CATCH-U-DNA

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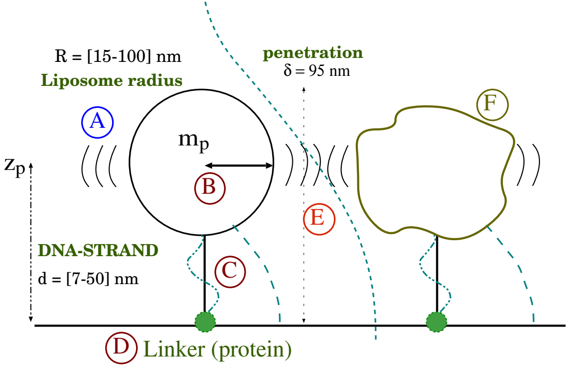
FETOPEN MEETING at Tours

- **Objectives**
  - Linker
  - DNA-strands
  - Liposomes
- Achievements
  - Theory
  - Computational models
  - Preliminary results
- Deviations
  - Accuracy
  - Computation times
- Future plans
  - Impedance analysis

Objectives

- M20. Molecular dynamics simulations of linker and DNA strands under GHz oscillatory shear flow
- M30. Hydrodynamic code resolving coarse-grained molecular description of liposomes in oscillatory flow

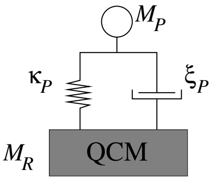


A: Fluid drag on the liposome
B: Mass and inertia of the liposome
C: Stiffness of the anchor (DNA)
D: Stiffness of the linker in contact with resonator
E: Hydrodynamics: flow distortion due to liposomes
F. Liposome flexibility

Achievements

Theory

- Simple spring model
- Fluid
- Liposome (rigid) + Fluid
- Improvements (future plans)



$$M_R \frac{d^2 x_R}{dt^2} = -\kappa_R x_R - \xi_R \frac{dx_R}{dt} + \kappa_P (x_P - x_R) + \xi_P (\frac{dx_P}{dt} - \frac{dx_R}{dt}),$$
$$M_P \frac{d^2 x_P}{dt^2} = -\kappa_P (x_P - x_R) - \xi_P (\frac{dx_P}{dt} - \frac{dx_R}{dt}).$$

In the frequency domain:

$$-\tilde{\omega}^2 M_R \hat{x}_R = -\kappa_R \hat{x}_R - \mathrm{i}\omega \xi_R \hat{x}_R + \kappa_P (\hat{x}_P - \hat{x}_R) + \mathrm{i}\omega \xi_P (\hat{x}_P - \hat{x}_R),$$
$$-\tilde{\omega}^2 M_P \hat{x}_P = -\kappa_P (\hat{x}_P - \hat{x}_R) - \mathrm{i}\omega \xi_P (\hat{x}_P - \hat{x}_R).$$

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

$$|\tilde{\omega} - \tilde{\omega}_R| \ll |\tilde{\omega}_R| \text{ and } \left|\frac{\kappa_P + \mathrm{i}\omega\xi_P}{\kappa_R + \mathrm{i}\omega\xi_R}\right| \ll 1,$$

we arrive at

$$\Delta\tilde{f} = \frac{1}{4\pi M_R}\tilde{\kappa}_P \frac{\tilde{\omega}_R}{\tilde{\omega}_R^2 - \tilde{\omega}_P^2}.$$

- *Inertial loading* $(\mathrm{Re}(\omega_P) >> \mathrm{Re}(\omega_R))$

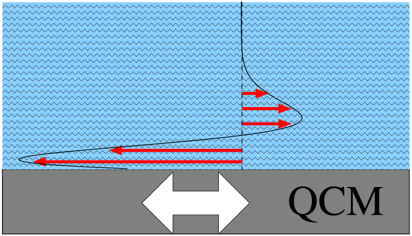
$$\Delta\tilde{f} \approx -\frac{\tilde{\omega}_R M_P}{4\pi M_R}.$$

