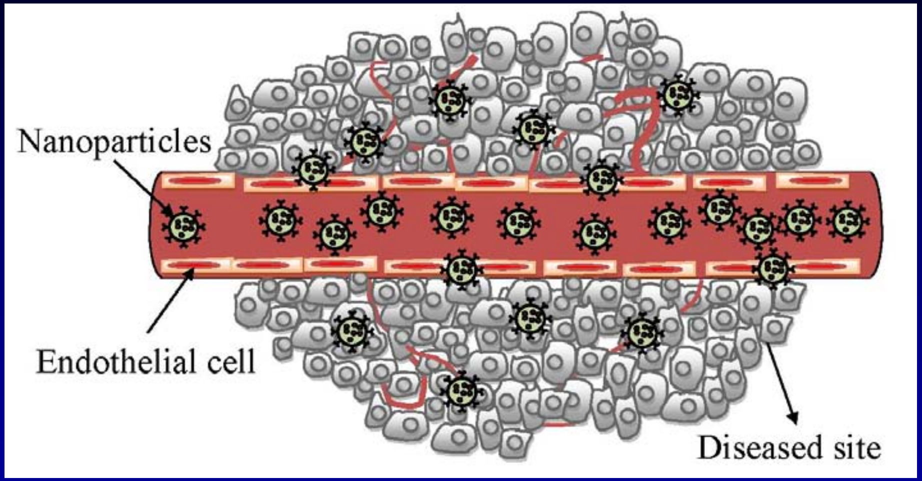
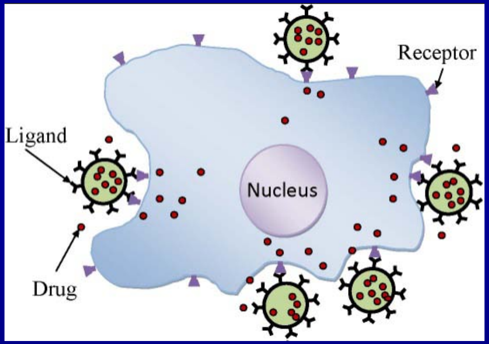
Nanoparticle thermal motion in a Newtonian fluid using fluctuating hydrodynamics

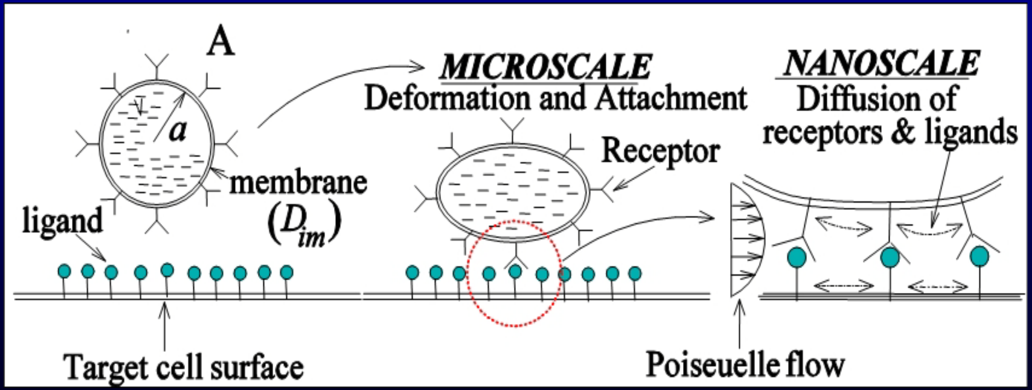
Uma Balakrishnan
Department of Mechanical Engineering and Applied Mechanics
University of Pennsylvania
E-mail: umab@seas.upenn.edu

Incompressible fluids, Turbulence and Mixing: In honour of Peter Constantin's 60th birthday,
Carnegie Mellon University, October 15, 2011

Targeted Drug Delivery







- Drug delivery by intravascular use of targeted nanocarriers holds promise for personalized medicine
- Clinical optimization of drug transport requires accurate description of carrier motion in the blood stream and near endothelial cells
- Synergistic computational approach is required to determine the translational and rotational motions of a nanocarrier
- Brownian motion and hydrodynamic interactions are important

Overview

Fluctuating Hydrodynamics Approach

Lattice Boltzmann method
(Ladd, Phys. Rev. Lett, 1993; JFM, 1994; Adhikari et al., Euro. Phys. Lett, 2005)

Stochastic Immersed Boundary method
(Atzberger et al., J. Compu. Phys., 2007)

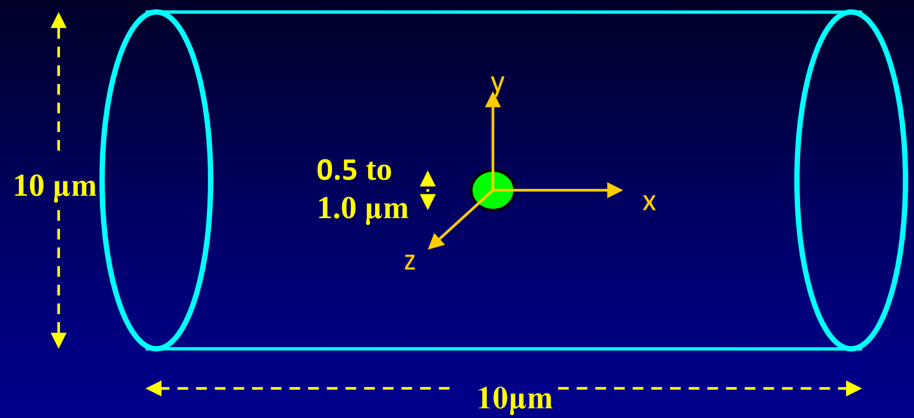
Finite element method
(Espanõl et al., J. Chem. Phys., 2009)

Finite Volume Method
(Sharma and Patankar, J.Chem. Phys., 2004)

Langevin Approach

(Iwashita et al., J. Phys. Soc. Jpn., 2008; Iwashita and Yamamoto, Phys. Rev. E, 2009).

