Supporting Information

Study on the Diffusion-Dominated Solid-Phase Microextraction Kinetics in Semi-Solid Sample Matrix

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Text S1. Derivation of eq. 3 in the main text. Due to the continuity of the mass flux through every cylinder cross section coaxial to the fiber in the fiber coting and the diffusion domain, we get,

$$C_s(r,t) = \frac{\ln r - \ln R_0}{\ln\frac{R_0+2\sqrt{D_s t}}{R_0}} C_{s,0} + \frac{\ln\left(R_0+2\sqrt{D_s t}\right) - \ln r}{\ln\frac{R_0+2\sqrt{D_s t}}{R_0}} \frac{C_f(R_0,t)}{K},\ R_0 \le r \le R_0 + 2\sqrt{D_s t} \qquad \text{(S1)}$$

and

$$C_f(r,t) = \frac{\ln r - \ln r_0}{\ln\frac{R_0}{r_0}} C_f(R_0,t) + \frac{\ln R_0 - \ln r}{\ln\frac{R_0}{r_0}} C_f(r_0,t),\ r_0 \le r \le R_0 \qquad \text{(S2)}$$

Replace eq S1 and eq S2 in eq 1 and eq 2 respectively, and combine eqs 1 and 2, the mass flux towards the SPME fiber can be expressed as,

$$\frac{dn}{dt} = 2\pi L D_s \frac{C_{s,0} - \frac{C_f(R_0,t)}{K}}{\ln\frac{R_0+2\sqrt{D_s t}}{R_0}} = 2\pi L D_f \frac{C_f(R_0,t) - C_f(r_0,t)}{\ln\frac{R_0}{r_0}} \qquad \text{(S3)}$$

Besides, the extracted amount in the fiber coating can be expressed by integrating the concentration of the analyte in the fiber coating,

$$n = \int_{r_0}^{R_0} 2\pi r L C_f(r,t)\, dr \qquad \text{(S4)}$$

Combining eqs S2, S3 and S4, the mass flux towards the fiber can be expressed as,

$$\frac{dn}{dt} = \frac{2\left(KV_f C_{s,0} - n\right)}{\frac{K(R_0^2 - r_0^2)\ln\frac{R_0+2\sqrt{D_s t}}{R_0}}{D_s} + \frac{R_0^2 - r_0^2 - 2r_0^2\ln\frac{R_0}{r_0}}{2D_f}} \qquad \text{(S5)}$$

where V_f is the volume of the fiber coating, $V_f = \pi L(R_0^2 - r_0^2)$. Then, the extracted amount in the fiber coating when the sampling reaches equilibrium can be expressed as $n_e = V_f K C_{s,0}$. Define $A = \frac{D_s\left(R_0^2 - r_0^2 - 2r_0^2\ln\frac{R_0}{r_0}\right)}{2KD_f\left(R_0^2 - r_0^2\right)}$ and $\alpha = \ln\frac{R_0+2\sqrt{D_s t}}{R_0} + A$, then, integrating eq S5, we can get eq. 3 in the main text.

Text S2. Derivation of eq. 4 in the main text. The mass flux during desorption is a function of time, which can be expressed according to Fick's first law of diffusion as follows:

$$J(t) = \frac{dq}{dt} = 2\pi r L D_s \frac{\partial C_s(r,t)}{\partial r},\ R_0 \le r \le R_0 + 2\sqrt{D_s t} \qquad \text{(S6)}$$

$$J(t) = \frac{dq}{dt} = 2\pi r L D_f \frac{\partial C_f(r,t)}{\partial r},\ r_0 \le r \le R_0 \qquad \text{(S7)}$$

where q is the residual amount in the fiber coating, L is the length of the fiber coating, r_0 and R_0 are the radii of the SSW core and the fiber, respectively, D_s and D_f are the diffusion coefficients in sample matrix and fiber coating, respectively, and $C_s(r,t)$ and $C_f(r,t)$ are the concentration in the sample matrix and in the fiber coating at a distance of r to the axis of the fiber after deploying the fiber in the sample matrix for a duration of t.

Also, K the partition coefficient between the fiber coating and the sample matrix, $K = \frac{C_f(R_0,t)}{C_s(R_0,t)}$. And the original analyte concentration in the sample matrix is zero. Then,

$$C_s(r,t) = \frac{\ln\left(R_0+2\sqrt{Dt}\right)-\ln r}{\ln\left(R_0+2\sqrt{Dt}\right)-\ln R_0}\frac{C_f(R_0,t)}{K},\ R_0 \le r \le R_0 + 2\sqrt{D_s t} \qquad \text{(S8)}$$

and

$$C_f(r,t) = \frac{\ln r-\ln r_0}{\ln R_0-\ln r_0}C_f(R_0,t) + \frac{\ln R_0-\ln r}{\ln R_0-\ln r_0}C_f(r_0,t),\ r_0 \le r \le R_0 \qquad \text{(S9)}$$

Replace eq S8 and eq S9 in eq S6 and eq S7, respectively, and combine eq S6 and eq S7, we get,

$$\frac{dq}{dt} = 2\pi L D_s \frac{-\frac{C_f(R_0,t)}{K}}{\ln\frac{R_0+2\sqrt{Dt}}{R_0}} = 2\pi L D_f \frac{C_f(R_0,t)-C_f(r_0,t)}{\ln\frac{R_0}{r_0}} \qquad \text{(S10)}$$