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

$$\Delta\tilde{f} \approx \frac{\tilde{\kappa}_P}{4\pi M_R \tilde{\omega}_R}.$$

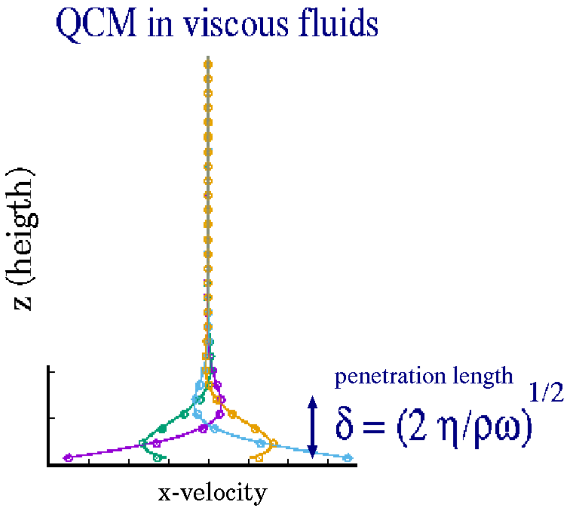
- *Zero crossing* $(\mathrm{Re}(\omega_P) \approx \mathrm{Re}(\omega_R)$,

$$\Delta\tilde{f} \approx \frac{M_P \tilde{\omega}_P}{8\pi M_R(\tilde{\omega}_R - \tilde{\omega}_P)}.$$



$$\rho \frac{\partial u(z,\ t)}{\partial t} = \eta \frac{\partial^2 u(z,\ t)}{\partial z^2}, \qquad \text{(fluid)}$$

$$\ddot{X} = -\omega_0^2\, X + \frac{\eta}{m_W}\ \frac{\partial u(z,\ t)}{\partial z}\bigg|_{z=0}, \qquad \text{(wall)}$$


QCM in viscous fluids
z (heigth)
x-velocity
penetration length
δ = (2 η/ρω)^1/2

$$u(z,\ t) = U_0 e^{\hat{\omega} t + \kappa z},\ \text{with}\ \kappa = \sqrt{\frac{\hat{\omega}\rho}{\eta}}.$$

$$X(t) = \frac{U_0}{\hat{\omega}} e^{\hat{\omega} t}.$$

One gets a condition for $\Lambda = \frac{\hat{\omega}}{\omega_0}$,

$$\Lambda^2 + 1 = C\Lambda^{3/2},$$

governed by the adimensional parameter

$$C = \sqrt{\frac{\eta\rho}{\omega_0 m_w}}$$

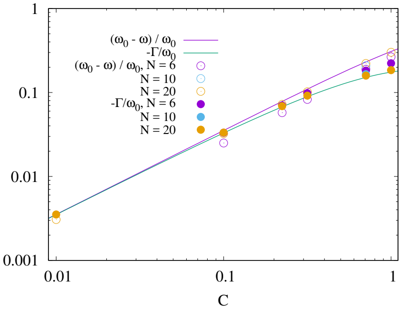
.

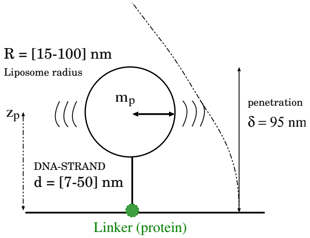
$$\frac{\Delta\omega}{\omega_0} = \frac{C}{2^{3/2}} \sim 10^{-5}! \qquad \text{(frequency shift)}$$

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

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

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





$$(m_R + m_P)\frac{d^2X}{dt^2} = -m_R\omega_0^2 X + \frac{\eta}{\sigma}\left(\frac{\partial v}{\partial z}\right)_{z=0} - \gamma\left(\frac{dX}{dt} - v(z_p,t)\right)$$

(wall and particle)

