Electronic Supplementary Material (ESI) for Soft Matter.

The interaction of protein-coated bionanoparticles and surface receptors reevaluated: How important is the number of bonds?

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Supporting information

1. Length of the entrance region

The average velocity at a flow rate of Q = 50 μl/min is $\bar{v}_x = Q/(2wh)$= 83.3 mm/s. From Eq. (3) in the main text, with the kinematic viscosity of water ν = 0.897 mm^2/s and the channel height $(2h) =$ 0.02 mm we obtain l_e = 9.6 x 10^{-4} mm.

2. Diffusivity of the bionanopartices

The diffusivity of influenza virus particles D is estimated from the Stokes-Einstein equation $D = \kappa T/(6\pi R_v \eta_w)$, where κ is Boltzmann's constant, 1.38066 x 10^{-23} J/K; T is the temperature, 298 K; η_w is the viscosity of pure water at 25 ^{o}C, 8.94 x 10^{-4} Pa·s; R_v is the radius of the bionanoparticles. The diameter of influenza virus particles is about 1275 ± 162 Å [1], the diameter of human IgG is about 15 nm, and the diameter of the synthetic bionanoparticles is about 143 nm tested by Malvern Zetasizer Nano ZS device. Based on these data, the diffusivity D is estimated as 3.76 x 10^{-12} m^2/s for the influenza virus, 0.389 x 10^{-12} m^2/s for human IgG, and 3.42 x 10^{-12} m^2/s for the human IgG coated nanoparticle.

3. Calculation

For the numerical solution of the model equations, the flow cell domain was spatially discretized equidistantly along the x-direction into 100 elements, i.e. $\Delta X = 0.01$ for each element. The backward difference scheme was applied to discretize Eq. (12) in the main text. Thereby, with application of the chain rule $\frac{\partial r^*}{\partial X} = \frac{\partial r^*}{\partial \delta_D^*}\frac{d\delta_D^*}{dX}$, Differential Algebraic Equations (DAE) were obtained which were solved by the ode15s solver in MATLAB 7.12.0 (R2011a). Correspondingly, the discretized form of the BIAcore output quantity is given here in terms of the dimensionless quantity $\Theta = m_{PR_n}(t)/\left([R^{max}]l_p w_p\right)$:

$$\Theta = \frac{l}{l_p}\sum_{i=6}^{95}\theta_{P,S,i}\Delta X \tag{1}$$

where the elements i = 6 up to i = 95 correspond to the probing area.

The two unknown parameters, Da and n, were estimated by least squares fitting of experimental time series of adsorption data, using the Gauß-Newton method. The sum of squares was defined as:

$$S = \sum_{j=1}^{m}\left(\Theta_{exp,j} - \Theta_j\right)^2 \tag{2}$$

$\Theta_{exp,j}$ stands for the experimentally observed (dimensionless) total amount of bionanoparticles adsorbed on the probing area at time point t_j, while Θ_j is the corresponding simulated data. m is the total number of points in a given time series. Please note that the experimental data were determined from the response units RU_V of the BIAcore device according to the calibration formula:

$$\Theta_{exp} = \frac{RU \times MW_{receptor}}{[R^{max}] \times MW_{bionanoparticle}} \tag{3}$$

1 RU = 1 pg/mm^2 = 1 x 10^{-12} g/mm^2 [2]. N_A is Avogadro constant, 6.02 x 10^{23} mol^{-1}. The weight of a single virus particle is MW_{virus} ~ 1.8 x 10^8 Da [1]. The weight of human IgG is 150 kDa. The weight of the human IgG coated nanoparticle is approximated as 5 x 10^8 Da.

