

CATCH-U-DNA: WP2, UAM group

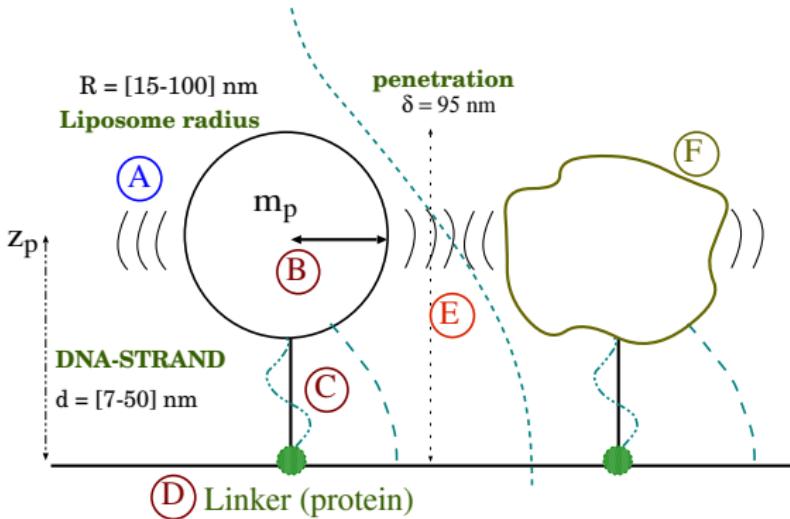
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CATCH-U-DNA Meeting at Brusselless

- M6. Analysis of DNA strands, **molecular** and **coarse grained** simulations
- M20. Molecular dynamics simulations of linker and DNA strands under GHz oscillatory shear flow
- M30. Hydrodynamic codes tp resolve dissipative molecular structures (liposomes) under QCM setup

Objectives



- A: Fluid drag on the liposome
- B: Mass and inertia of the liposome
- C: Stiffness of the anchor (DNA)
- D: Stiffness of the linker in contact with resonator
- E: Hydrodynamics: flow distortion due to liposomes
- F: Liposome flexibility

Analyses

- Ring-down analysis: resolve overdamped wall motion

$$x(t) = X_0 \exp(-\Gamma t) \cos(2\pi f t) \quad (1)$$

$X_0 \sim 2\text{nm}$.

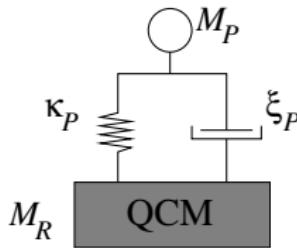
- Impedance analysis: impose oscillatory wall motion

$$\frac{\Delta \tilde{f}}{f_0} = \frac{i}{\pi} \frac{Z_L}{Z_Q} \quad (2)$$

$$\Delta\omega = -\frac{2\pi A}{x_0} \langle x(t) F_{wall}(t) \rangle \quad (3)$$

$$\Delta\Gamma = -\frac{2\pi A}{v_0} \langle v(t) F_{wall}(t) \rangle \quad (4)$$

Theory: QCM simple model



$$\tilde{\omega}_R^2 = \frac{1}{M_R} (\kappa_R + i\omega\xi_R), \quad \tilde{\omega}_P^2 = \frac{1}{M_P} (\kappa_P + i\omega\xi_P),$$

- *Inertial loading* ($\text{Re}(\omega_P) \gg \text{Re}(\omega_R)$)

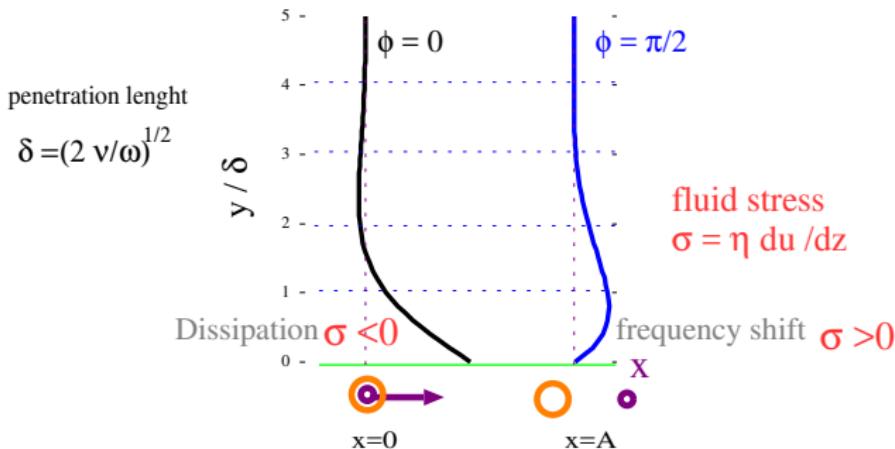
$$\Delta\tilde{\omega} \approx -\frac{\tilde{\omega}_R M_P}{2M_R} < 0.$$