Schematic Representation

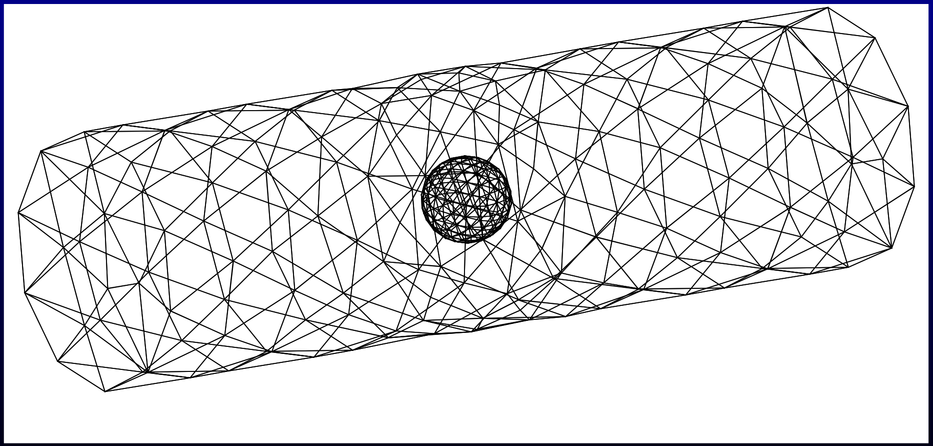


$$k_B = 1.3806\times10^{-23}\ \mathrm{J\,K^{-1}};\ T = 310\,\mathrm{K};\ \mu = 10^{-4}\ \mathrm{kg/ms};\ \rho_\mathrm{f} = 10^3\ \mathrm{kg/m^3};\ 990\ \mathrm{kg/m^3} \le \rho_\mathrm{p} \le 1010\ \mathrm{kg/m^3}$$

$$U_{\max} = 10^{-4}\ \text{to}\ 10\ mm/s;\ \mathrm{Re}_f = 5\times10^{-7}\,\text{to}\,5\times10^{-2};\ \mathrm{Re}_p = 2.5\times10^{-8}\,\text{to}\,2.5\times10^{-3}\,\text{(Poiseuille flow)}$$

Finite Element Discretization

Direct Numerical Simulation (DNS): Arbitrary Lagrangian–Eulerian technique based on combined formulation of the fluid and particle momentum equations – ALE moving, unstructured, finite-element mesh



Governing Equations and Boundary Conditions: Fluctuating Hydrodynamics Approach

Governing equations for the fluid motion and rigid particles

$$\nabla \cdot \mathbf{u} = 0$$

$$\rho_f \frac{D\mathbf{u}}{Dt} = \rho_f \mathbf{f} + \nabla \cdot \sigma = 0$$

$$\sigma = -p\mathbf{I} + \mu\left[\nabla\mathbf{u} + (\nabla\mathbf{u})^T\right] + \mathbf{S}$$

(Random Stress)

(Landau and Lifshitz, 1959)

$$m_i \frac{d\mathbf{U}_i}{dt} = -\int_{\partial\Omega_i(t)} \sigma \cdot \mathbf{n}\, ds$$

$$\frac{d(\mathbf{I}_i\omega_i)}{dt} = -\int_{\partial\Omega_i(t)} (\mathbf{x} - \mathbf{X}_i) \times (\sigma \cdot \mathbf{n})\, ds$$

Boundary conditions

$$\mathbf{u} = \mathbf{u}_p \text{ on } (\partial\Omega)_u$$

$$\sigma \cdot \mathbf{n} = 0 \text{ on } (\partial\Omega)_\sigma$$

$$\mathbf{u} = \mathbf{V}_i + \omega_i \times (\mathbf{x}_i - \mathbf{X}_i) \text{ for } \mathbf{x} \in \partial\Omega_i(t)$$

Initial conditions

$$\mathbf{u} = \mathbf{u}_0 \text{ on } \Omega_0(0)$$

$$\langle \mathbf{S}_{ij} \rangle = 0; \quad \langle \mathbf{S}_{ik}(\mathbf{x}_1, t_1)\mathbf{S}_{lm}(\mathbf{x}_2, t_2)\rangle = 2k_B T\mu(\delta_{il}\delta_{km} + \delta_{im}\delta_{kl})\delta(t_1 - t_2)\delta(\mathbf{x}_1 - \mathbf{x}_2)$$

