Supporting Information

Host-Guest Induced Chiral Amplification in Highly-Selective Nano-sensing

Zhuo Liu[†], Siyun Zhang[‡], Ming Cheng[‡], Lei Yang[‡], Guang Li[‡], Weiwei Xu[‡], Haonan Qu[‡], Feng Liang[†], Jing Cheng[*‡] and Haibing Li[*‡]*

[†]. The State Key Laboratory of Refractories and Metallurgy, School of Chemistry & Chemical Engineering, Wuhan University of Science and Technology, Wuhan 430081, China

[‡]. Key Laboratory of Pesticide and Chemical Biology (CCNU), Ministry of Education, College of Chemistry, Central China Normal University, Wuhan 430079, Hubei Province, P. R. China

E-mail: feng_liang@whu.edu.cn

chengjingok@mail.ccnu.edu.cn

lhbing@mail.ccnu.edu.cn

Contents of Supporting Information:

1.Materials.

Poly ethylene terephthalate (PET, 12 μm thick) membranes were irradiated with Au ions of 11.1 MeV/nucleon kinetic energy at the UNILAC linear accelerator (GSI, Darmstadt, Germany). 1-Ethyl-3-(3-dimethyllaminopropyl) carbodiimide hydrochloride(EDC·HCl,≥99.0%),N-hydroxysulfosuccinimide (NHS,≥98.0%),R-phenylethylamine(R-PEA),sodium hydroxide(NaOH),methanoic acid (HCOOH), potassium chloride(KCl), sodium hydrogen phosphate($Na_2HPO_4·12H_2O$), sodium dihydrogen phosphate(NaH_2PO_4) were purchased from Sinopharm Chemical Reagent Shanghai Co., Ltd. (SCRC, China). All chemical reagents were used as received. electrolyte solution was prepared in MilliQ water (18.2 MΩ). Current-voltage curves were measured by a Keithley 6487 picoammeter (Keithley Instruments, Cleveland, OH). Contact Angle is measured by OCA 20 Contact Angle Tester. Scanning electron microscopy (SEM) images were recorded using a JSM-6700F Scanning electron microscope.