- *Elastic coupling* ($\text{Re}(\omega_P) \ll \text{Re}(\omega_R)$)

$$\Delta\tilde{\omega} \approx \frac{\tilde{\kappa}_P}{2M_R \tilde{\omega}_R} > 0.$$

Theory: QCM in Newtonian fluids

Fluid velocity profiles phase: $\phi = \omega t$



$$m_W \ddot{X} = -\omega_0^2 m_W X + A\eta \left. \frac{\partial u(z, t)}{\partial z} \right|_{z=0}, \quad (\text{wall})$$
$$\rho \frac{\partial u(z, t)}{\partial t} = \eta \frac{\partial^2 u(z, t)}{\partial z^2}, \quad (\text{fluid})$$

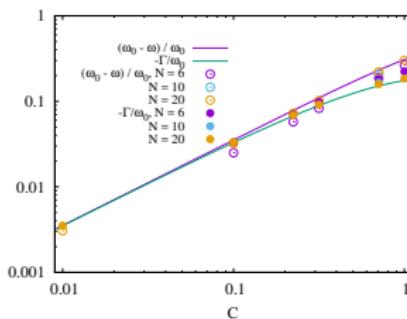
Theory: QCM in Newtonian fluids

$$\frac{\Delta\omega}{\omega_0} = \frac{C}{2^{3/2}} \sim 10^{-5}! \quad (\text{frequency shift})$$

$$\frac{\Delta\Gamma}{\omega_0} = \frac{C}{2^{3/2}} \sim 10^{-5} \quad (\text{dissipation})$$

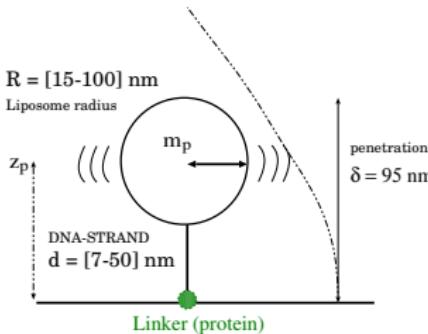
$$C = \sqrt{\frac{\eta\rho}{\omega_0 m_w}} \quad (\text{Inverse number of oscillations to decay})$$

$$C_{\text{exp}} \sim 10^{-4}$$



Deviation: FLUAM-incompressible cannot handle such inertia. We used
FLUAM-compressible

Theory: QCM fluid+ rigid liposome



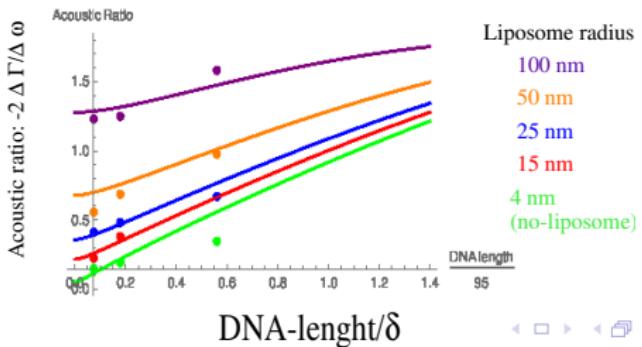
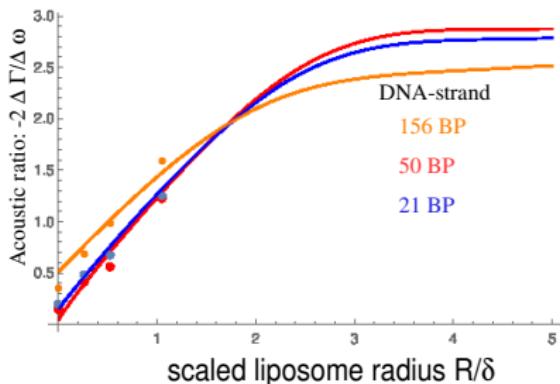
$$m_T \ddot{X} = -m_R \omega_0^2 X + \eta \left. \frac{\partial u(z, t)}{\partial z} \right|_{z=0} + F_{drag}$$