Time Scales

Hydrodynamic time scale:
(a – radius of a nanoparticle
ν – viscosity of the fluid)

$$\tau_\nu = \frac{a^2}{\nu}$$

Nanoparticle of radius
a = 250 nm

$$\tau_\nu = 6.25 \times 10^{-8} s$$

Brownian relaxation time scale:
(m – mass of a nanoparticle
$\varsigma^{(F)}$ – Stokes friction coefficient)

$$\tau_b = \frac{m}{\varsigma^{(F)}}$$

Nanoparticle of radius
a = 250 nm

$$\tau_b = 1.38 \times 10^{-8} s$$

Brownian diffusion time scale:

$$\tau_d = \frac{a^2 \varsigma^{(F)}}{k_B T}$$

Nanoparticle of radius
a = 250 nm

$$\tau_d = 6.88 \times 10^{-2} s$$

Time scale for simulation:

$$\Delta t << \tau_b, \tau_\nu, \tau_d$$

DNS: Fluctuating Hydrodynamics – Equipartition Theorem

Translational and rotational temperatures of the nanoparticle are obtained:

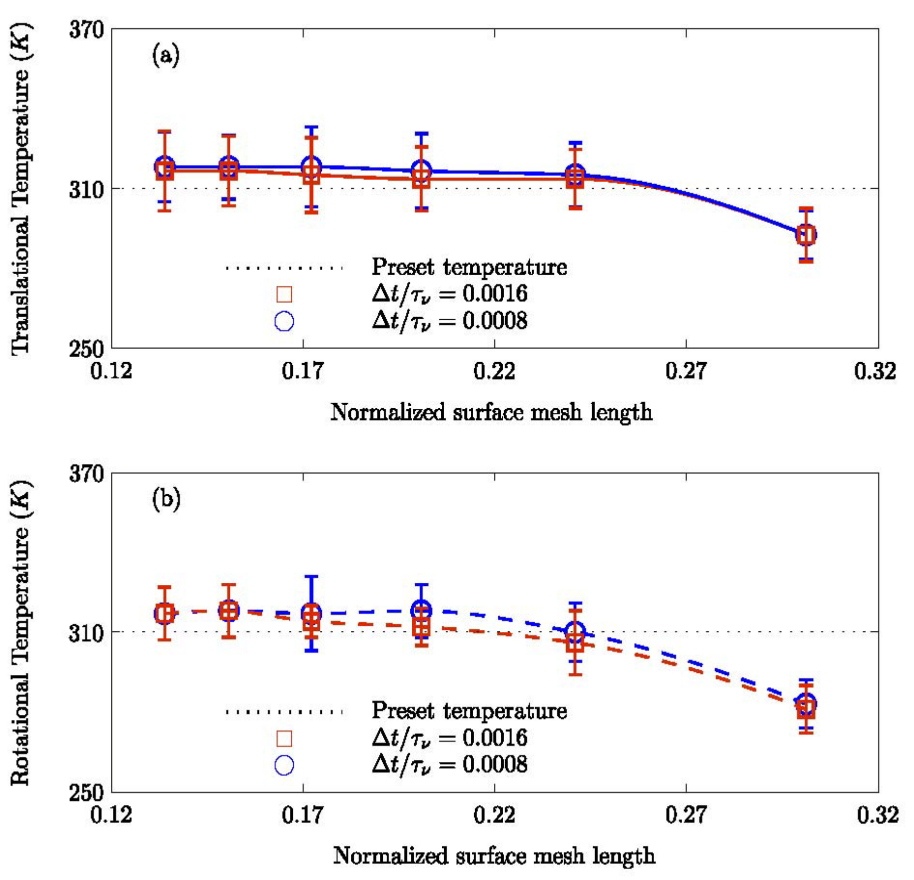
$$T^{(t)} = \frac{m\left\langle \mathbf{U}^2 \right\rangle}{3k_B}; \quad T^{(r)} = \frac{\mathbf{I}\left\langle \omega^2 \right\rangle}{3k_B}$$

- To account for compressibility effects in the translation motion of the particle, its mass is augmented by an added mass (mass of the displaced fluid)

$$T^{(t)} = \frac{M\left\langle \mathbf{U}^2 \right\rangle}{3k_B}; \quad T^{(r)} = \frac{\mathbf{I}\left\langle \omega^2 \right\rangle}{3k_B}$$

DNS: Fluctuating Hydrodynamics – Equipartition Theorem (Mesh Convergence)

Quiescent Medium

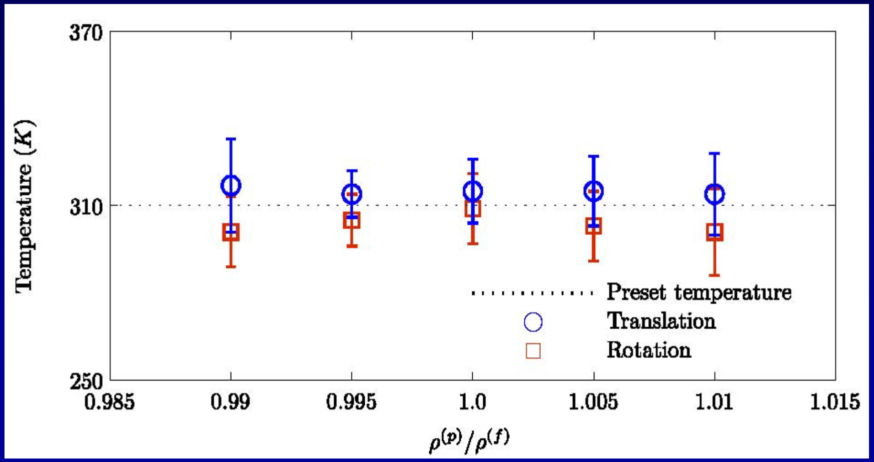


- The translational and rotational temperatures of the particle in a stationary medium as a function of the normalized surface mesh length and for different time step of integration
- The rotational motion of the nanoparticle is unaffected by the incompressibility of the fluid.
- The error bars have been plotted from standard deviations of the temperatures obtained with 15 different realizations (5 realizations in each direction).

