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Supplemental Information

Single-Bond Association Kinetics Determined by Tethered Particle Motion: Concept and Simulations

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S1 Implementing hydrodynamic effects near a surface

As mentioned is section 4.3.1, the drag on the particle near a surface is no longer the isotropic drag, but the drag increases in a distinct matter for the parallel and perpendicular component. In particular, we use the relations

$$\gamma_{\parallel} = \frac{\gamma_0}{1 - \frac{9}{16}q + \frac{1}{8}q^3 - \frac{45}{256}q^4 - \frac{1}{16}q^5}, \tag{15}$$

$$\gamma_{\perp} = \frac{\gamma_0}{1 - \frac{9}{8}q + \frac{1}{2}q^3 - \frac{57}{100}q^4 + \frac{1}{5}q^5}, \tag{16}$$

for the parallel drag $\gamma_{\parallel}$ and the perpendicular drag $\gamma_{\perp}$ for a particle near a wall at $z = 0$. Here $q = R/z$, η is the dynamic viscosity of the solvent and $\gamma_0 = 6\pi\eta R$, the Stokes drag in an unbounded liquid.

We define $c_{\parallel}$ and $c_{\perp}$

$$c_{\parallel} = \frac{1}{1 - \frac{9}{16}q + \frac{1}{8}q^3 - \frac{45}{256}q^4 - \frac{1}{16}q^5}, \tag{17}$$

$$c_{\perp} = \frac{1}{1 - \frac{9}{8}q + \frac{1}{2}q^3 - \frac{57}{100}q^4 + \frac{1}{5}q^5}, \tag{18}$$

so that $\gamma_{\parallel} = c_{\parallel}\gamma_0$ and $\gamma_{\perp} = c_{\perp}\gamma_0$.

In the LAMMPS code (24) this can be implemented by adjusting the random force and the drag force in the file fix_langevin.cpp.

```
//For loops loops over all atoms in bin
//and applies random force, after that
//drag force is applied.
for (int i = 0; i < nlocal; i++) {
//Assign the perpendicular and parrallel
//component a value depending on the z-coordinate
zs = R_bead/(R_bead+x[i][2]);
//This is a rescaled version of z,
//convenient for the expressions of the parr and perp drag
//Use Faxen's law and an interpolation formula given by Schaffer et al.
//to determine both coeffs
cparr = 1/(1-0.5625*zs+0.125*pow(zs,3)-0.175781*pow(zs,4)-0.0625*pow(zs,5));
cperp=1/(1-1.125*zs+0.5*pow(zs,3)-0.57*pow(zs,4)+0.2*pow(zs,5));
  if (mask[i] & groupbit) {
    if (Tp_TSTYLEATOM) tsqrt = sqrt(tforce[i]);
    if (Tp_RMASS) {
      gamma1 = -rmass[i] / t_period / ftm2v;
      gamma2 = sqrt(rmass[i]) * sqrt(24.0*boltz/t_period/dt/mvv2e) / ftm2v;
      gamma1 *= 1.0/ratio[type[i]];
      gamma2 *= 1.0/sqrt(ratio[type[i]]) * tsqrt;
    } else {
```

```
        gamma1 = gfactor1[type[i]];
        gamma2 = gfactor2[type[i]] * tsqrt;
      }

      fran[0] = sqrt(cparr)*gamma2*(random->uniform()-0.5);
      fran[1] = sqrt(cparr)*gamma2*(random->uniform()-0.5);
      fran[2] = sqrt(cperp)*gamma2*(random->uniform()-0.5);

     fdrag[0] = cparr*gamma1*v[i][0];
     fdrag[1] = cparr*gamma1*v[i][1];
     fdrag[2] = cperp*gamma1*v[i][2];
```