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

Analytical solution

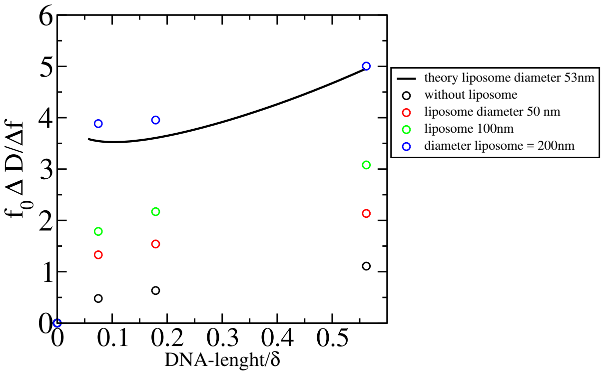
$$\frac{\Delta\omega}{\omega_0} = -\frac{m_P}{2m_R} - 3\,c\,e^{-z}\sin(z)\frac{\phi(R)}{R} \qquad \text{(freq. shift over fluid)}$$

$$\frac{\Delta\Gamma}{\omega_0} = \frac{3\,c\,\phi(R)}{R}\left(1 - e^{-z}\cos(z)\right) \qquad \text{(Damp shift over fluid)}$$

- z and R in units of $\delta = (2\nu/\omega_0)^{1/2}$
- Fraction area of liposomes $\phi(R) = \pi R^2 N/A$
- C-parameter: $c = [\eta\rho/(2\omega_0\sigma^2)]^{1/2} \sim 2 \times 10^{-5}$
- Mass ratio $m_P/m_R = \phi(\sigma_P/\sigma_R) \sim \phi(\rho_P/\rho_R)(R/d_R) \sim 10^{-[4-5]}$

Acoustic ratio

$$\mathrm{AR} = \frac{\Delta\Gamma}{\Delta\omega} = \frac{6c\,(e^z - \cos(z))}{e^z mR + 6c\sin(z)}$$



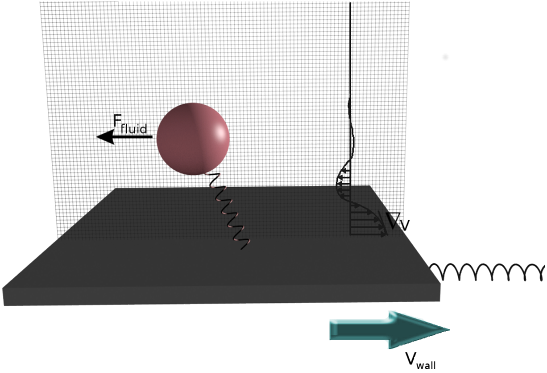
$f_0 \Delta D/\Delta f$
DNA-lenght/δ
0
1
2
3
4
5
6
0
0.1
0.2
0.3
0.4
0.5
theory liposome diameter 53nm
without liposome
liposome diameter 50 nm
liposome 100nm
diameter liposome = 200nm

Achievements: Computational methods

- Continuum-particle models
  - `BD`: One-way coupling, Brownian dynamics for particles
  - `Langevin`: One-way coupling, Langevin dynamics for particles
  - `FLUAM-i`: Incompressible fluid + Immersed boundary (IB)
  - `FLUAM-c`: Compressible fluid + Immersed boundary (IB)
  - `LB`: Lattice Boltzmann with bounce-back coupling for particles (collab. Juan Aragonés UAM)
- Particle based models
  - `MD`: Molecular Dynamics: all-atom molecular dynamics (GROMACS) (collab. Ivan Korotin Queen Mary Univ., London)
  - `CG-MD` Coarse-grained molecular Dynamics (UAMMD)
  - `DPD` Dissipative particle dynamics (UAMMD)

Scheme	Coupling	Aprox.	Cost-per-run
`Langevin`	One-way	No-hydro	10 minutes
`BD`	One-way	No inertia	hours
`FLUAM-i`	Two-way	Incompressible	30 mins (impedance)
`FLUAM-c`	Two-way	Compressible	2-3 days
`LB`	Two-way	compressible	?
`MD`	Two-way	All-Atom	1-2 days
`DPD`	Two-way	Coarse-grained	20 minutes?

