Colloidal Potentials Mediated by Specific Biomolecular Interactions

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Supporting Information

Calculating K_D for Harmonic Well Potentials

The procedure for determining K_D was developed based on the work by Luo and Sharp.[1] For the case of a simple harmonic well potential, U_H, has the form,

$$U_H = U_M + 0.5\Delta q \cdot \mathbf{F} \cdot \Delta q \tag{S1}$$

where Δq are the translational and rotational coordinates of reactant A, B, and their complex AB, and $\mathbf{F}$ is the force constant matrix defined as,

$$\mathbf{F} = kT\left[\sigma_{ij}^{\,2}\right]^{-1} = k_s J_3 \tag{S2}$$

where σ_{ij} is the coordinate fluctuation covariance matrix, k_s is the spring constant, and J_3 is a 3x3 unit matrix (a matrix of ones). The association constant, K_A, can be computed for a harmonic well potential as,

$$K_A = \frac{1}{8\pi^2}\int H(r) e^{-U_H(r)/kT} dr \tag{S3}$$

where $H(r)$ =1 in the bound state and 0 otherwise. The integral is solved analytically as,

$$\int e^{-U_H(r)/kT} dr = e^{-U_M/kT}\sqrt{(2\pi)^n \left|\sigma_{ij}^{\,2}\right|} \tag{S4}$$

where $|\sigma_{ij}|=(kT/k_s)^3$ is the determinant of σ_{ij} and n is the degrees of freedom in the system. With biomolecules allowed to diffuse in 3 dimensions and non-orientation dependent binding, substituting Eq. (S4) into Eq. (S3) yields,

$$K_A^{-1} = K_D = \left(2\pi kT/k_S\right)^{(-3/2)} \exp\left(\left|U_M\right|/kT\right) \tag{S5}$$

allowing for direct computation of K_D as a function of k_s and U_M.

Calculating K_D for Harmonic Well + Hard Sphere Potentials

As described in the Theory section, the second virial coefficient, B_2, is calculated for ligands with hard core + harmonic well (HCHW) potentials (*i.e.*, $a_L>0$) to estimate their effective interaction strength. The second virial coefficient for ligands with hard cores, $B_{2,HCHW}$, is calculated with Eq. (4) as,

$$B_{2,HCHW} = (16/3)\pi a_L^3 + 12\int_{a_L}^{a_L+\delta}\left[1-\exp\left[-U_{RL}(r,a_L)/kT\right]\right] r^2 dr \tag{S6}$$

An equivalent harmonic well potential is then found by determining a simple harmonic well (HW) potential (*i.e.*, $a_L=0$) with the same B_2 as the ligand including a hard core. The second virial

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coefficient of a HW potential (without a hard core), $B_{2,HW}$, is calculated with Eq. (4) as,

$$B_{2,HW} = 12\int_0^{\delta}\left[1-\exp\left[-U_{RL}(r,0)/kT\right]\right]r^2 dr \tag{S7}$$

To find an equivalent HW potential, U_M in U_{RL} (Eq. 1) is adjusted at constant k_s until $B_{2,HW}$ is equal to $B_{2,HCHW}$. These two potentials are then considered equivalent and the K_D of the harmonic well calculated from Eq. (3) assigned to the ligand including a hard core.

3D Rotational Receptor Moves

In order to maintain uniform spacing between the receptors and the surface while making 3D receptor rotational moves, the rotations made must be uniform in Euclidean space. The following algorithm was developed by Arvo to make random, uniform rotational moves[2]:

1. Rotate randomly about the z axis by applying the rotation matrix, R:

$$R = \begin{vmatrix} \cos(2\pi\delta_1) & \sin(2\pi\delta_1) & 0 \\ -\sin(2\pi\delta_1) & \cos(2\pi\delta_1) & 0 \\ 0 & 0 & 1 \end{vmatrix} \tag{S8}$$

   where δ_1 is a random variable that ranges from 0 to the maximum rotational step size, s_{rot}.

2. Rotate randomly from the position (0, 0, $a + h_R$) to a random position by using the Householder matrix, H:

$$H = I - 2vv^T \tag{S9}$$

   where v is the matrix,

$$v = \begin{vmatrix} \cos(2\pi\delta_2)\sqrt{\delta_3} \\ \sin(2\pi\delta_2)\sqrt{\delta_3} \\ \sqrt{1-\delta_3} \end{vmatrix} \tag{S10}$$

3. The final rotation can be defined with matrix, M as:

$$M = -HR \tag{S11}$$

The random variables δ_2 and δ_3 also range from 0 to s_R. A maximum value of 1 x 10^{-3} for s_R was found empirically to not disturb the equilibrium ligand coverage and allowed for unbiased configurational sampling as shown in Figure S1.

Colloid-Ligand Cluster Moves

In order to allow our colloids to freely diffuse with dense coverages of ligands on their surface, cluster moves were used to translate all interacting colloids and ligands when attempting colloidal MC moves. The following algorithm was used to decide whether to accept or reject the cluster moves:

1. Determine number of ligands, n_L, bound to a receptor on the colloid ($r < a_L + \delta$)

2. Move n_L ligands on colloid with same translation and rotation as attempted by the colloid and receptors in that step.
3. Calculate total change in energy due to the cluster move, ΔE, for colloid and the n_L ligands bound.

$$\Delta E = \Delta E_C + \sum_{i=1}^{n_L} E_{L,i} \tag{S12}$$

where ΔE_C is the change in energy of the colloid and ΔE_L is the change an energy of a ligand.