4. Derivations of the reduced model equations

By inserting Eq. (22) into Eq. (15) in the main text and integration, an implicit equation for $\theta_{P,s}$ is obtained:

$$1 - n\theta_{P,s} = e^{-nDa\tau} e^{nDa\frac{\delta_D^*}{3}\theta_{P,s}} \tag{4}$$

Furthermore, an approximate explicit equation can be derived via Taylor series expansion of the exponential term $e^{nDa\frac{\delta_D^*}{3}\theta_{P,s}}$ at $\theta_{P,s} = 0$:

$$\theta_{P,s} = \frac{1 - e^{-nDa\tau}}{n\left(1 + Da\frac{\delta_D^*}{3}e^{-nDa\tau}\right)} \tag{5}$$

Finally, putting Eq. (5) into Eq. (1) and taking the analytical solution of δ_D^* in the main text (Eq. (20)), the output quantity sounds:

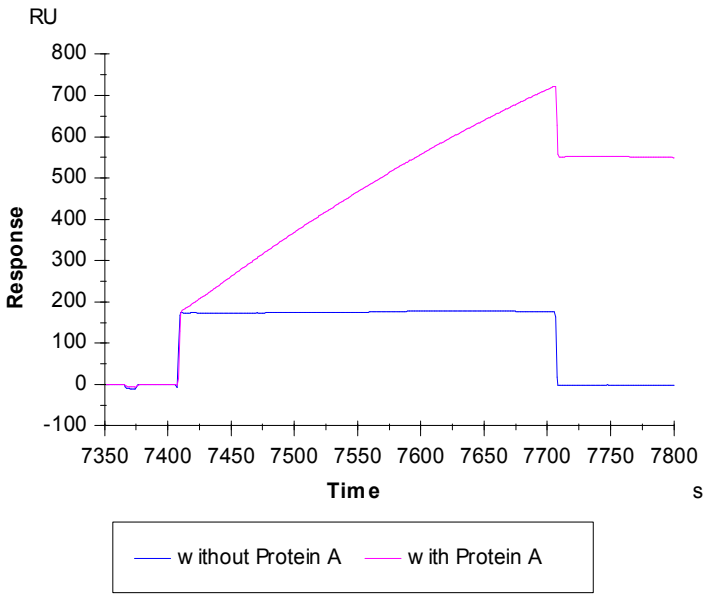
$$\Theta = \frac{l}{nl_p}\left(1 - e^{-nDa\tau}\right)\int_{0.05}^{0.95} \frac{1}{1 + Da\frac{e^{-nDa\tau}}{3}\sqrt[3]{5\left(\frac{l}{h}\right)^2\frac{1}{Pe}}X^{1/3}}dX \tag{6}$$

5. Surface coverage ratio

The surface coverage ratio is calculated to divide the number of the total bond ligands summed up from the amount of adsorbed bionanoparticles by the capacity of the receptor surface, $[R^{max}]$. For the experimental case of the synthetic bionanoparticle shown in Fig. 7 (main text), the number of bonds is estimated to be about 6000 as shown in Table 1 (main text), and $[R^{max}]$ = 1.56 x 10^{10} receptors/mm^2. The final RU is 540 and 1 RU = 1178 particles/mm^2 according to Eq. (3). Then, 6000*540*1178/1.56 x 10^{10} ≈ 0.24.

6. Evidence of the attachment of human IgGs to nanoparticles

The related experimental data of Fig. 7b, i.e., the sensorgram monitored by surface plasmon resonance technology, is displayed as follows:



For the measurement of the multivalent adsorption of human IgG-coated particles on the lectin-immobilized surface, two flow cells were simultaneously used. One cell surface was immobilized with Protein A (see the pink curve) and the other was without Protein A (see the blue curve). The particle solution was injected through these two flow cells at the same time. The final experimental data displayed in Fig. 7b were obtained by online subtracting data of the blue curve from data of the pink curve. The experimental data of these two curves clearly show that the responding signals of particles increase on the surface with Protein A while those almost do not change on the surface without Protein A. This difference was caused by the presence of human IgGs and, thus, verifies that human IgGs were coated onto the nanoparticle surface.

References

1. K. Nicholson, R. G. Webster and A. J. Hay, *Textbook of influenza*, Blackwell Science, Oxford, 1998.

2. *Biacore sensor surface handbook*, GE Healthcare Bio-Sciences AB, Uppsala, Sweden, 2008.