torque



Mobility : (intermonolayer slip varied)







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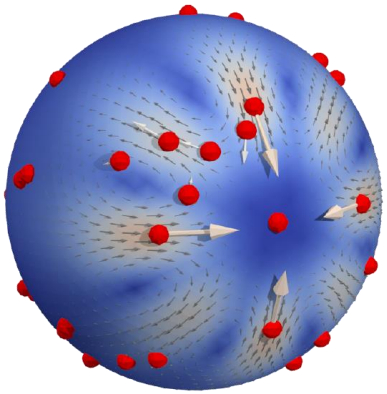
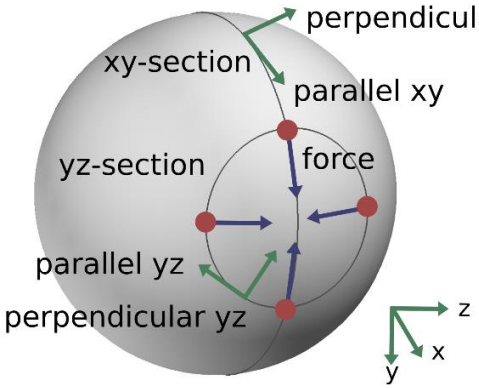
Many Particle Interactions

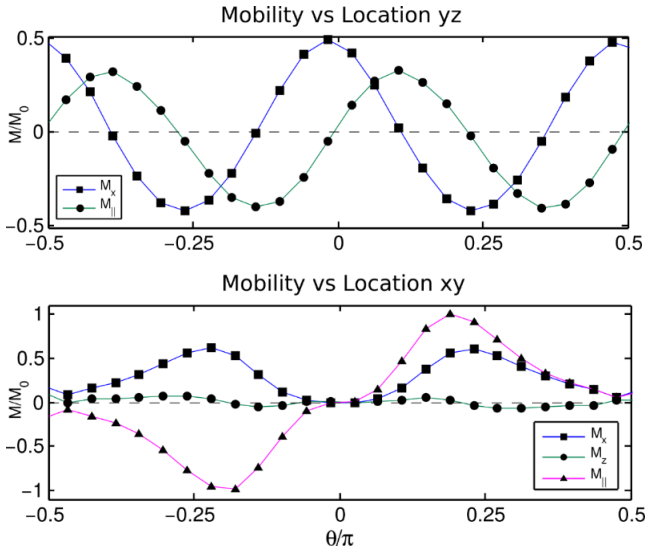
Many Particle Systems



Mobility Cross-Section



Mobility vs Position



Multiple-particle Dynamics within Vesicles

$$\frac{d\mathbf{X}}{dt} = \mathbf{M}\mathbf{F} + k_B T \nabla \cdot \mathbf{M} + \mathbf{F}_{thm}$$

$$\langle \mathbf{F}_{thm}(s)\mathbf{F}_{thm}(t)^T \rangle = 2k_B T \mathbf{M}\delta(t-s).$$

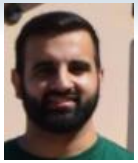
$\mathbf{M}$
solution flow

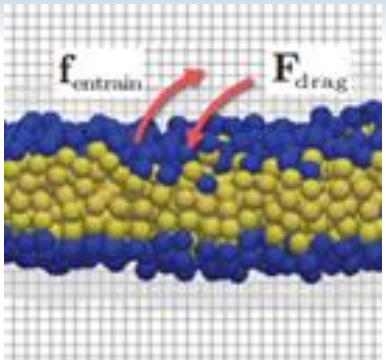
Lipid Bilayer Hydrodynamics

$$\begin{cases} \mu_m\left[-\boldsymbol{\delta}\mathbf{d}\mathbf{v}_+^\flat + 2K_+\mathbf{v}_+^\flat\right] + \mathbf{t}_+^\flat - \gamma\left(\mathbf{v}_+^\flat - \mathbf{v}_-^\flat\right) \\ \quad = \mathbf{d}p_+ - \mathbf{b}_+^\flat = -\mathbf{c}_+^\flat, & \mathbf{x} \in \Gamma_+ \\ \boldsymbol{\delta}\mathbf{v}_+^\flat = 0, & \mathbf{x} \in \Gamma_+, \\ \\ \mu_m\left[-\boldsymbol{\delta}\mathbf{d}\mathbf{v}_-^\flat + 2K_-\mathbf{v}_-^\flat\right] + \mathbf{t}_-^\flat - \gamma\left(\mathbf{v}_-^\flat - \mathbf{v}_+^\flat\right) \\ \quad = \mathbf{d}p_- - \mathbf{b}_-^\flat = -\mathbf{c}_-^\flat, & \mathbf{x} \in \Gamma_- \\ \boldsymbol{\delta}\mathbf{v}_-^\flat = 0, & \mathbf{x} \in \Gamma_-. \end{cases}$$

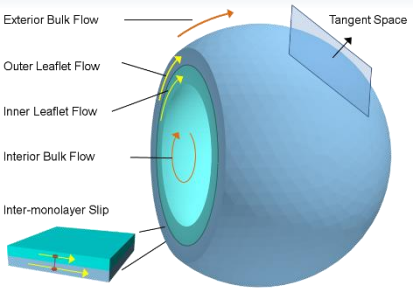
- Mobility obtained from solving bilayer hydrodynamic equations.
- Illustration : attracting cluster of particles on spherical surface.
- Finite domain size + incompressibility requires re-circulation of fluid.
- Rich dynamics on spherical surface from finite domain size + topology (vortex for any tangential flow, packing restrictions).
- Protein assembly, collective kinetics, etc…

Conclusions

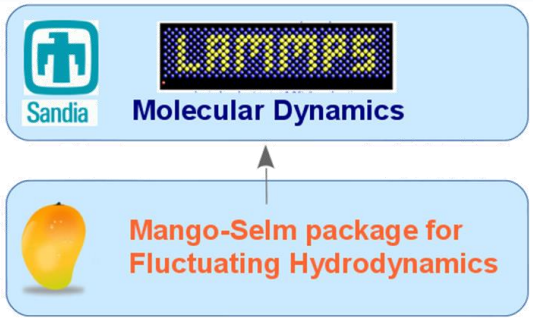





Coarse-Grained Lipid Models
Fluctuating Hydrodynamics Approaches



Continuum Mechanics of Bilayer Membranes
Fluctuating Hydrodynamics Approaches



http://mango-selm.org/

Summary

- Stochastic Eulerian Lagrangian Method (SELM) for fluctuating hydrodynamic descriptions of mesoscale systems.
- SELM incorporates into traditional hydrodynamic and CFD approaches the role of thermal fluctuations.
- Developed both coarse-grained and continuum approaches for lipid bilayer membranes.
- Many other applications: polymeric fluids, colloidal systems, electrokinetics, microfluidics.
- Open source package in LAMMPS MD for SELM simulations: http://mango-selm.org/

Recent Students / Post-docs

- J. K. Sigurdsson
- B. Gross
- G. Tabak
- P. Plunkett
- Y. Wang
- K. Sikorski
- Inderbir Sidhu

Funding

- NSF CAREER
- DOE CM4
- Keck Foundation

more information: http://atzberger.org/

Publications

Hydrodynamic Coupling of Particle Inclusions Embedded in Curved Lipid Bilayer Membranes, J.K. Sigurdsson and P.J. Atzberger, (submitted), (2016) http://arxiv.org/abs/1601.06461

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