Quasi-two-dimensional diffusion of interacting protein monomers and dimers: a MPC simulation study

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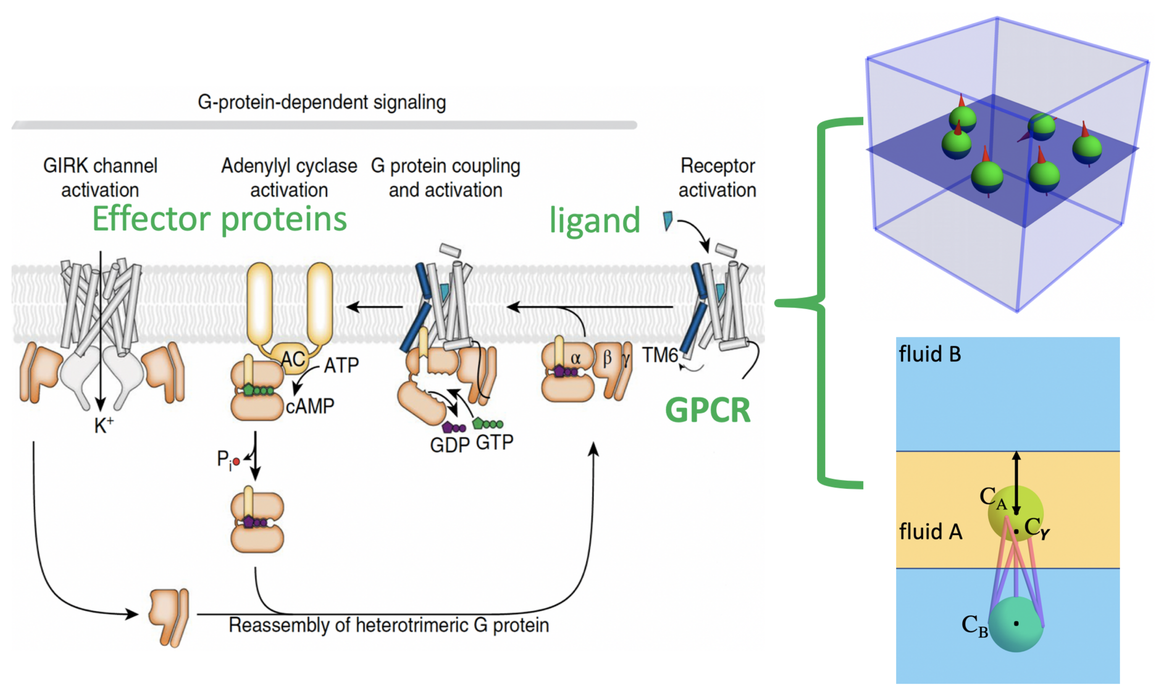
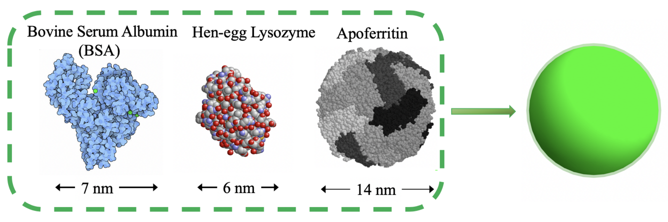
Abstract: Modeling lateral diffusion of proteins at a membrane

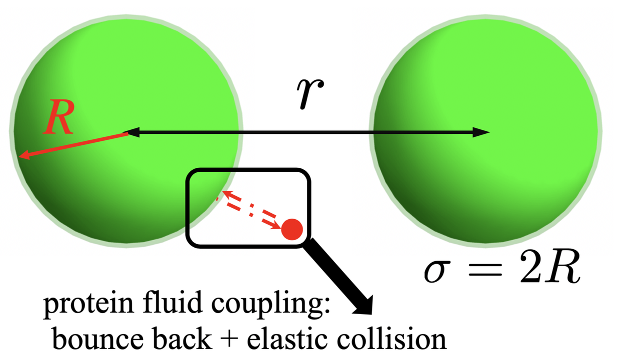
- **Diffusion of proteins along a membrane:** e.g., in postsynaptic signal transduction where specific proteins diffuse along a postsynaptic membrane, triggering a cascade of biochemical processes.
- **Minimalistic model:** Interacting Brownian particles embedded in a three-dimensional (3D) Newtonian bulk fluid but confined to a planar monolayer.
  - Onset of large-scale collective diffusion under quasi-two-dimensional (Q2D) confinement
  - Hydrodynamic retardation effects in concentrated Q2D protein solutions.
- **More detailed model:** Non-spherical proteins diffusing at a fluid-fluid interface.
  - Effects of membrane-cytosol viscosity difference on diffusion of proteins.