$$F_{drag} = - \left[\gamma \left(1 + \frac{\delta}{R} \right) u + 3\pi R^2 \sqrt{2\eta\rho/\omega} \left(1 + \frac{2R}{\delta} \right) \frac{du}{dt} \right]$$

$$v(0, t) = \frac{dX}{dt} \text{ and } v(\infty, t) = 0$$

Theory: Analytical solution rigidly cleaved liposome

Experimental AR scaled by a factor 3



- **Continuum-particle models**

- **Langevin**: One-way coupling, Langevin dynamics for particles
- **FLUAM**: Fluctuating hydrodynamics + immersed boundary Method
- **LB**: Lattice Boltzmann with bounce-back coupling for particles

- **Particle based models**

- **MD**: All-atom molecular dynamics (GROMACS)
- **CG-MD** Coarse-grained MD (UAMMD)
- **DPD** Dissipative particle dynamics (UAMMD)

Achievements: Methods

Impedance analysis: about 10 times faster calculations

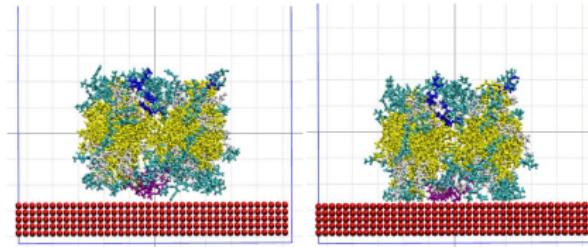
Scheme	Coupling	Aprox.	OK
FLUAM-i	Two-way	Incompressible	✓
FLUAM-c	Two-way	Compressible	✓
MD	Two-way	All-Atom	✓
DPD	Two-way	Coarse-grained	✓

Molecular dynamics of QCM ring-down simulations

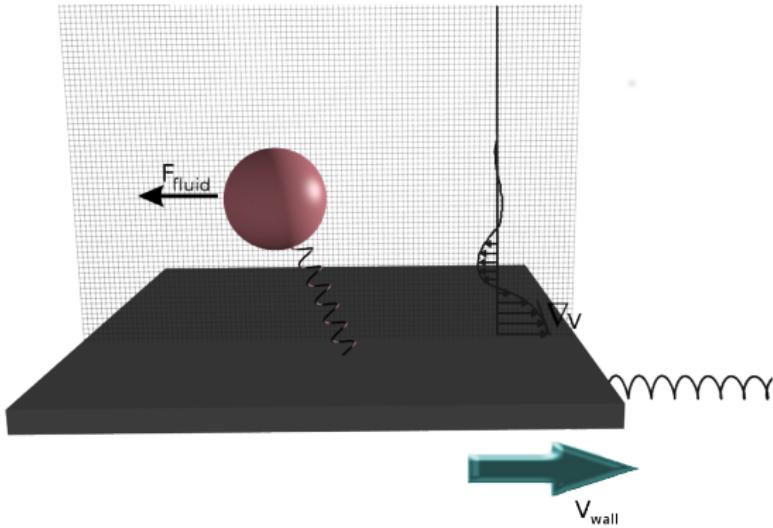
All-atom molecular dynamics of streptavidin in QCM

Experiments [Milioni et al. Anal. Chem. 2017, 10.1021. Shifts respect the fluid frequency and dissipation $\Delta\hat{f} = \hat{f} - \hat{f}_f$. $\Delta D = 2\Delta\Gamma/\omega_0$.

Data	$10^6 f_0$ [MHz]	$10^6 \Delta D$	$\Delta f/f_0$	$-f_0 \Delta D / \Delta f$	$-\Delta D / \Delta f$
Exp.	35	0.06	-4.14	0.014	0.00040
MD	10^3	2930	-5440	0.53	0.00053
MD	10^4	-2360	668	3.52	0.00035



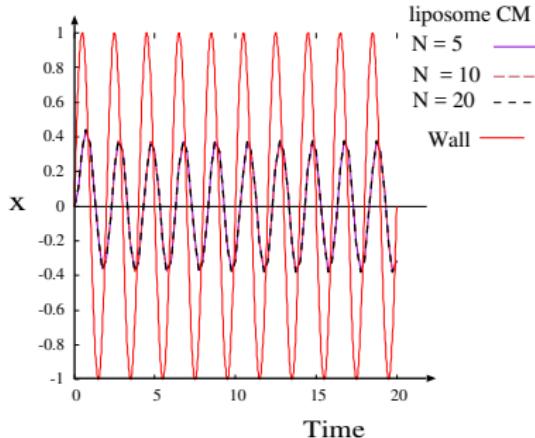
FLUAM: Immersed Boundary method: CFD-particle solver