Immersed Boundary method: CFD-particle solver



$$
\begin{aligned}
\text{Fluid} \quad &: \quad \rho\left[\frac{\partial \mathbf{v}}{\partial t} + \mathbf{v}\cdot\nabla\mathbf{v}\right] = -\nabla p(\rho) + \eta\nabla^2\mathbf{v} - \sum_i \mathbf{F}_i^{(fl)}\,\mathrm{S}(\mathbf{q}_i - \mathbf{r}) \\
\text{DNA beads} \quad &: \quad m_e^{(i)}\frac{d^2\mathbf{q}_i}{dt^2} = \mathbf{F}_i^{(fl)} + \mathbf{F}_{springs} \\
\text{Quarzt wall} \quad &: \quad m\ddot{x} = k_w x - \eta A \left.\frac{\partial v_x(z,t)}{\partial z}\right|_{z=0} - K_0\,(x - X_0)
\end{aligned} \tag{1}
$$

- Explicit solution of wall dynamics: $x(t)$
- Rigid boundary to the fluid with velocity $v_x(z=0,t) = dx/dt$
- Drag evaluated numerically: POTENTIAL ERRORS!

`Langevin: The inertia of the particle is resolved`

- **Quarzt wall**

$$m\ddot{x} + k_w x - \eta A \left. \frac{\partial v_x(z,t)}{\partial z} \right|_{z=0} - K\left(\mathbf{R}_0 - \mathbf{r}_w\right) \cdot \hat{\mathbf{x}} = 0.$$

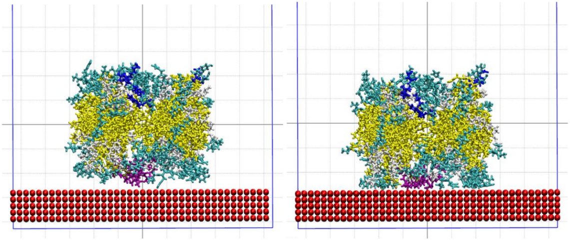
- **Fluid not affected by the particle**: One-way coupling

$$\rho_f \frac{\partial v_x}{\partial t} = \eta \frac{\partial^2 v_x}{\partial z^2}$$

- **Polymer, Langevin dynamics**

$$m_p \frac{d\mathbf{R}^2}{dt} = -\chi\left(\dot{\mathbf{R}} - v_x(Z_i;t)\right)\hat{\mathbf{x}} + \mathbf{F}_{\mathrm{s}}(\mathbf{R}) - K\left(|\mathbf{R}_0 - \mathbf{X}_w|\right)\hat{\mathbf{R}}_{0w} + d\tilde{R}_i$$

Molecular dynamics of QCM ring-down simulations
All-atom molecular dynamics of streptavidin in QCM



	Pure SPC water, 1 GHz		Water + Protein, 1 GHz		Water + Protein, 10 GHz	
	value	fit error	value	fit error	value	fit error
$\Gamma,\ ps^{-1}$	1.97E-05	+/- 3.9E-08	2.89E-05	+/- 9.3E-08	1.23E-04	+/- 6.38E-08
$\omega,\ ps^{-1}$	0.0062625	+/- 4.0E-08	0.0062283	+/- 9.2E-08	0.062667	+/- 6.41E-08
$\omega_0,\ ps^{-1}$	0.0062832		0.0062832		0.062832	
$\omega_0-\omega,\ ps^{-1}$	2.07E-05	+/- 4.0E-08	5.49E-05	+/- 9.2E-08	1.65E-04	+/- 6.41E-08
$2\Gamma/(\omega_0-\omega)$	**1.90**	< 0.5%	**1.05**	< 0.5%	**1.49**	< 0.1%
$\Gamma_{analytical},\ ps^{-1}$	2.22E-05		2.22E-05		2.22E-04	