2. Synthesis of WAP5.

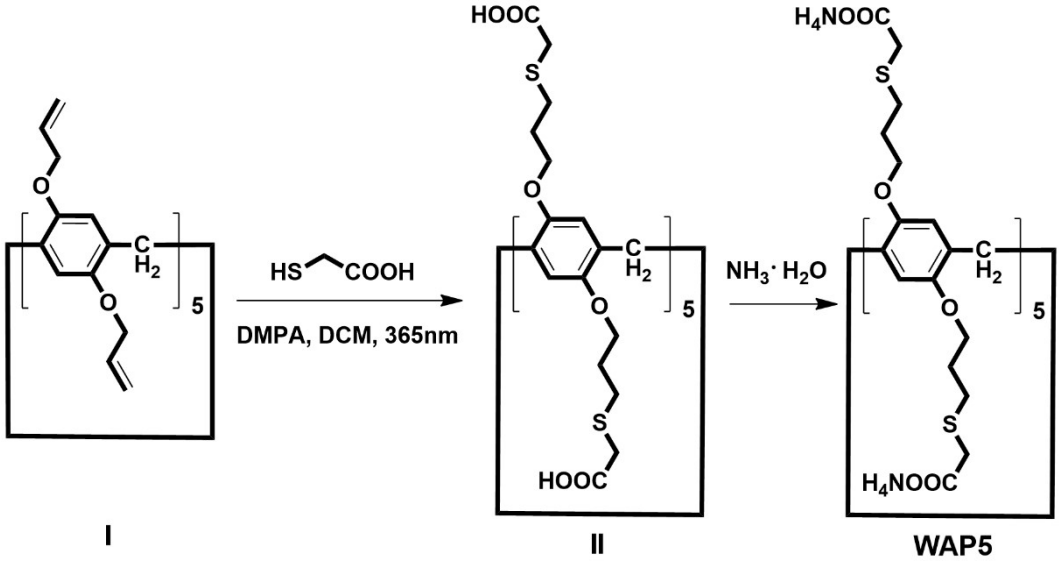

Figure S1. Synthetic routes of WAP5

Synthesis of II

Ammonium salts of the water-soluble Pillar[5]arene are used in our work. As shown in Figure S1, In a 100mL three-neck flask, Pillar[5]arene Ⅰ (100 mg, 0.1 mmol), thioglycolic acid (368 mg, 4 mmol) and photoinitiator 2, 2-dimethoxy-2-phenylacetophenone DMPA (50mg, 0.2 mmol) were added. Add 40 mL DCM, stir to dissolve in N2 atmosphere. The mixture reacted for 0.5 h in nitrogen atmosphere and 365nm UV light. Excess thioglycolic acid (25mL×3) was washed with saturated salt. The organic phase was dried with anhydrous magnesium sulfate and the solvent was removed by decompression. The residue was separated and purified by column chromatography (dichloromethane/methanol, V/V =4/1), and 0.15 g white solid was obtained with a yield of 78%.1H NMR (400 MHz, DMSO) δ (ppm): 12.53 (s, 10H , COOH), 6.80 (s, 10H , Ar-H), 4.06, 3.66(m, 20H , HOOC-CH_2), 3.80 (s, 10H, Ar-CH_2), 3.28-3.23 (m, 20H, OCH_2), 2.88-2.82 (m, 20H, S-CH_2), 2.09-2.00 (m, 20H, CH_2-CH_2-CH_2). 13C NMR (100 MHz, DMSO) δ (ppm): 172.08, 149.02, 127.82, 114.12, 66.70, 33.92, 30.66, 28.93, 28.75. MALDI-TOF-MS: Calcd. for m/z: 1930.43. Found: 1953.26 [M+Na]+. Anal. Calcd for $C_{85}H_{110}O_{30}S_{10}$: C, 52.85. H, 5.71. S, 16.58. found: C, 52.80. H, 5.99. S, 16.43.

Synthesis of WAP5

in a 100mL three-necked flask, the Pillar[5]arene Ⅱ (19mg, 1 mmol) modified by carboxyl groups and concentrated ammonia (13.3 mol/L, 5 ml) were dissolved in 10mL methanol and stirred at room temperature for 2 h. The solvent and ammonia were removed at reduced pressure to obtain a light yellow solid 2.01g with a yield of 95%.1H NMR (400 MHz, D_2O) δ (ppm): 6.60 (s, 10H, Ar-H), 3.69 (s, 20H, HOOC-CH_2, s, 10H, Ar-CH_2), 3.09 (m, 20H, O-CH_2), 2.55 (m, 20H, S-CH_2), 1.76 (m, 20H, CH_2-CH_2-CH_2).

3. Experimental

Fabrication of the single conical nanochannel.

We use the asymmetric track-etching technique to prepare the single conical nanochannel in PET membrane (Poly ethylene terephthalate,12 μm thick, GSI, Darmstadt, Germany), which was irradiated with a single heavy ion (Au) of energy 11.4 MeV/nucleon at the UNILAC linear accelerator. Every profile of PET membrane was irradiated with UV light (λ= 365 nm) for 1 hour. Then the PET membrane was immobilized between two tetrafluoroethylene cells of a U-shaped electrolyzer at 35℃. The etching solution (9 M NaOH) was filled in one cell, and the preventing solution (1 M KCl + 1 M HCOOH) was filled in the other. Next, a DC voltage (+1.0 V) was applied across the membrane for monitoring the current during etching. (Figure S4)

Preparation of the chiral host-guest-based nanochannel.

The host-guest system of WAP5 and R-PEA was introduced into an etched nanochannel by two steps. The first step was to modify the etched nanochannel with chiral guest R-PEA, generating the chiral monomolecular functionalized nanochannel (R-PEA channel). The second step was to assembly the achiral macrocyclic host WAP5 on the inner surface of R-PEA channel (Figure S6). First, the etched PET membrane was immersed in a 4mL aqueous solution containing 30 mg 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (EDC) and 6 mg N-hydroxyl-succinimide (NHS) at room temperature for activating the carboxyl groups on the inner surface of etched nanochannel. After 50 minutes, the membrane was rinsed with water and immersed in 1mM R-PEA aqueous solution for 12 hours for chiral modification. Secondly, the R-PEA channel was put into 1mM WAP5 aqueous solution for 3 hours for the self-assemble of host-guest system. Then we tested the properties of chiral host-guest-based nanochannel (R-PEA⊂WAP5 channel) by ion current (I-V curve), contact angle (CA) and X-ray photoelectron spectroscopy (XPS).