1. Globular protein model



Globular proteins $\Longrightarrow$ Brownian spheres



◇ Proteins confined in-plane are interacting by short-range attraction (SA) and long-range electrostatic repulsion (LR):

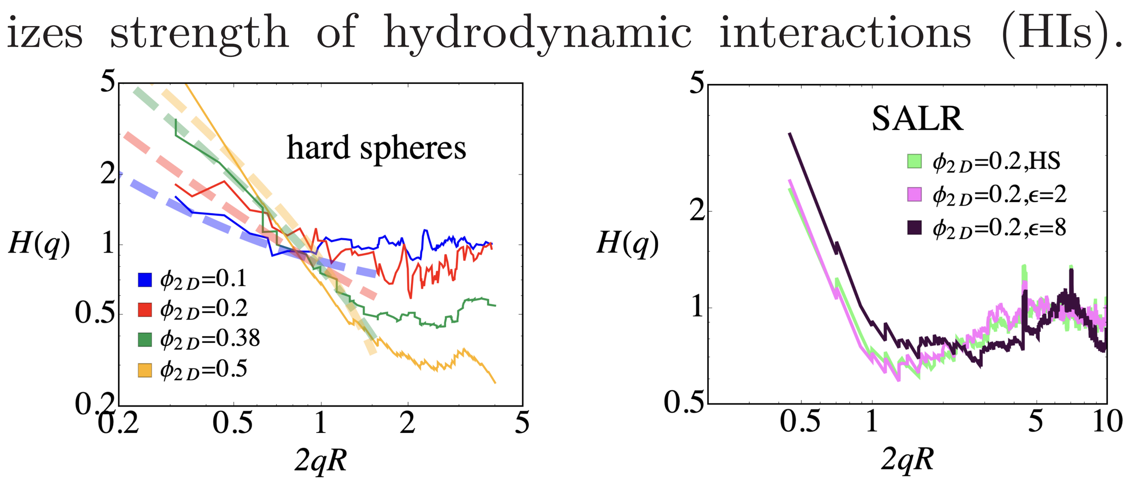
$$\beta U(r) = 4\epsilon\left[\left(\frac{\sigma}{r}\right)^{100} - \left(\frac{\sigma}{r}\right)^{50}\right] + \ell_B Z_{eff}^2 \frac{e^{-r/\lambda}}{r}$$

hardcore + short-range attraction — long-range repulsion

◇ Fluid motion is described by multiparticle collision dynamics (MPC) [1].

2. Anomalous enhancement of H(q)

Hydrodynamic function $H(q)$: Characterizes strength of hydrodynamic interactions (HIs).