The translational and rotational temperatures of the nanoparticle agree with the preset temperature of the fluid to within 5% error.

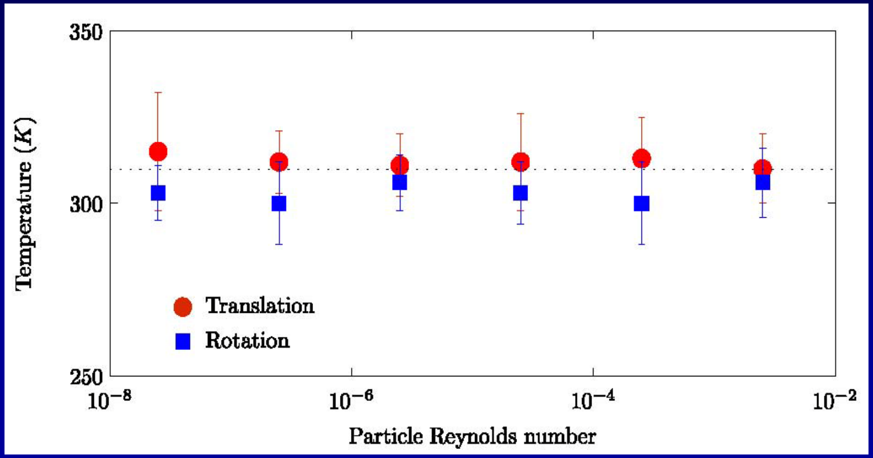
DNS: Fluctuating Hydrodynamics – Equipartition Theorem

Quiescent Medium



The translational and rotational temperatures of nearly neutrally buoyant Brownian particles, thermally equilibrated, in a quiescent fluid medium are independent of the density of the particle in relation to that of fluid.

Poiseuille Flow



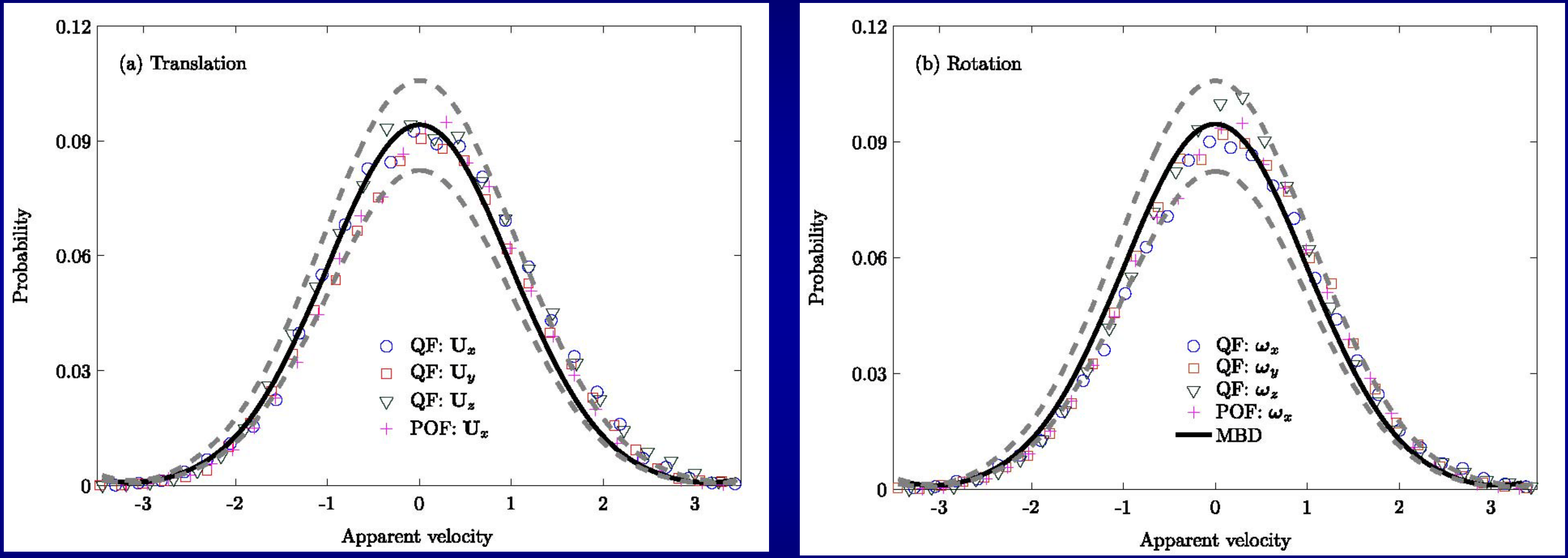
The translational and rotational temperature equilibration of a nanoparticle initially placed at the center of a cylindrical tube as a function of the particle Reynolds number for Poiseuille flow

The translational and rotational temperatures of the nanoparticle agree with the preset temperature of the fluid to within 5% error.