Besides, the residual amount from the fiber coating can be expressed as follows:

$$q = \int_{r_0}^{R_0} 2\pi r L C_f(r,t)dr \qquad \text{(S11)}$$

Then, combine eqs S9, S10 and S11, we get,

$$\frac{C_f(R_0,t)}{K} = \frac{q}{\pi L\left(K\left(R_0^2-r_0^2\right)+\frac{D_s\left(R_0^2-r_0^2-2r_0^2\ln\frac{R_0}{r_0}\right)}{2D_f\ln\frac{R_0+2\sqrt{Dt}}{R_0}}\right)} \qquad \text{(S12)}$$

Replace eq S12 in eq S10, we get,

$$\frac{dq}{dt} = -\frac{2\pi L D_s q}{\pi L\left(K\left(R_0^2-r_0^2\right)+\frac{D_s\left(R_0^2-r_0^2-2r_0^2\ln\frac{R_0}{r_0}\right)}{2D_f\ln\frac{R_0+2\sqrt{Dt}}{R_0}}\right)} \qquad \text{(S13)}$$

Then, integrating eq S13,

$$\frac{q}{q_0} = \exp\left\{-\frac{R_0^2}{K\left(R_0^2-r_0^2\right)}\left[\sum_{n=1}^{\infty}\frac{\left(2^n e^{-2A}-e^{-A}\right)\left(\alpha^n-A^n\right)}{n\cdot n!}-\left(e^{-2A}-e^{-A}\right)\ln\frac{\alpha}{A}\right]\right\} \qquad \text{(S9)}$$

where q_0 is the amount originally loaded in the fiber coating, $A = \frac{D_s\left(R_0^2-r_0^2-2r_0^2\ln\frac{R_0}{r_0}\right)}{2KD_f\left(R_0^2-r_0^2\right)}$

and $\alpha = \ln\frac{R_0+2\sqrt{D_s t}}{R_0} + A$.

Text S3. Chemicals and materials. Fluoxeitne (FLX) and norfluoxetine (NFLX) were purchased from Toronto Research Chemical Inc. (New York, ON, Canada). Tolfenamic acid (TOLF) and mefenamic acid (MEF) were purchased from Tokyo Chemical Industry Co. Ltd. (Tokyo, Japan). Stainless steel wires (SSWs, 200 μm in diameter, medical grade) were purchased from Small Parts Inc. (Miami Lakes, FL, USA). Polydimethylsiloxane (PDMS) tube (i.d. 212 μm, o.d. 300 μm) was purchased from Helixmark (Carpinteria, CA, USA). Agarose powder and HPLC grade methanol were purchased from Sigma-Aldrich Co. Ltd. (St. Louis, MO, USA). Sodium azide was purchased from Tianjin Fuchen Chemical Reagents Factory (Tianjin, China). Unless with specific statement, other reagents were all purchased from Guangzhou Chemical Factory (Guangzhou, China).

Preparation of SPME fibers. Custom-made PDMS fibers were prepared as follows: Briefly, SSWs were cut into pieces of about 3 cm, and cleaned by sonication in acetone and deionized water for 15 min respectively. After the well-cut PDMS tubes (1.0 cm) were swelled in hexane for half a minute at room temperature, the PDMS tubes were wore on the SSWs. Prior to use, the freshly prepared PDMS fibers were cleaned in methanol for 30 min.

Extraction and desorption in agarose gel. Agarose powder was dissolved in phosphate buffer saline (PBS) solution (pH=7.3, containing 0.1% sodium azide) by heating in water bath at 90 ℃ for half an hour. After the solution (containing 0.8% w/v agarose) cooled down to about 50 ℃, stock solution of the analytes (1000 $\mu g \cdot mL^{-1}$ for each analyte, in methanol) was spiked in agar solution, and the final

concentration of each analyte was 100 ng·mL^{-1}. Then, the solution was transferred to 10 mL sample vials with an aliquot of 8.0 mL of the spiked solution in each vial. Subsequently, the vials were sealed with polytetrafluoroethylene septum by using stainless steel caps. After the agarose gel solidified thoroughly at room temperature, the caps were removed, and the custom-made PDMS fibers were deployed in agar gel with one piece of fiber in each vial for extracting the target analytes.

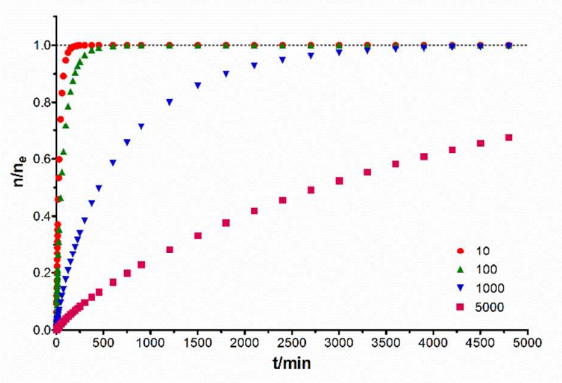
The desorption experiment was similar to the extraction experiment, except that PDMS fibers were previously loaded in the aqueous solutions of the analytes (400 ng·mL^{-1} for each analyte) for 36 h, and subsequently desorbed in blank agarose gel without previously spiking analytes in it. All the extraction and desorption experiments were conducted under room temperature.

Partition coefficients between fiber coating and agarose gel. In the previous study (*Anal. Chim. Acta* **2012**, *742*, 2-9), the equilibrium extraction amounts of pharmaceuticals from PBS solution and agarose gel were nearly the same, which indicated that the partition coefficients between fiber coating and PBS solutions are equal to those between fiber coating and agar gel. Equilibrium extraction was conducted in PBS solutions (100 ng·mL^{-1} for each analyte) for 80 h under vortex. The partition coefficients of the analytes were calculated as the ratios of the concentrations of the analytes in fiber coating and PBS solution at equilibrium.