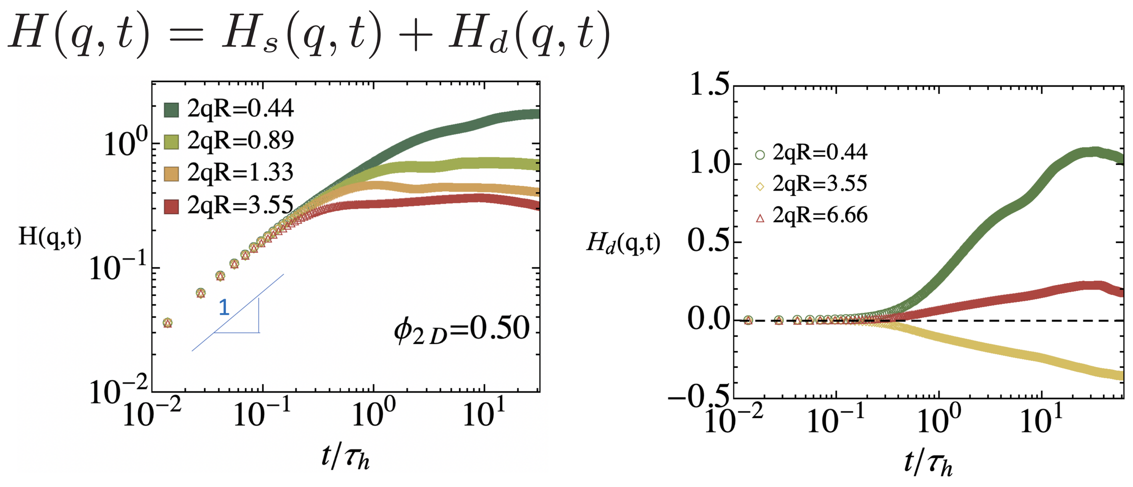


◇ Divergence of $H(q)$ as q^{-1} for $qR \lesssim 1$:

◇ Well captured by theoretical predictions (dashed) for Q2D hard-sphere systems.

◇ SALR system: typical q^{-1} behavior at small q. Stronger attraction gives rise to higher amplitude of $H(q \approx 0)$.

Time-dependent hydrodynamic function:
$H(q,t) = H_s(q,t) + H_d(q,t)$

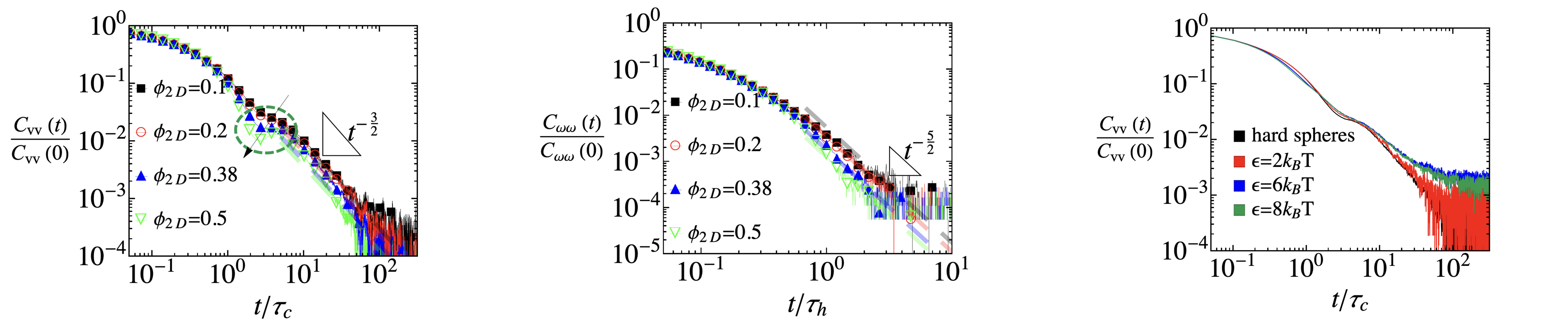


◇ Onset of HIs at $t \sim \tau_h$ (single protein vorticity diffusion time).

◇ $H_d(qR \lesssim 1, t) > 0$: enhancement of HIs. $H_d(1 \lesssim qR \lesssim \pi, t) < 0$, backflow-induced anti-correlations. $H_d(qR \approx \pi, t) > 0$: protein drags along its neighbours.

3. Hydrodynamic retardation in concentrated Q2D protein systems

Vorticity diffusion: Long-time tail in (angular) velocity autocorrelation functions $C_{VV}(t)$ ($C_{\omega\omega}(t)$).



