Electronic Supplementary Material (ESI) for Soft Matter

Supporting Information

1. Stability of Particle Size

Size distribution of particle was also measured after diluting 10 times or stored at 4 °C for 10 days. Figure S1 shows the size distribution of 305-nm nanomedicine at the experiment concentration (Day 0), diluting 10 times, and after 10 days. There was no significant change after dilution or 10-days storage at 4 °C.

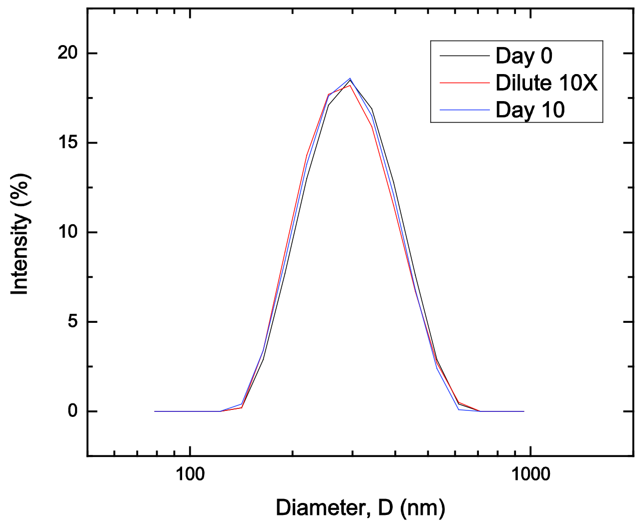

Figure S1. Size distribution of 305-nm nanomedicine at Day 0 and Day 10, and after diluting 10 times at Day 0.

2. Numerical Calculation of the Average Adsorption Rate Constant k_a.

In the main manuscript, we derived the following expression for the adsorption rate constant, k_a:

$$k_a = \frac{D^{2/3}}{Gamma\left(\frac{4}{3}\right)}\left(\frac{6K}{9bS}\right)^{1/3} \quad [S1]$$

where $K = \frac{Q}{\pi b}$ and $S = \int_{\tau=-\infty}^{\tau} h_\sigma h_\tau d\tau$. Diffusivity, D, can be calculated from the particle size using Stokes-Einstein equations:

$$D = \frac{k_B T}{6\pi R\eta} \quad [S2].$$

To calculate the average k_a over the measurement area of QCM-D (i.e. r≤ 3mm), the area integration is performed as follows:

$$< k_a >= \int_{x=-r}^{x=r} \int_{y=0}^{y=\sqrt{r^2-x^2}} k_a \, dy \, dx \quad [S3]$$

This integration was numerically carried out Matlab as described below.

```
clear all;
a=0.005; % radius of the chamber, m
```

```
b=0.00064; % thickness of the chamber, m
r=0.003; % radius of measurement area, m
dx=0.00001; % step size of x and y for integral, m
du=0.01; % u, v were used for τ, σ, du is the step size of u for integral
M=0;
for x=0-r:dx:r
   ym=sqrt(r^2-x^2);
   for y=0:dx:ym
      u=log(sqrt((x+a)^2+y^2)/sqrt((a-x)^2+y^2));
      v=atan((a+x)/y)+atan((a-x)/y); % convert (x, y) to (τ, σ)
      S=0;
      for i=-10:du:u
         S=S+1/(cosh(i)-cos(v))^2*du;
      end
      ka=1/0.893*(6/pi/b^2/a^2/S/9)^(1/3); % local ka without D
      M=M+ka;
   end
end
N=M*dx*dx/pi/0.003^2*2 % average ka without D
%%<ka>=N*D^(2/3)*Q^(1/3)
```

3. Calculation of Mass Transport due to Diffusion at Different Directions

The concentration profile inside the QCM-D chamber was calculated to be:

$$\frac{c}{c_0} = \frac{\int_0^{\eta} e^{-m^3}\,dm}{Gamma\left(\frac{4}{3}\right)} \qquad \text{[S4].}$$

The mass transport due to diffusion at different directions can be calculated by taking the second derivative of the concentration with respect to the direction of interest.

3.1 Diffusion at z-direction

$$-D\left[\left(\frac{\partial c}{\partial z}\right)|_z - \left(\frac{\partial c}{\partial z}\right)|_{z+dz}\right] h_\sigma d\sigma h_\tau d\tau = D\frac{\partial^2 c}{\partial z^2} * dV \qquad \text{[S5]}$$

$$\frac{\partial c}{\partial z} = \frac{c_0}{Gamma\left(\frac{4}{3}\right)} e^{-\eta^3}\frac{\partial \eta}{\partial z} = \frac{c_0}{Gamma\left(\frac{4}{3}\right)} e^{-\eta^3}\left(\frac{6K}{9DbS}\right)^{1/3} \qquad \text{[S6]}$$

$$\frac{\partial^2 c}{\partial z^2} = \frac{c_0}{Gamma\left(\frac{4}{3}\right)} e^{-\eta^3} * (-3\eta^2)\left(\frac{6K}{9DbS}\right)^{2/3} \qquad \text{[S7]}$$