DNS: Fluctuating Hydrodynamics – Maxwell-Boltzmann Distribution

Frequency distribution of velocity of a nanoparticle: Maxwell-Boltzmann distribution

Quiescent Medium and Poiseuille flow



- The probability density distribution of the translational and rotational velocities of the fluctuating nanoparticle follow the Maxwell-Boltzmann distribution.
- Each degree of freedom individually follows a Gaussian distribution.

DNS: Fluctuating Hydrodynamics – Velocity Autocorrelation Function (VACF)

At Short times:

$$\left\langle \mathbf{U}(t)\mathbf{U}(0)\right\rangle = \frac{3k_B T}{M} e^{-\zeta^{(t)} t/M}; \quad \left\langle \omega(t)\omega(0)\right\rangle = \frac{3k_B T}{\mathbf{I}} e^{-\zeta^{(r)} t/\mathbf{I}}$$

(Zwanzig and Bixon, Phys. Rev. A 2, 2005 (1970))

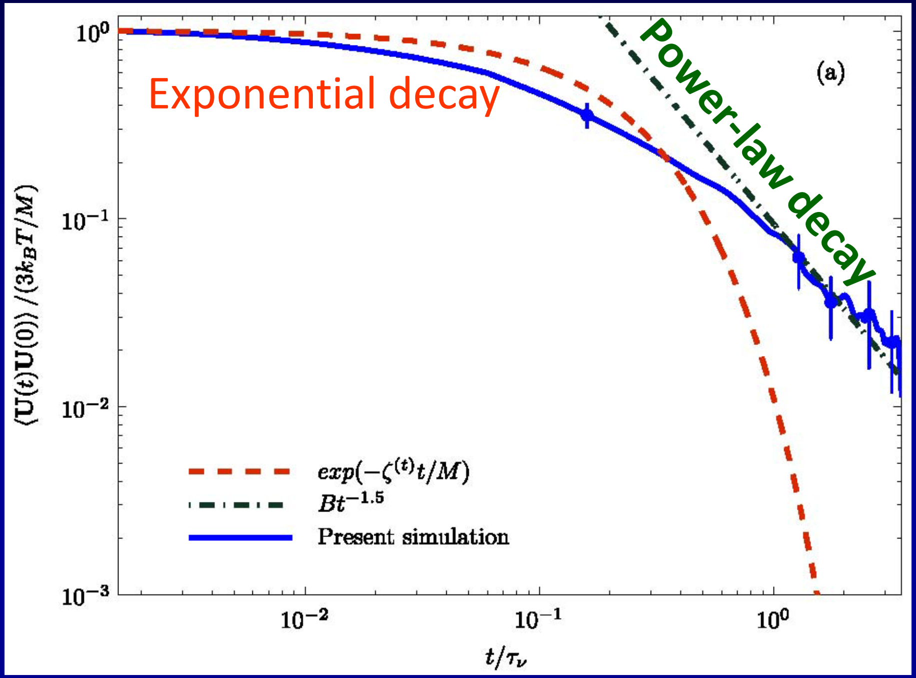
At long times:

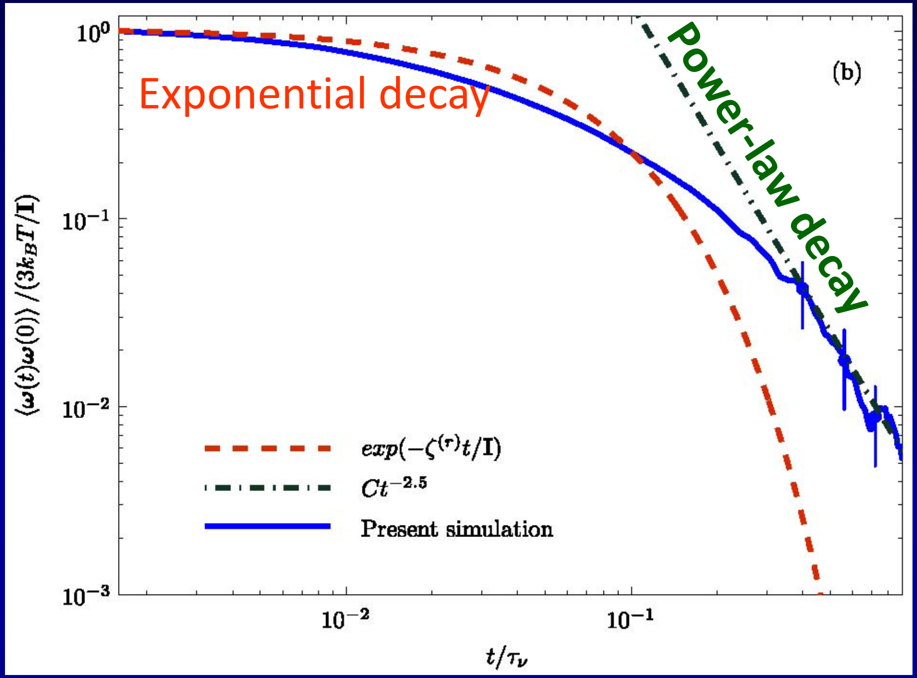
$$\left\langle \mathbf{U}(t)\mathbf{U}(0)\right\rangle \simeq \left(\frac{k_B T \rho^{(f)1/2}}{4\pi^{3/2}\mu^{3/2}} \right) t^{-3/2}; \quad \left\langle \omega(t)\omega(0)\right\rangle \simeq \left(\frac{3k_B T \rho^{(f)3/2}}{32\pi^{3/2}\mu^{5/2}} \right) t^{-5/2}$$