Instrumental analysis. Instrumental analysis was referred to our previous study (*Anal. Chem.* **2015**, *87*, 3453-3459) without any modification.

Figure S1. SPME kinetics under different K, where $D_s = 5 \times 10^{-10}$ m^2 s^{-1}, $D_s/D_f = 1000$ (A); SPME kinetics under different D_s, where $K = 100$, $D_s/D_f = 1000$ (B); and SPME kinetics under different D_s/D_f, where $K = 100$, $D_s = 5 \times 10^{-10}$ m^2 s^{-1} (C). In all the modelling, $R_0 = 150$ μm and $r_0 = 106$ μm.

A)



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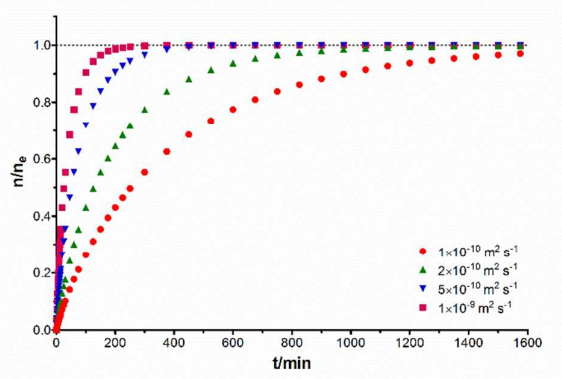

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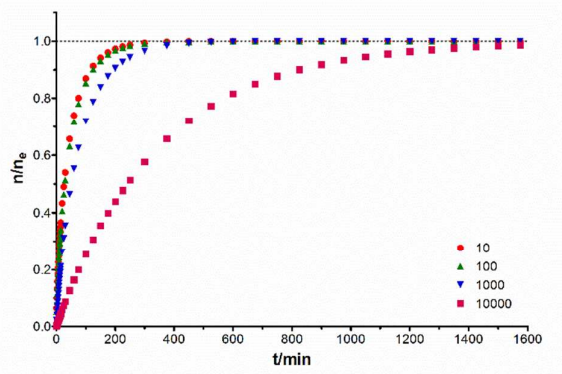
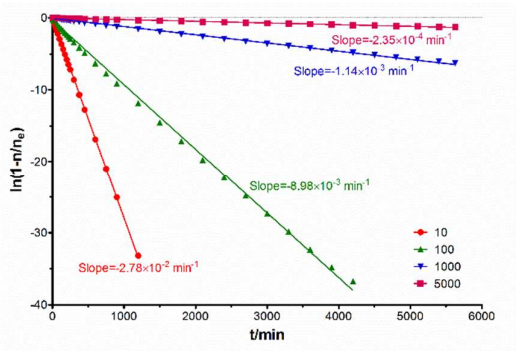
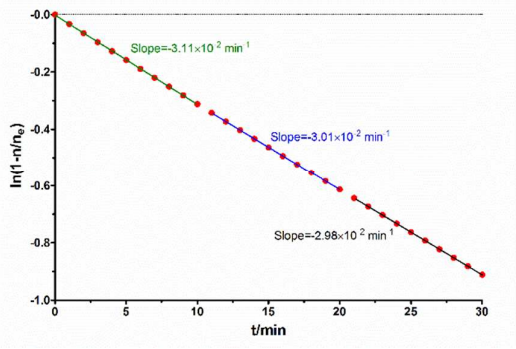


Figure S2. Plots of $\ln(1 - n/n_e)$ to t by varying K. The full view (A) and the view of the first 30 min (B-E); $K = 10$ (B), $K = 100$ (C), $K = 1000$ (D), and $K = 5000$ (E).

A) B)





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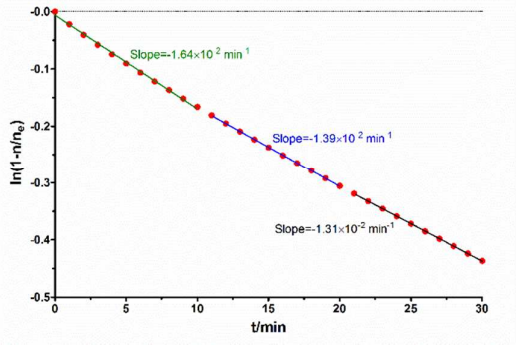

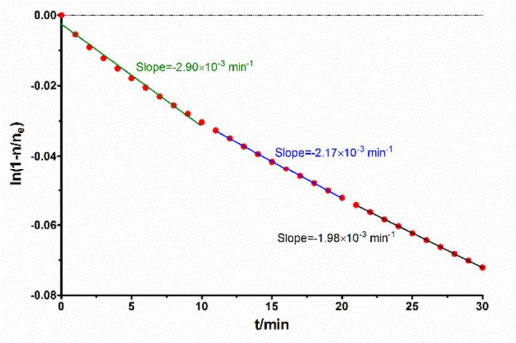
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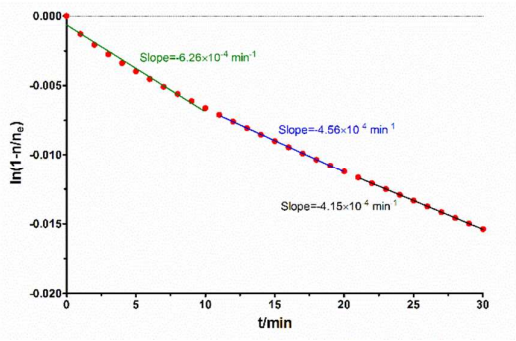
ln(1-n/ne)
t/min