If the desired coordinate for the wall is not the z-component, this can be incorporated by requiring the arguments 'face' and 'coord' to describe the location of the wall and process this by

```
  //Check if the wall face is set in a valid way
  if (strcmp(arg[iarg],"xlo") == 0) wallface = XLO;
  else if (strcmp(arg[iarg],"xhi") == 0) wallface = XHI;
  else if (strcmp(arg[iarg],"ylo") == 0) wallface = YLO;
  else if (strcmp(arg[iarg],"yhi") == 0) wallface = YHI;
  else if (strcmp(arg[iarg],"zlo") == 0) wallface = ZLO;
  else if (strcmp(arg[iarg],"zhi") == 0) wallface = ZHI;
  else error->all(FLERR, "Wall face should be a coordinate with 'lo' or 'hi'");
  dim = wallface / 2; //0 for x, 1 for y, 2 for z
  side = wallface % 2; //0 for lo, 1 for hi
```

And then apply them to the component in the relevant direction

```
//Assign the perpendicular and parrallel
//component a value depending on the coordinate
//in the direction of the wall
//This is a rescaled version of the coordinate,
//convenient for the expressions of the parr and perp drag
if (!side) xs = R_bead/(x[i][dim]-coord0);
else      xs = R_bead/(coord0 - x[i][dim]);
if (xs<0.0) error->all(FLERR, "Rescaled component is negative");
if (xs>1.0) error->all(FLERR, "Bead is intersecting wall");

//Use Faxen's law and an interpolation formula given by
//Schaffer et al. to determine both coeffs
cparr = 1.0/(1.0-0.5625*xs+0.125*pow(xs,3)-0.175781*pow(xs,4)-0.0625*pow(xs,5));
cperp=1.0/(1.0-1.125*xs+0.5*pow(xs,3)-0.57*pow(xs,4)+0.2*pow(xs,5));
if (dim ==0){
        cx = cperp;
```

```
  cy = cparr;
  cz = cparr;
}
else if (dim==1){
  cx = cparr;
  cy = cperp;
  cz = cparr;
}
else if (dim==2){
  cx = cparr;
  cy = cparr;
  cz = cperp;
}
```

S2 Optimizing engineering parameters

In designing a TPM system it is worthwhile to investigate the influence of several engineering parameters to maximize the number of potential binding events. In this respect, the tether length l and the particle diameter R are relevant parameters, but the used frame rate may aso be of significant influence. We present a way to optimize such experiments.

For a maximum number of binding events to occur, the reactive surface on the substrate and the reactive surface on the particle should be within encounter distance as much as possible. We aim to define a parameter that quantifies the amount of surface on the particle and the substrate being within encounter distance. Since the system is axisymmetric, we may define a contact parameter ζ as

$$\zeta = \int_{A_s} \int_{A_p} P_{\text{enc}}(d_p, d_s) \mathrm{d}A_{ring,p} \mathrm{d}A_{ring,s}, \tag{19}$$

where P_{enc} represents the probability that a binding spot on the particle and a binding spot on the substrate are within interaction range. $\mathrm{d}A_{ring,p}$ and $\mathrm{d}A_{ring,s}$ are ring-shapen area elements on the particle and the substrate over which we integrate.

For a maximum number of potential binding events, ζ should be maximized. For fixed particle diameter of 1 μm and fixed frame rate of 30 Hz, we have calculated ζ for several tether lengths L and this lead to the trivial optimal tether length $L = 0$. In other words, with a longer tether the particle will encounter the substrate less often and the extra available potential encounter positions are not able to make up for this.

However, in designing the optimal measurement set-up, the contact area is not the only important parameter. Namely, not every secondary bond is detectable and we want to optimize the number of *detectable* bonds. The specific position of the binding molecules determines the step size $R_{step} = |\vec{R}(t + \Delta t) - \vec{R}(t)|$, the in-plane distance that the particle travels between two frames, which is used to detect secondary bonds. In order to encompass this effect and include only the potential detectable bonds, we define a refined contact parameter

$$\xi = \int_{d_{s,min}}^{d_{s,max}} \int_{A_p} P_{\text{enc}}(d_p, d_s) \mathrm{d}A_{ring,p} \mathrm{d}A_{ring,s}, \tag{20}$$

where $d_{s,min}$ is the minimum d_s that leads to a detectable bond and $d_{s,max}$ is the maximum possible d_s. Our preliminary results delivered an optimal tether length of 60 nm for a particle diameter of 1 μm and frame rate 30 Hz (35).