(Hauge and Martin-Löf, J. Stat. Phys. 7, 259 (1973))

DNS: Fluctuating Hydrodynamics – Velocity Autocorrelation Function (VACF)

Quiescent Medium





- The translational VACF follows an exponential decay in the range for $t < 0.343\ \tau_\nu$ and an algebraic tail for $t > 1.202\ \tau_\nu$
- The rotational VACF follows an exponential decay, for $t < 0.115\ \tau_\nu$ and an algebraic tail for $t > 0.495\ \tau_\nu$
- The error bars have been plotted from standard deviations of the decay at particular time instants obtained with 45 different realizations

DNS: Fluctuating Hydrodynamics – Mean Square Displacement (MSD)

Translation:

$$\left\langle \Delta \mathbf{x}^2 \right\rangle = \frac{3k_B T}{M} t^2 \quad \text{(ballistic limit)}$$

$$= 6D_\infty^{(t)} t \quad \text{(diffusive regime; Stokes-Einstein relation)}$$

(Zwanzig, Nonequilibrium Statistical Mechanics, 2001)

Rotation:

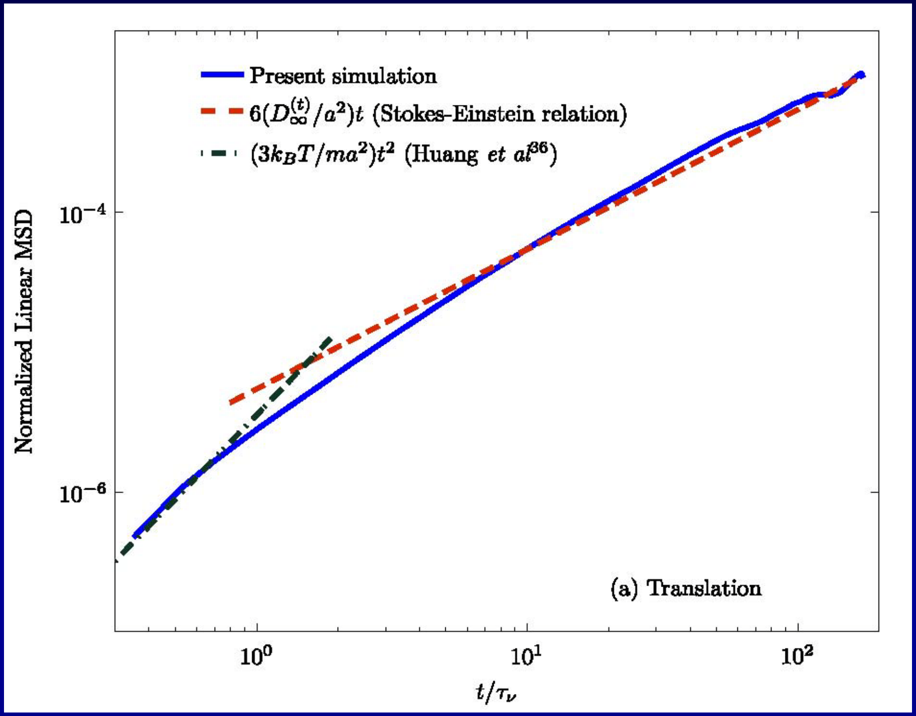
$$\left\langle \Delta \theta^2 \right\rangle = \frac{3k_B T}{\mathbf{I}} t^2 \quad \text{(ballistic limit)}$$

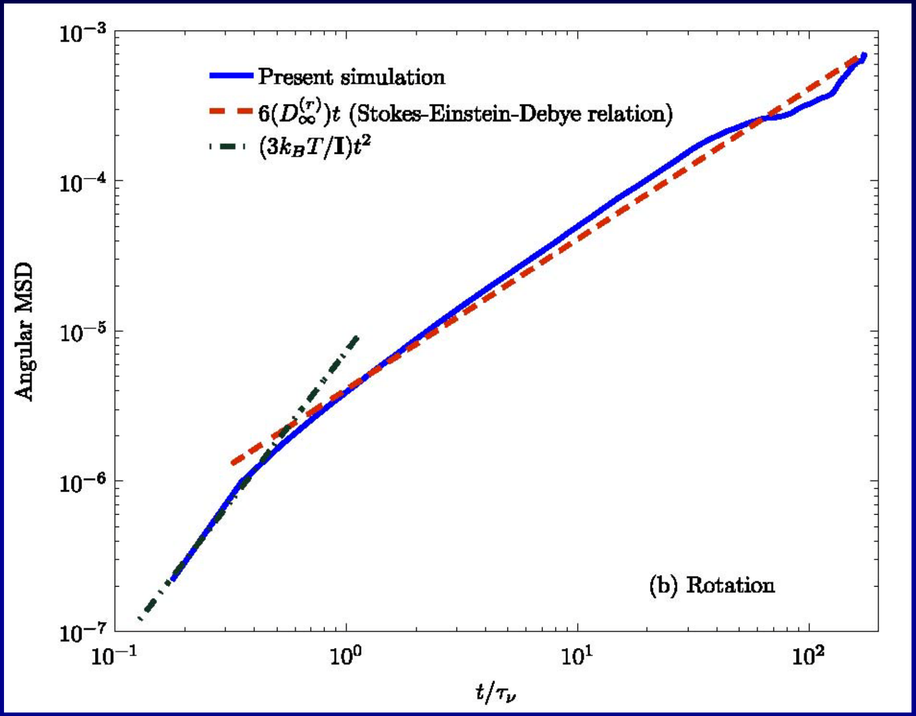
$$= 6D_\infty^{(r)} t \quad \text{(diffusive regime; Stokes-Einstein-Debye relation)}$$