E)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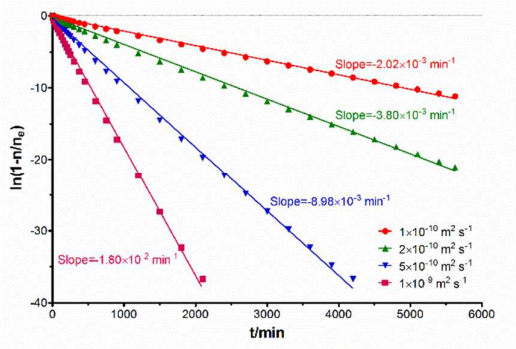
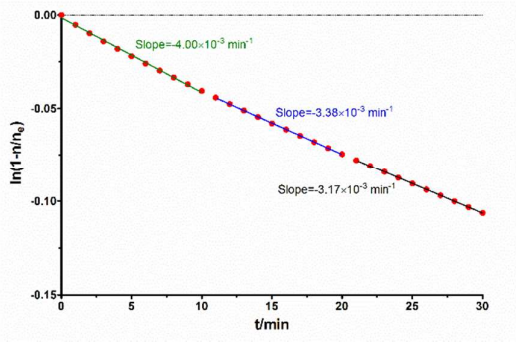
ln(1-n/ne)
t/min

Figure S3. Plots of $\ln(1-n/n_e)$ to t by varying D_s. The full view (A) and the view of the first 30 min (B-E); $D_s = 1\times10^{-10}$ m^2 s^{-1} (B), $D_s = 2\times10^{-10}$ m^2 s^{-1} (C), $D_s = 5\times10^{-10}$ m^2 s^{-1} (D), and $D_s = 1\times10^{-9}$ m^2 s^{-1} (E).

A) B)





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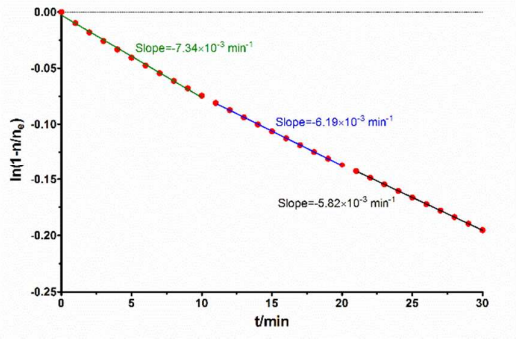

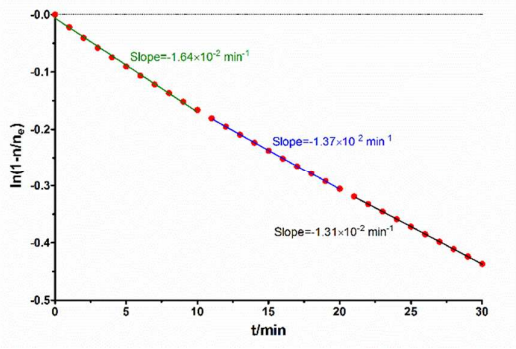
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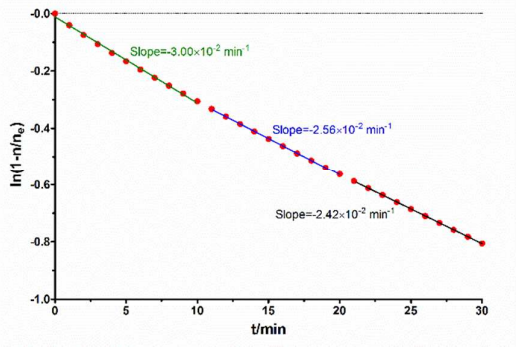
ln(1-n/ne)
t/min

E)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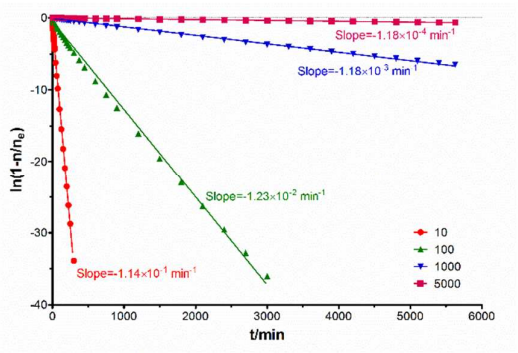
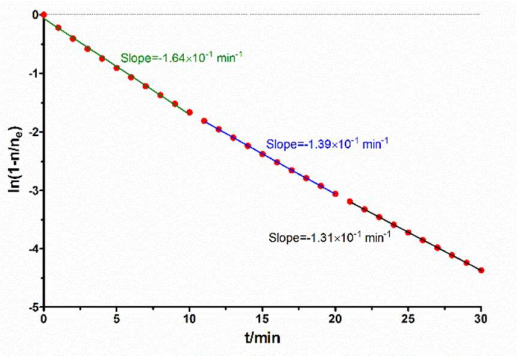
Slope=-2.42×10-2 min-1
ln(1-n/ne)
t/min

Figure S4. Plots of $\ln(1-n/n_e)$ to t by varying D_s/D_f. The full view (A) and the view of the first 30 min (B-E); $D_s/D_f = 10$ (B), $D_s/D_f = 100$ (C), $D_s/D_f = 1000$ (D), and $D_s/D_f = 10000$ (E).