3.2 Diffusion at τ-direction

$$-D\,[(\frac{\partial c}{h_\tau \partial \tau})|_\tau - (\frac{\partial c}{h_\tau \partial \tau})|_{\tau+d\tau}]h_\sigma d\sigma dz = D\frac{\partial}{h_\tau \partial \tau}\left(\frac{\partial c}{h_\tau \partial \tau}\right) * dV \quad [S8]$$

$$\frac{\partial c}{h_\tau \partial \tau} = \frac{c_0}{Gamma\left(\frac{4}{3}\right)}e^{-\eta^3}\frac{1}{h_\tau}\frac{\partial \eta}{\partial \tau} = \frac{c_0}{Gamma\left(\frac{4}{3}\right)}e^{-\eta^3}\eta\frac{1}{3}S^{-1}h_\sigma \quad [S9]$$

$$\frac{\partial}{h_\tau \partial \tau}\left(\frac{\partial c}{h_\tau \partial \tau}\right) = \frac{c_0}{Gamma\left(\frac{4}{3}\right)}e^{-\eta^3}\left[\frac{1}{3S}\frac{\partial \eta}{\partial \tau} - \frac{\eta h_\tau h_\sigma}{3S^2} + \frac{\eta}{3S}\frac{\partial h_\sigma}{h_\tau \partial \tau} - \eta^3 S^{-1}\frac{\partial \eta}{\partial \tau}\right] \quad [S10]$$

3.3 Diffusion at σ-direction

$$-D\,[(\frac{\partial c}{h_\sigma \partial \sigma})|_\sigma - (\frac{\partial c}{h_\sigma \partial \sigma})|_{\sigma+d\sigma}]h_\tau d\tau dz = D\frac{\partial}{h_\sigma \partial \sigma}\left(\frac{\partial c}{h_\sigma \partial \sigma}\right) * dV \quad [S11]$$

$$\frac{\partial c}{h_\sigma \partial \sigma} = \frac{c_0}{Gamma\left(\frac{4}{3}\right)}e^{-\eta^3}\frac{1}{h_\sigma}\frac{\partial \eta}{\partial \sigma} = \frac{c_0}{Gamma\left(\frac{4}{3}\right)}e^{-\eta^3}\frac{1}{h_\sigma}\eta\frac{1}{3}S^{-1}\int_{\tau=-\infty}^{\tau}\frac{\partial}{\partial \sigma}(h_\sigma h_\tau)d\tau \quad [S12]$$

Let $\int_{\tau=-\infty}^{\tau}\frac{\partial}{\partial \sigma}(h_\sigma h_\tau)d\tau = M$ [S13]

$$\frac{\partial}{h_\sigma \partial \sigma}\left(\frac{\partial c}{h_\sigma \partial \sigma}\right) = \frac{c_0}{Gamma\left(\frac{4}{3}\right)}e^{-\eta^3}\left[\frac{-\eta M}{3(h_\sigma)^3 S}\frac{\partial h_\sigma}{\partial \sigma} + \frac{M}{3{h_\sigma}^2 S}\frac{\partial \eta}{\partial \sigma} - \frac{\eta M^2}{3{h_\sigma}^2 S^2} + \frac{\eta}{3{h_\sigma}^2 S}\frac{\partial M}{\partial \sigma} - \frac{\eta^3 M}{{h_\sigma}^2 S}\frac{\partial \eta}{\partial \sigma}\right] \quad [S14]$$

where $\eta = z\left(\frac{6K}{9DbS}\right)^{1/3} = z\left(\frac{6K}{9DbS}\right)^{1/3};\ K = \frac{Q}{\pi b}$; and $S = \int_{\tau=-\infty}^{\tau} h_\sigma h_\tau d\tau.$ [S15]

$$\frac{\partial \eta}{\partial \tau} = z\left(\frac{6K}{9Db}\right)^{1/3}\frac{1}{3}S^{-\frac{2}{3}}h_\sigma h_\tau = \eta\frac{1}{3}S^{-1}h_\sigma h_\tau \quad [S16]$$

$$\frac{\partial \eta}{\partial \sigma} = z\left(\frac{6K}{9Db}\right)^{1/3}\frac{1}{3}S^{-\frac{2}{3}}\int_{\tau=-\infty}^{\tau}\frac{\partial}{\partial \sigma}(h_\sigma h_\tau)d\tau = \eta\frac{1}{3}S^{-1}\int_{\tau=-\infty}^{\tau}\frac{\partial}{\partial \sigma}(h_\sigma h_\tau)d\tau = \eta\frac{1}{3}S^{-1}M \quad [S17]$$

$$\frac{\partial \eta}{\partial z} = \left(\frac{6K}{9DbS}\right)^{1/3} = \frac{\eta}{z} \quad [S18]$$

Table S1 summarizes the calculated diffusion induced mass transport at τ-, σ-, and z-directions for selection locations. As can readily be seen, the magnitude of the mass transport due to diffusion at z-direction was much larger than that at τ- and σ-directions.