Liposomes (FLUAM)

1GHz

FLUAM: convergence

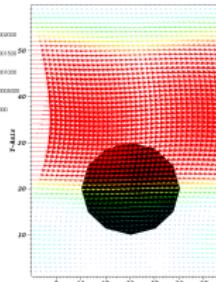
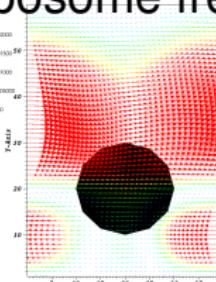
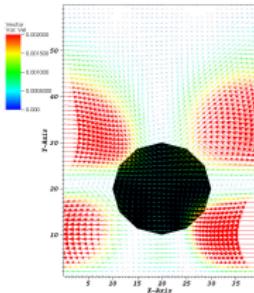


Spatial Resolution: number of cells in penetration lenght: $N = \delta/h$

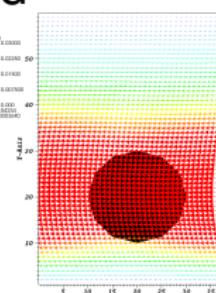
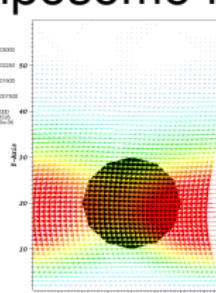
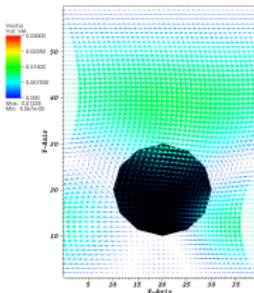
-	with	liposome	without	liposome
N	$\Delta\Gamma$	Δf	$\Delta\Gamma$	Δf
10	0.0520	-0.0537	0.05037	-0.05408
20	0.0530	-0.0519	0.05022	-0.05241
40	0.0541	-0.0507	0.05018	-0.05149