A) B)





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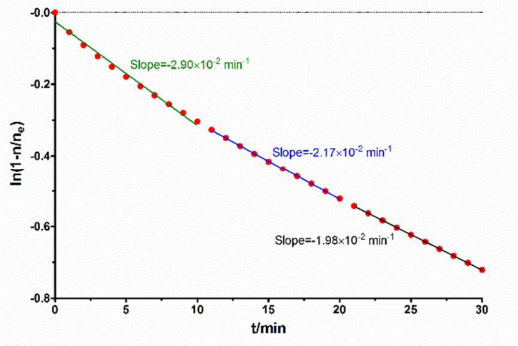

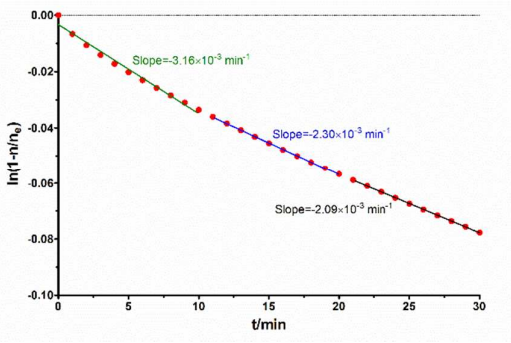
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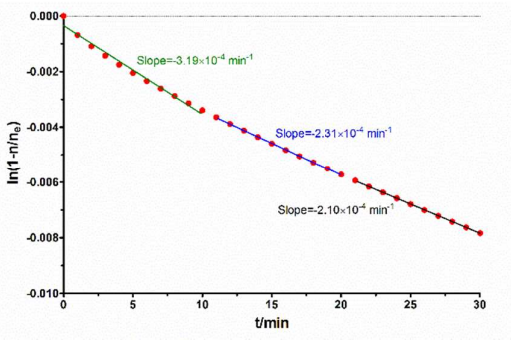
Slope=-2.09×10-3 min-1
ln(1-n/ne)
t/min

E)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Slope=-2.10×10-4 min-1
ln(1-n/ne)
t/min

Figure S5. Extraction and desorption time profiles of NFLX in agarose gel (A), and plots of $\ln\left(1-\frac{n}{n_e}\right)$ to time for NFLX (B); Extraction and desorption time profiles of MEF in agarose gel (C), and plots of $\ln\left(\frac{q}{q_0}\right)$ to time for MEF (D); Extraction and desorption time profiles of FLUFEN in agarose gel (E), and plots of $\ln\left(\frac{q}{q_0}\right)$ to time for FLUFEN (F). Error bars represent the standard deviations (n=3).

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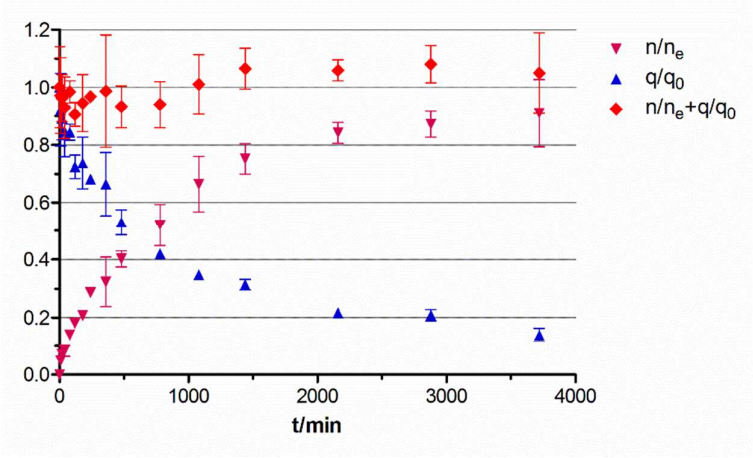

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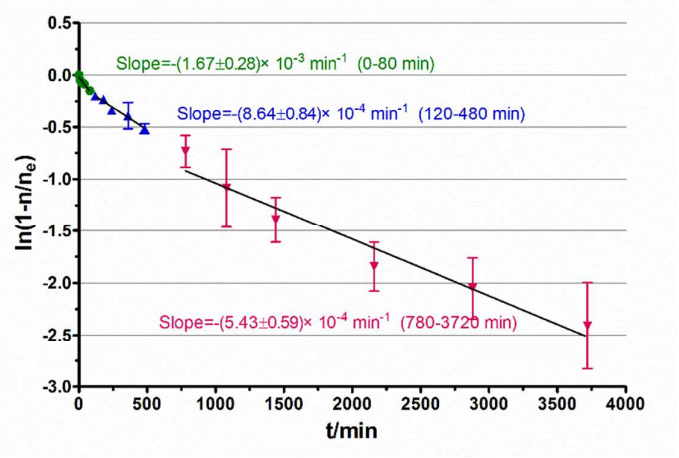