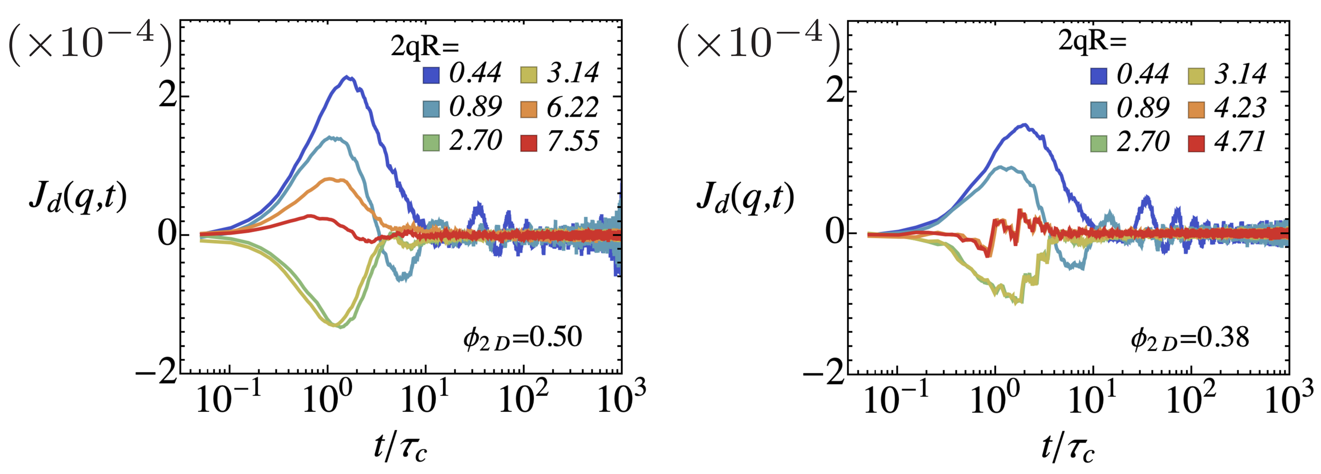
◇ Positive $t^{-3/2}$ ($t^{-5/2}$) long-time tail in (A)VAFs for concentrated Q2D hard-sphere systems at $t > \tau_h$.

◇ Area fraction (ϕ_{2D})-dependence of (A)VAFs is roughly captured using $\eta_{eff} = (1 + 2.5\phi_{2D})\eta$ for single-protein (A)VAF functions (dashed).

◇ Slower long-time decay of Q2D-SALR systems for stronger attraction.

Role of sound propagation: Distinct longitudinal current-current correlation function

$$J_d(q,t) = \frac{1}{Nq^2}\left\langle \sum_{i=1}^{N}\sum_{j=1}^{N} \mathbf{q}\cdot\mathbf{V}_i(t)\mathbf{V}_j(0)\cdot\mathbf{q}\exp\left[i\mathbf{q}\cdot(\mathbf{R}_i - \mathbf{R}_j)\right]\right\rangle$$



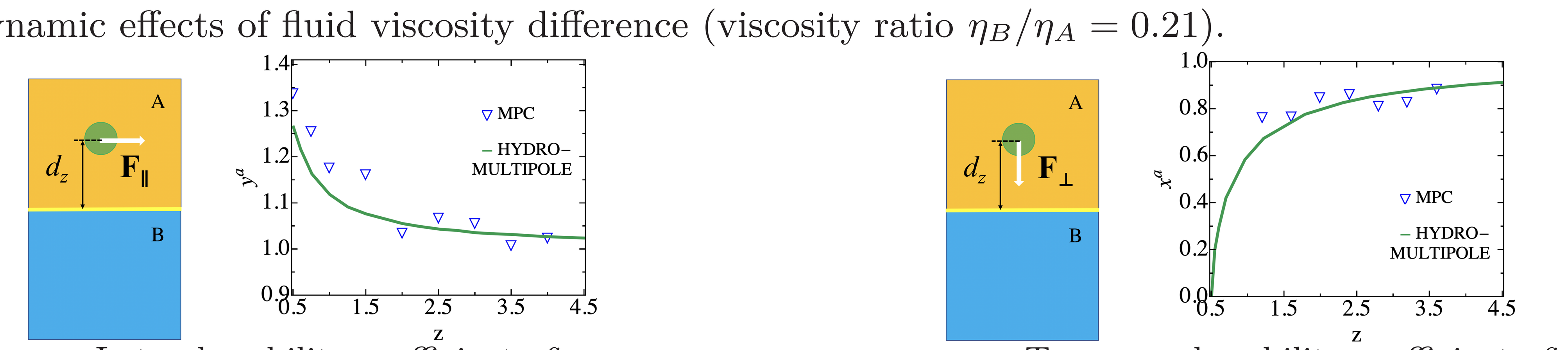
◇ Anti-correlations (dashed ellipse) in VAFs for Q2D hard-sphere systems at larger ϕ_{2D} due to multiple scattering of sound.