(Heyes et al., J. Phys.: Condens. Matter 10, 10159 (1998))

DNS: Fluctuating Hydrodynamics – Mean Square Displacement (MSD)

Quiescent Medium

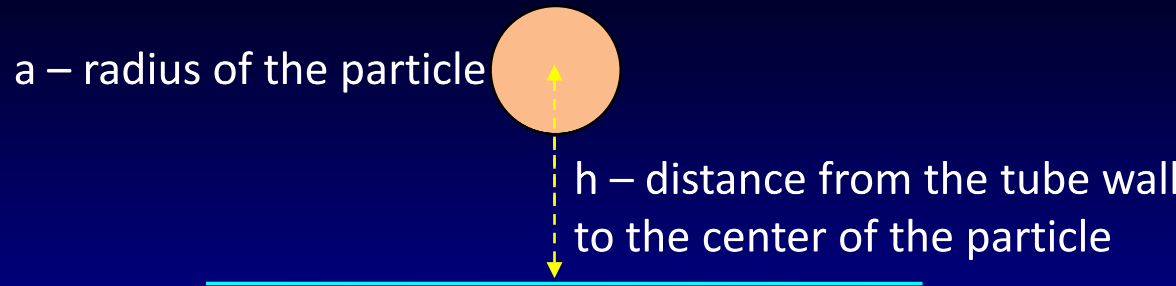




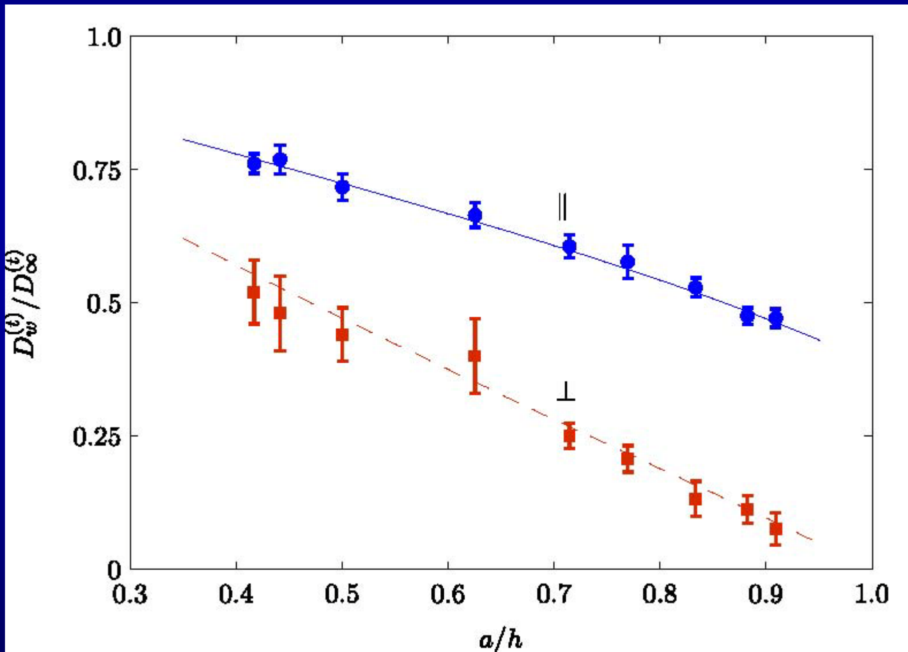
In the ballistic regime, $0.346\ \tau_\nu < t < 0.63\ \tau_\nu$ (translation), and $0.174\ \tau_\nu < t < 0.316\ \tau_\nu$ (rotation), the translational and rotational motions of the particle follow $(3k_BT/M)\,t^2$ and, $(3k_BT/\mathbf{I})\,t^2$ respectively.

In the diffusive regime, $t \gg \tau_b$, and when $t \geq 7\ \tau_\nu$ (translation) and $t \geq 1.2\ \tau_\nu$ (rotation), the translational and rotational MSDs increase linearly in time to follow Stokes-Einstein and Stokes-Einstein-Debye relation, respectively.