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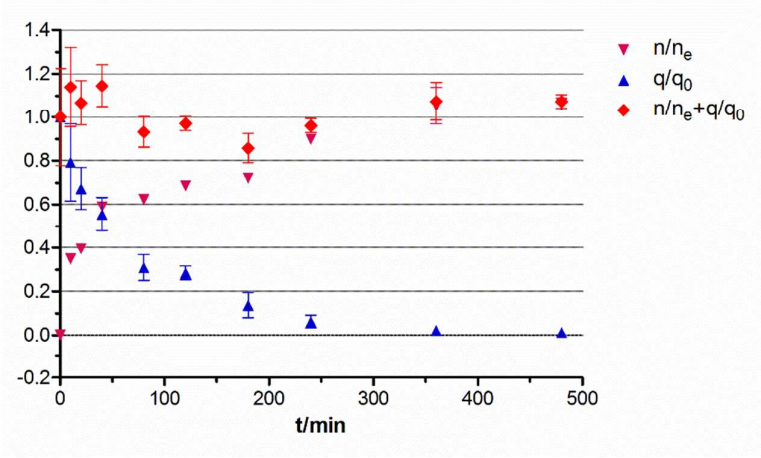
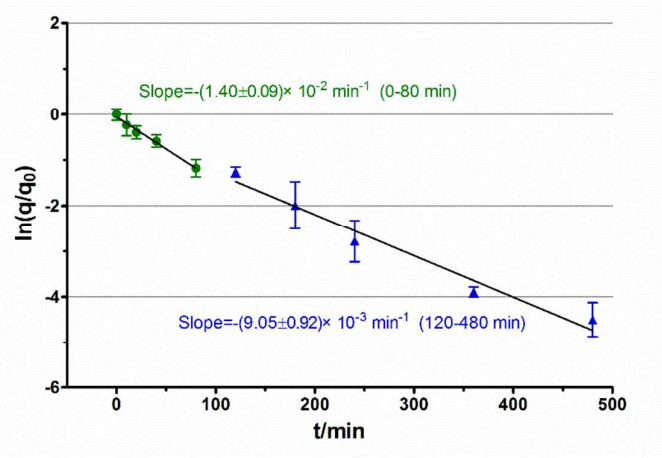

n/n$_e$
q/q$_0$
n/n$_e$+q/q$_0$
t/min

D)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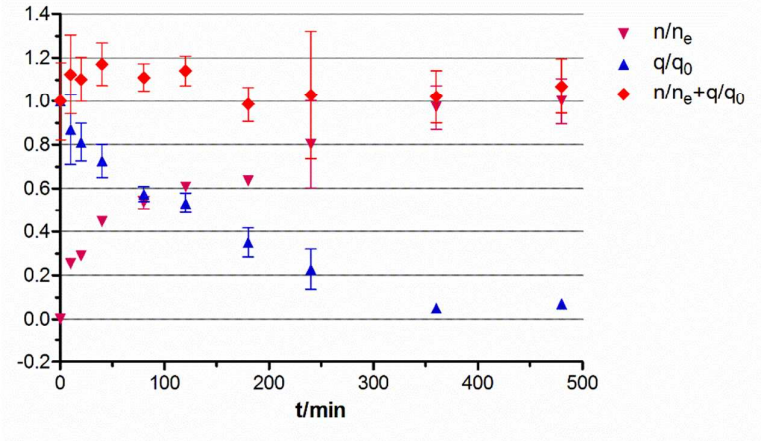
Slope=-(9.05±0.92)× 10^{-3} min^{-1} (120-480 min)
ln(q/q$_0$)
t/min

E)


n/n$_e$
q/q$_0$
n/n$_e$+q/q$_0$
t/min

F)

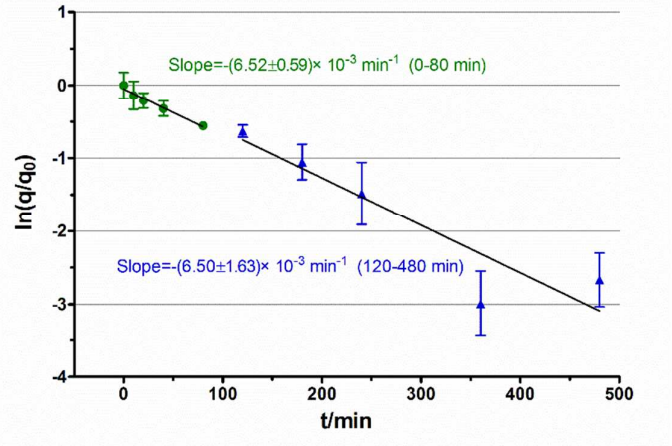
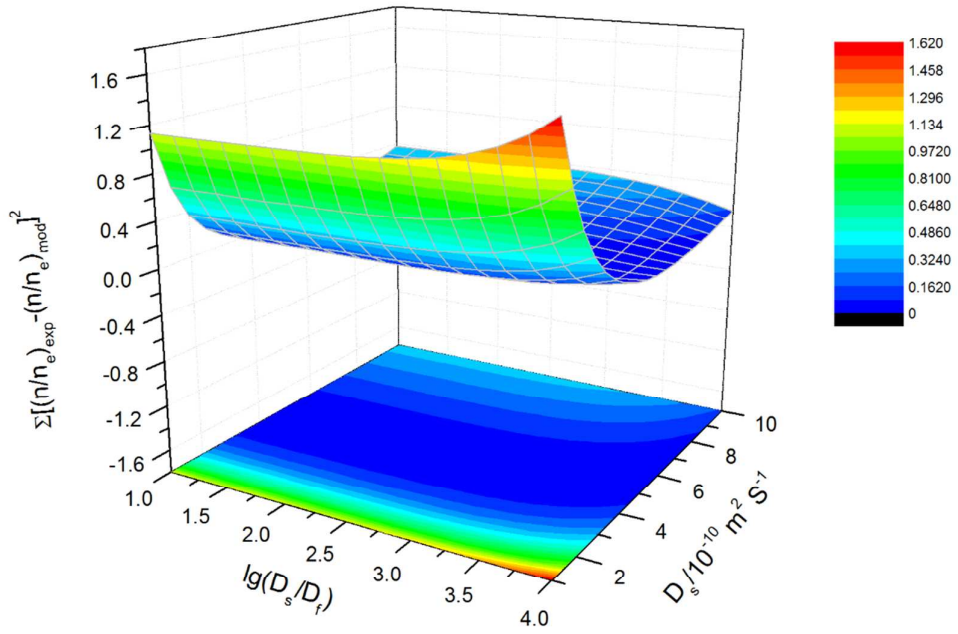
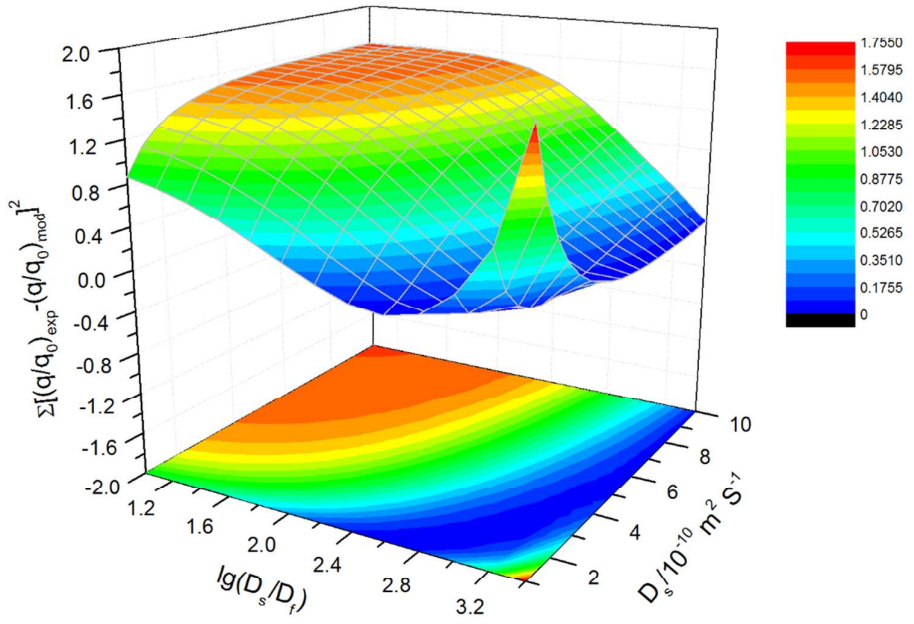