◇ Sound damping at small q persists much longer than single-particle sonic time τ_c.

◇ Small, intermediate, and large wavenumber regions are observed consistent with those of $H_d(q,t)$.

4. MPC results for lateral protein diffusion near fluid-fluid interface

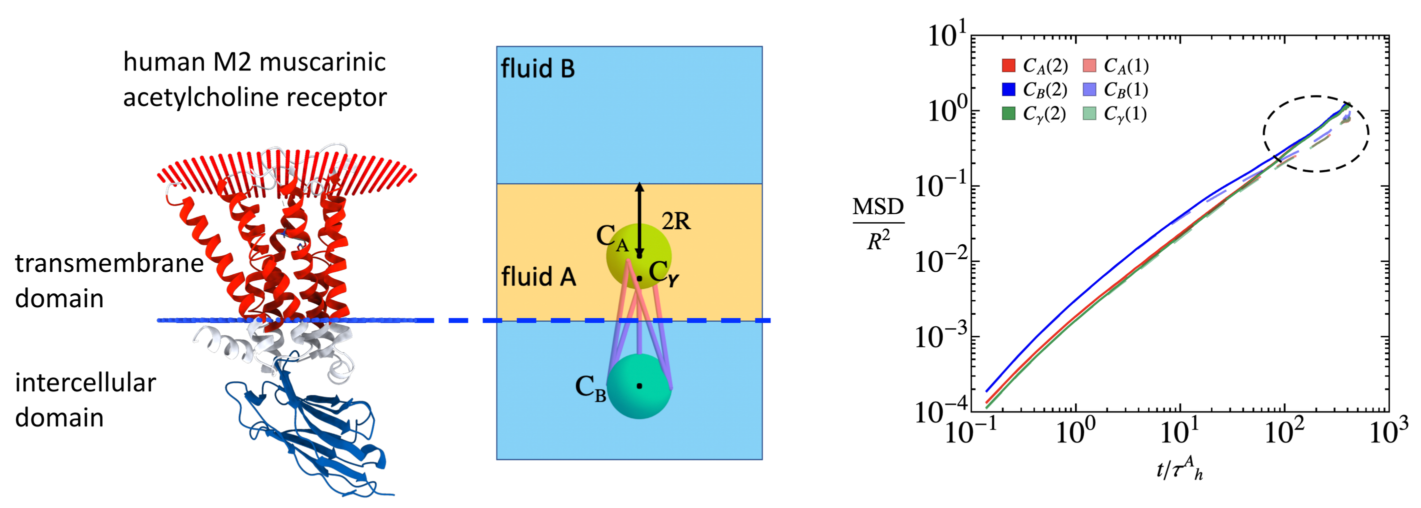
Coarse-grained protein-membrane-cytosol model using MPC
Hydrodynamic effects of fluid viscosity difference (viscosity ratio $\eta_B/\eta_A = 0.21$).



Lateral mobility coefficient y^a — Transversal mobility coefficient x^a

Solid curves are numerical calculations from Ref. [2].

Dumbbell model of a GPCR at fluid-fluid interface ($\eta_B/\eta_A = 0.21$)



◇ Mean-squared displacement (MSD) of bead centers C_A and C_B, and hydrodynamic center of mobility C_γ. C_γ has smallest MSD, for $1 \ll t/t_h^A \ll 10^2$.

◇ For $t \gg t_h^A$: MSD enhanced in presence of two interfaces (solid curves, marked by dashed ellipse).

References & Acknowledgement

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