Table S1. Calculated diffusion induced mass transport at τ-, σ-, and z-directions for some selected points

	Position	Diffusion (kg/s)	D_z/D_σ	(x,y,z) m
τ	0	1.35E-05	-2.16E+04	(0, 2E-3, 1E-5)
σ	2.356194	-2.45E-05		
z	1.00E-05	5.30E-01		
τ	0	1.35E-05	-2.16E+04	(0, -2E-3, 1E-5)
σ	3.926991	-2.45E-05		
z	1.00E-05	5.30E-01		
τ	-1	4.72E-05	-6.10E+04	(-2.6E-3, 1.5E-3, 1E-5)
σ	2.356194	-3.33E-05		
z	1.00E-05	2.03E+00		
τ	-1	8.25E-89	2.35E+05	(-2.6E-3, 1.5E-3, 1E-4)
σ	2.356194	8.08E-91		
z	1.00E-04	1.90E-85		
τ	-1	9.10E-06	-6.51E+03	(-2.6E-3, 1.5E-3, 1E-5)
σ	2.356194	-4.30E-05		
z	1.00E-05	2.80E-01		
τ	0	1.40E-06	-2.11E+03	(0, 1.5E-3, 1E-6)
σ	2.356194	-2.70E-06		
z	1.00E-06	5.70E-03		

The following Matlab code was used to numerically calculate the mass transport due to diffusion shown above.

```
function y = Diffusion(x1,x2,x3)
%x1=tao, x2=sigma, x3=z
%y1,y2,y3: diffusion at x1,x2,x3
c0=500;
a=0.005;
Q=2.5E-9;
b=0.64E-3;
D=5.45E-12; %diffusion coefficient for 90-nm partilces
gamma=0.893; %Gamma(4/3)
K=Q/pi/b;
s=0;%s=S/a^2
m=0;%m=ds/dx2
n=0;%n=dm/dx2
dx1=0.01;
      for   i=-30:dx1:x1
            s=s+1/(cosh(i)-cos(x2))^2;
            m=m-2/(cosh(i)-cos(x2))^3*sin(x2);
            n=n+6/(cosh(i)-cos(x2))^4*sin(x2)*sin(x2)-2/(cosh(i)-cos(x2))^3*cos(x2);
      end
S=dx1*s*a^2;
M=dx1*m*a^2;
N=dx1*n*a^2;
h=a/(cosh(x1)-cos(x2));
eta=x3*(6*K/9/D/b/S)^(1/3);
etax1=eta/3/S*h^2; %d(eta)/dx1
etax2=eta/3/S*M; %d(eta)/dx2
```

```
y1=1/3/S*etax1-1/3*eta/S^2*h^2+1/3*eta/S/h*(-1)*a/(cosh(x1)-cos(x2))^2*sinh(x1)-
eta^3/S*etax1;
y2=M*eta/h^3/3/S*a/(cosh(x1)-cos(x2))^2*sin(x2)+etax2*M/h^2/3/S-
M^2*eta/3/h^2/S^2+N*eta/h^2/3/S-eta^3*M*etax2/h^2/S;
y3=-3*eta^4/x3^2;
y=-1*D*[y1 y2 y3]*c0/gamma*exp(-3*eta^3);
end
```

4. List of Variables and Abbreviations

a: the distance from inlet/outlet to center of the QCM chamber, m

b: the depth of the QCM chamber gap, m

c: the mass concentration of nanomedicine in solution, g/m^3

c_0: the mass concentration of nanomedicine in inlet solution, g/m^3

D: diameter of nanomedicine, m

D_c: the diffusion coefficient, m^2/s

h_σ, h_τ: scale factors for σ coordinate and τ coordinate, m

K: $Q/\pi b$, m^2/s

k_B: Boltzmann constant, m^2 kg s^{-2} K^{-1}

k_a: the rate constant of adsorption, m/s

k_r: the rate constant of removal, 1/s

m_s: the mass concentration of nanomedicine in bulk solution, g/m^3

r_1, r_2: distance of a point to two foci F_1 and F_2, m

Q: flow rate of fluid, m^3/s

R: radius of nanomedicine, m

$R(c)$: unknown intrinsic kinetic rate expression for particle adsorption, g/m^2s

S: the sweep area from $\tau = -\infty$ (inlet) to $\tau = \tau$ with the width of $h_\sigma d\sigma$, m^2

T: temperature, K

t: time, s

u: $z\times[6Kd\sigma/(9bDS)]1/3$, similarity variable used for solving Equation 17

v_σ, v_τ, v_z: fluid velocities at σ, τ and z coordinate, m/s

η: the fluid viscosity, kg/(m·s)

θ: the ratio of non-deformed to total nanomedicine mass on the surface of the sensor ($\theta=\Gamma_\alpha/\Gamma$).

Γ_α: the concentration of α-particles (reversibly bound particles) on the sensor surface, g/m^2

Γ: the concentration of nanomedince on the sensor surface, g/m^2

Γ^*: the maximum surface concentration of nanomedicine that can cover the surface, g/m^2