Slope=-(6.52±0.59)× 10^{-3} min^{-1} (0-80 min)
Slope=-(6.50±1.63)× 10^{-3} min^{-1} (120-480 min)
ln(q/q$_0$)
t/min

Figure S6. Fitting of the experimental result of extracting NFLX from agarose gel (A), fitting of the experimental results of desorption of MEF (B) and FLUFEN (C) preloaded in fibers to agarose gel, by varying D_s from 1×10^{-10} m^2 s^{-1} to 1×10^{-9} m^2 s^{-1} with the step length of 5×10^{-11} m^2 s^{-1}, and $\lg(D_s/D_f)$ from 1 to 4 with the step length of 0.2. The subscripts "exp" and "mod" refer to the experimental results in the agarose gel, and the corresponding results estimated from the mathematical model, respectively.

A)



B)


2.0
1.6
1.2
0.8
0.4
0.0
-0.4
-0.8
-1.2
-1.6
-2.0
$\Sigma[(q/q_0)_{exp}-(q/q_0)_{mod}]^2$
1.2
1.6
2.0
2.4
2.8
3.2
$lg(D_s/D_f)$
2
4
6
8
10
$D_s/10^{-10}\ m^2\ S^{-1}$
1.7550
1.5795
1.4040
1.2285
1.0530
0.8775
0.7020
0.5265
0.3510
0.1755
0

C)