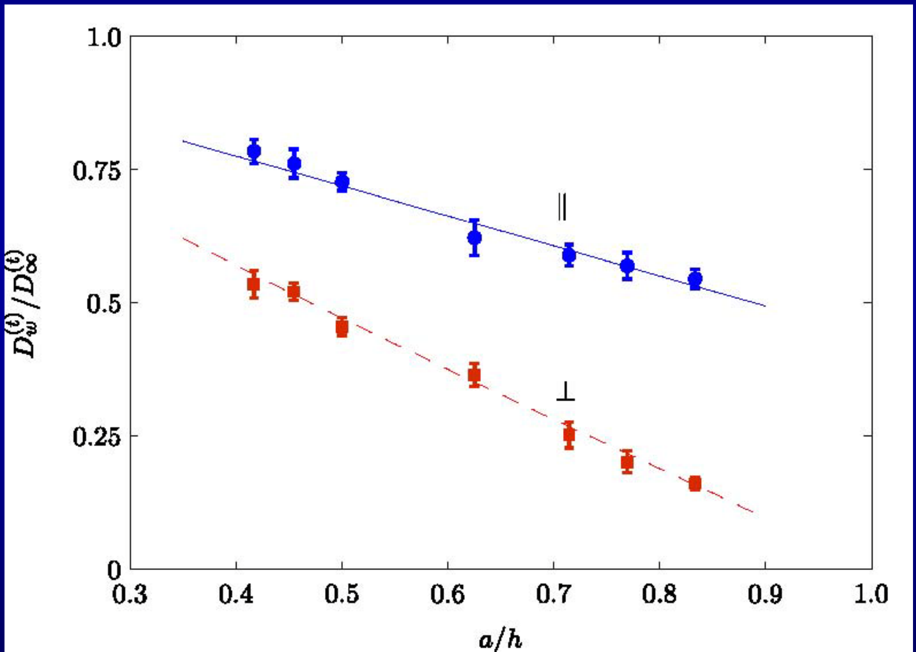
DNS: Fluctuating Hydrodynamics – Wall Interactions



Quiescent Medium



Poiseuille Flow



Parallel (x direction) and perpendicular (y direction) diffusion coefficients of neutrally buoyant particles of different radii initially placed at various distances from the tube wall, both in a quiescent medium and Poiseuille flow are in good agreement with the analytical predictions of Happel and Brenner (1983).

DNS: Fluctuating Hydrodynamics

• Frequency distribution of velocity of a nanoparticle:	Maxwell-Boltzmann distribution
• Temperature of a particle:	Equipartition theorem
• Velocity autocorrelation function: (VACF)	Exponential decay (initial time) Power-law decay (long time)
• Mean square displacement (MSD)	Stokes-Einstein & Stokes-Einstein-Debye relations
• Wall effects	Parallel and perpendicular diffusivity of the particle agrees with Happel and Brenner's analytical prediction

(Uma et al., Physics of Fluids, 23, 073602 (2011);
Uma et al., Proceedings of the 21st National and 10th ISHMT-ASME Heat and Mass Transfer conference, Paper No. ISHMT_USA_020 (2011))

DNS: Other Approaches

Generalized Langevin Dynamics with Correlated noise

(Uma et al., The Journal of Chemical Physics, 135, 114104 (2011);
Uma et al., Proceedings of the ASME 3rd Micro/Nanoscale Heat and Mass Transfer International Conference, Paper No. MNHMT2012-75019 (2012))

Hybrid Approach: Combination of fluctuating hydrodynamics and Generalized Langevin dynamics

(Uma et al., Molecular Physics, in review (2011))

Approach	Remarks
Fluctuating Hydrodynamics (FHD)	Satisfies equipartition theorem, VACF, MSD and wall effects. Compressibility effects are accounted by adding the virtual mass with the particle mass
Generalized Langevin Dynamics (GLD) with correlated noise	Thermostat satisfies equipartition theorem in a small plateau region, and satisfies VACF. Alters dynamics with a scaling factor depends on the radius of the particle
Hybrid: Combination of FHD and GLD	Thermostat satisfies equipartition theorem in a small plateau region. Also satisfies VACF, and MSD. Wall effects are yet to determine.

Modeling nanocarrier binding through receptor ligand interactions

J. Liu, N. Agrawal, A. Calderon, P.S. Ayyaswamy, D.M. Eckmann and R. Radhakrishnan, Multivalent binding of nanocarrier to endothelial cells under shear flow*, Biophys. J.* 101 (2): 319-326 (2011)

J. Liu, G. Weller, B. Zern, P.S. Ayyaswamy, D.M. Eckmann, V.R. Muzykantov and R. Radhakrishnan, Computational model for nanocarrier binding to endothelium validated using in vivo, in vitro and atomic force microscopy experiments, *Proc. Natl. Acad. Sci. USA* 107 (38): 16530-16535 (2010)

Review of physiological factors in drug delivery

T.N.Swaminathan, J.Lin, B.Uma, P.S.Ayyaswamy, R.Radhakrishnan and D.M.Eckmann, Dynamic factors controlling carrier anchoring on vascular cells, International Union of Bio-chemistry and Molecular Biology Life (IUBMB Life), 63(8), 640647, (2011)

V.R.Muzykantov, R.Radhakrishnan and D.M.Eckmann, Dynamic factors controlling targeting nanocarriers to vascular endothelium, *Current Drug Metabolism,* In Press: (2011)

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Prof. P.S.Ayyaswamy
Department of Mechanical Engineering and Applied Mechanics
ayya@seas.upenn.edu

Prof. D.M. Eckmann
Department of Anesthesiology and Critical Care
David.Eckmann@uphs.upenn.edu

Prof. R. Radhakrishnan
Department of Bioengineering
rradhak@seas.upenn.edu

Dr. T.N. Swaminathan
Department of Mechanical Engineering and Applied Mechanics

Other Collaborators:
Dr. Jin Liu
Department of Bioengineering

Prof. V.R.Muzykanto
Department of Anesthesiology and Critical Care

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Thanks for your attention !!!!!!