FLUAM liposome 3D hydrodynamics: flow-gradient plane

Liposome free



Liposome fixed

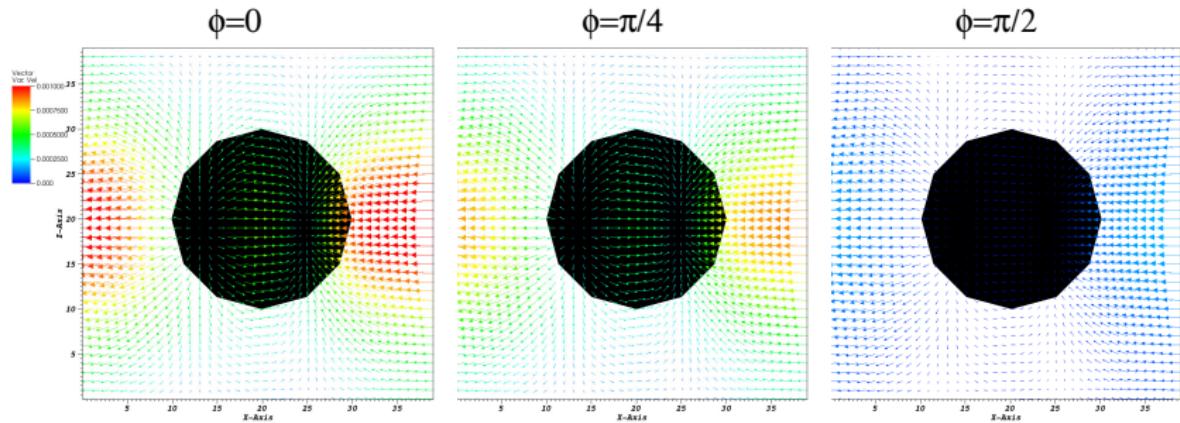


$\phi=0$

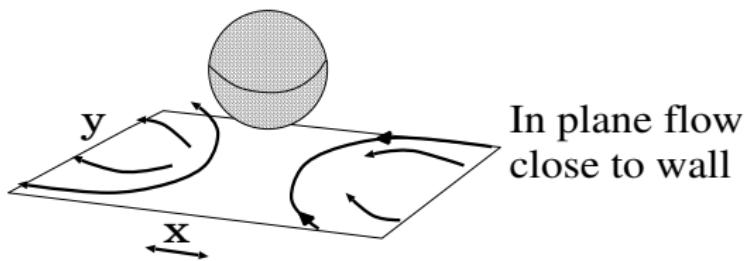
$\phi=\pi/4$

$\phi=\pi/2$

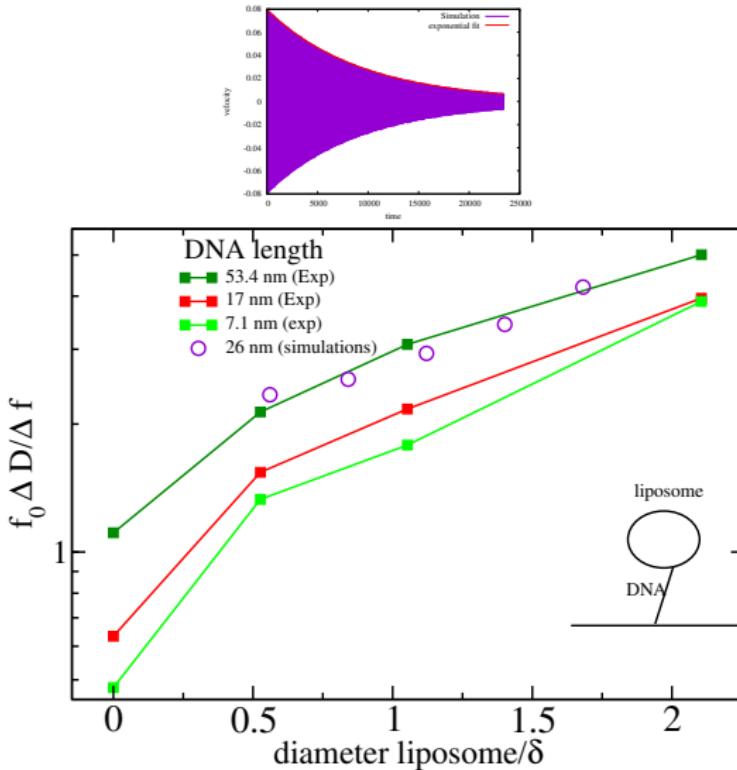
FLUAM, 3D hydrodynamics: close to resonator plane



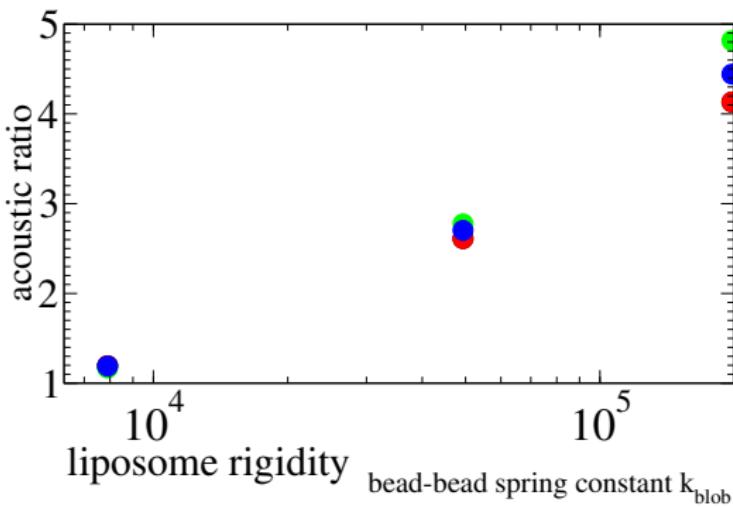
Free liposome



Liposomes: FLUAM ring-down simulations



Effect of liposome rigidity: FLUAM (impedance analysis)



Liposome rigidity increases dissipation: in agreement with experiments

- All-atom MD
 - Effect of linker adhesion energy
 - Linker with short DNA strand
- Continuum-particle methods (FLUAM)
 - Protein linker and DNA via a elastic network model
 - **Liposomes:** DNA-strand rigidity and length, liposome flexibility, study of liposome equilibrium distribution, effect of concentration, **test new dissipative structures**
 - **DNA-strands:** relation of AR with intrinsic viscosity
- Dissipative particle dynamics (DPD) and Lattice Boltzmann (LB)
 - Benchmarking, study possible benefits of these models.

- Marc Meléndez Schofield
- Adolfo Vazquez-Quesada
- Raul Pérez Peláez
- Proteins in collab with Ivan Korotin and Sergei Karavasov, Queen Mary University (London)

Thanks for your attention!