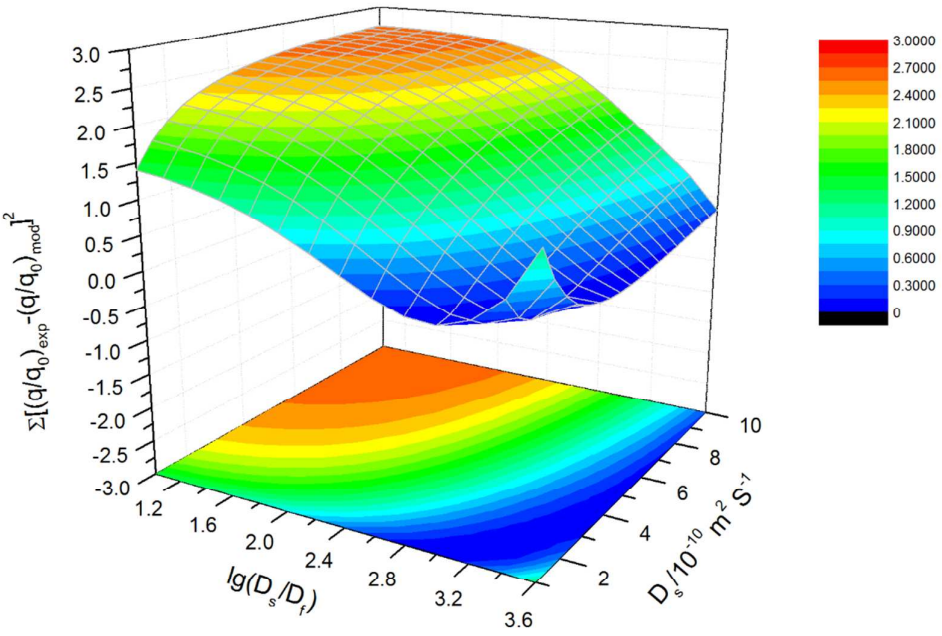
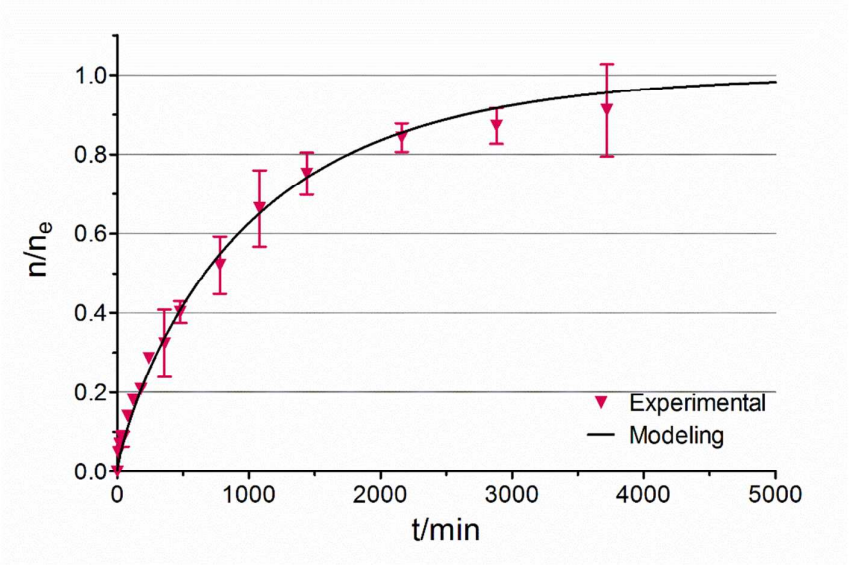
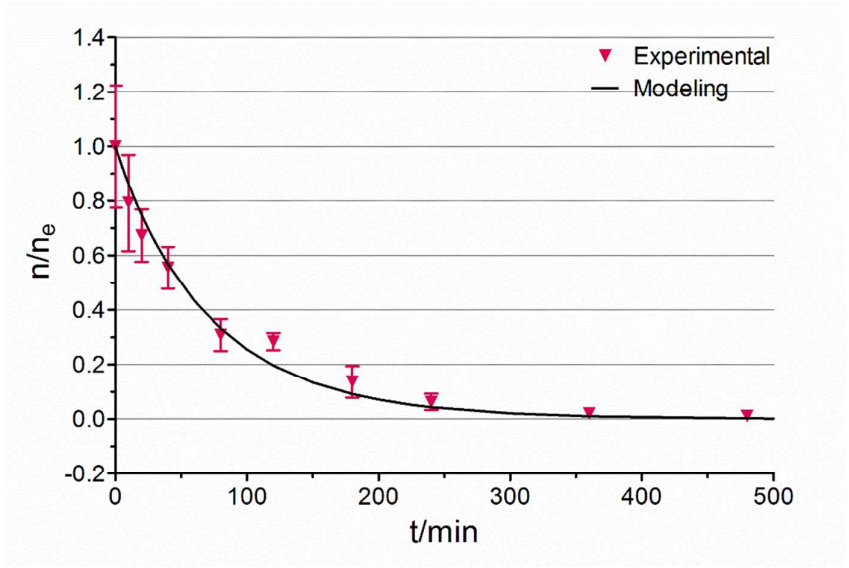

3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
-2.0
-2.5
-3.0
$\Sigma[(q/q_0)_{exp}-(q/q_0)_{mod}]^2$
1.2
1.6
2.0
2.4
2.8
3.2
3.6
$lg(D_s/D_f)$
2
4
6
8
10
$D_s/10^{-10}\ m^2\ S^{-1}$
3.0000
2.7000
2.4000
2.1000
1.8000
1.5000
1.2000
0.9000
0.6000
0.3000
0

Figure S7. Comparison of the experimental results with the modeled time profiles with the best fitting diffusion coefficients for the extraction of NFLX from the agarose gel (A), the desorption of preloaded MEF from the fiber (B), and the desorption of preloaded FLUFEN from the fiber (C).

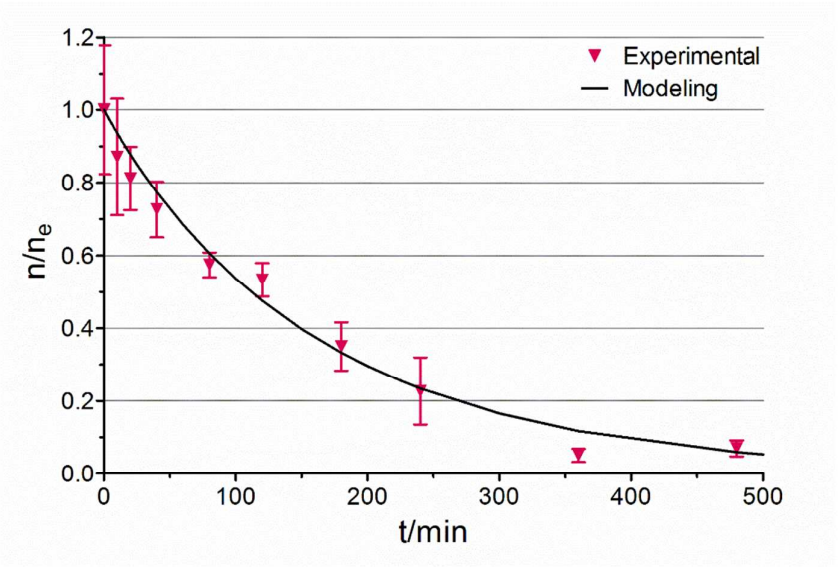
A)



B)



C)


Experimental
Modeling
n/n_e
t/min
0.0
0.2
0.4
0.6
0.8
1.0
1.2
0
100
200
300
400
500