4. If ΔE is less than or equal to zero or $e^{(-\Delta E)}$ is greater than a random integer, the cluster move is accepted.

By applying the metropolis criterion to these cluster moves, the potential for biasing in these moves was avoided. Figure S2 shows on a single diffusing colloid with coverages up to ~99%, MC move efficiency of the colloid (open triangles down) and ligands was still maintained with a minimum of ~78% acceptance rates (open circles).

Calculating Number, Energy, and Orientation of Ligand Bridges

The interaction of ligands with receptors is strictly limited to one receptor on each particle. If a ligand comes within range of a receptor ($r < a_L + \delta$), the net interaction is zero if it is currently occupying a receptor on the same particle. All ligands interacting with two receptors (one on each particle) are identified as a bridge. The number of bridges, N_B, was tracked in each step as a function of L in all MC-US simulations. The average number of bridges as a function of L, $\langle N_B \rangle(L)$, can be calculated as,

$$\left\langle N_B \right\rangle(L) = \sum^{n(L)} N_B(L) / n(L) \tag{S13}$$

where $n(L)$ is the total number of bridging events at separation L. The energy of each ligand bridge is calculated as,

$$U_B = U_{RL,i}(r_i) + U_{RL,j}(r_j) \tag{S14}$$

which is simply the sum of the interactions with the receptors that make up the bridge, receptor i and receptor j, that can be calculated with Eq. (3). Since colloids only make translational moves in the x-direction, we can determine the bridge orientation with respect to the colloidal surfaces as the orientation of the bridge in the x-direction. The orientation of each bridge is calculated with respect to the colloids in the x-direction by first determining the root mean-square distance between the receptors i and j, r_{ij}, calculated as,

$$r_{ij} = \sqrt{(x_i - x_j)^2 + (y_i - y_j)^2 + (z_i - z_j)^2} \tag{S15}$$

and the root mean-square distance between receptors i and j in the x-direction, $r_{ij,x}$, calculated as,

$$r_{ij,x} = \sqrt{(x_i - x_j)^2} \tag{S16}$$

We can then calculate the bridge orientation, ϕ, between receptors i and j with respect to the colloidal surfaces as,

$$\phi = 2\arcsin\left(r_{ij,x}/r_{ij}\right) \tag{S17}$$

Histograms of U_B and ϕ were then populated as a function of L from each of the 12 bins of the MC-US simulation results.

Supplementary Figure Captions

Figure S1. Schematic of receptor position (green circle) in spherical coordinates where α and ψ are the polar and azimuthal angles of each receptor with respect to the center of the colloid (blue circle). Histograms of sampled (A) α and (B) ψ in 2000 representative configurations for MC colloidal surface adsorption simulation at [C] = 10 μM, a_L = 5nm, and $U_M = 11kT$ ($\theta \approx 0.99$).

Figure S2. MC move efficiency (open circles) and fraction coverage, θ, (open triangles down) for MC colloidal surface adsorption simulation at [C] = 10 μM, a_L = 5nm, and $U_M = 11kT$.

Supplementary References

1. Luo, H.; Sharp, K. On the calculation of absolute macromolecular binding free energies. *Proceedings of the National Academy of Sciences of the United States of America* **2002,** *99*, 10399-404.
2. Arvo, J. Fast Random Rotation Matrices. *Graphics Gems III* **1992**, 117-120.

Figure S1

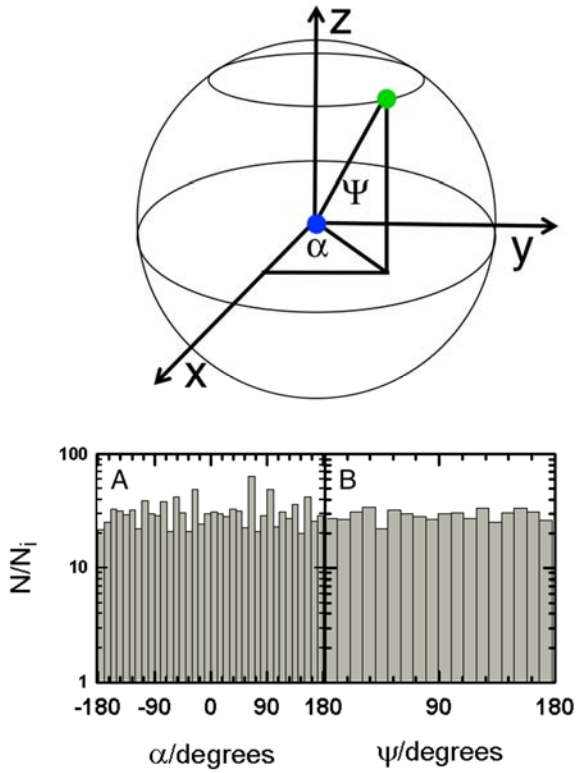

Figure S2