Ion Current Measurements.

The PET membrane with chiral nanochannel was immobilized in the U-shaped electrolyzer. Transmembrane ion current was measured by Keithley 6487 picoammter, using Ag/AgCl electrodes and the electrolyte of 0.03 M PBS (pH=7.4). Then a voltage from −2 to +2 V was applied to record the ion current as I-V curves. Each test was repeated 5 times to monitor the average current value at different voltages

4. ^{1}H NMR analysis of interaction of R-PEA and WAP5.

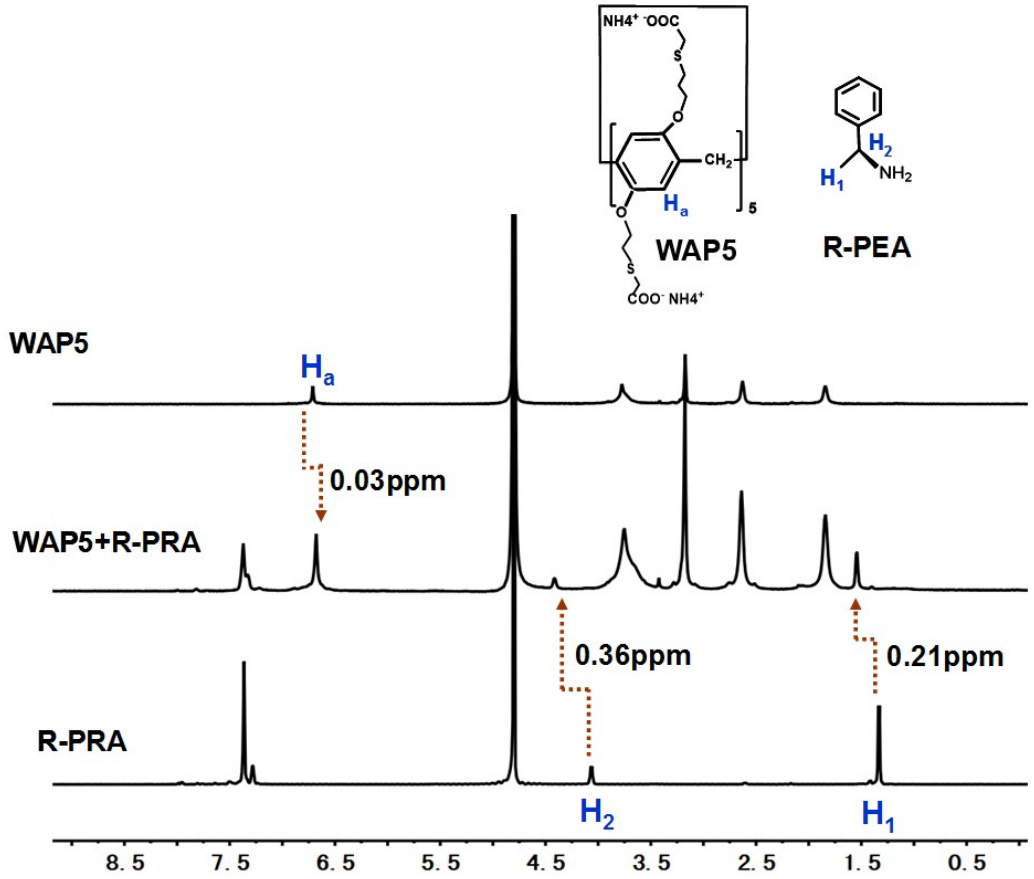

Figure S2. ^{1}H NMR of the interaction of pillar[5]arene with R-PEA

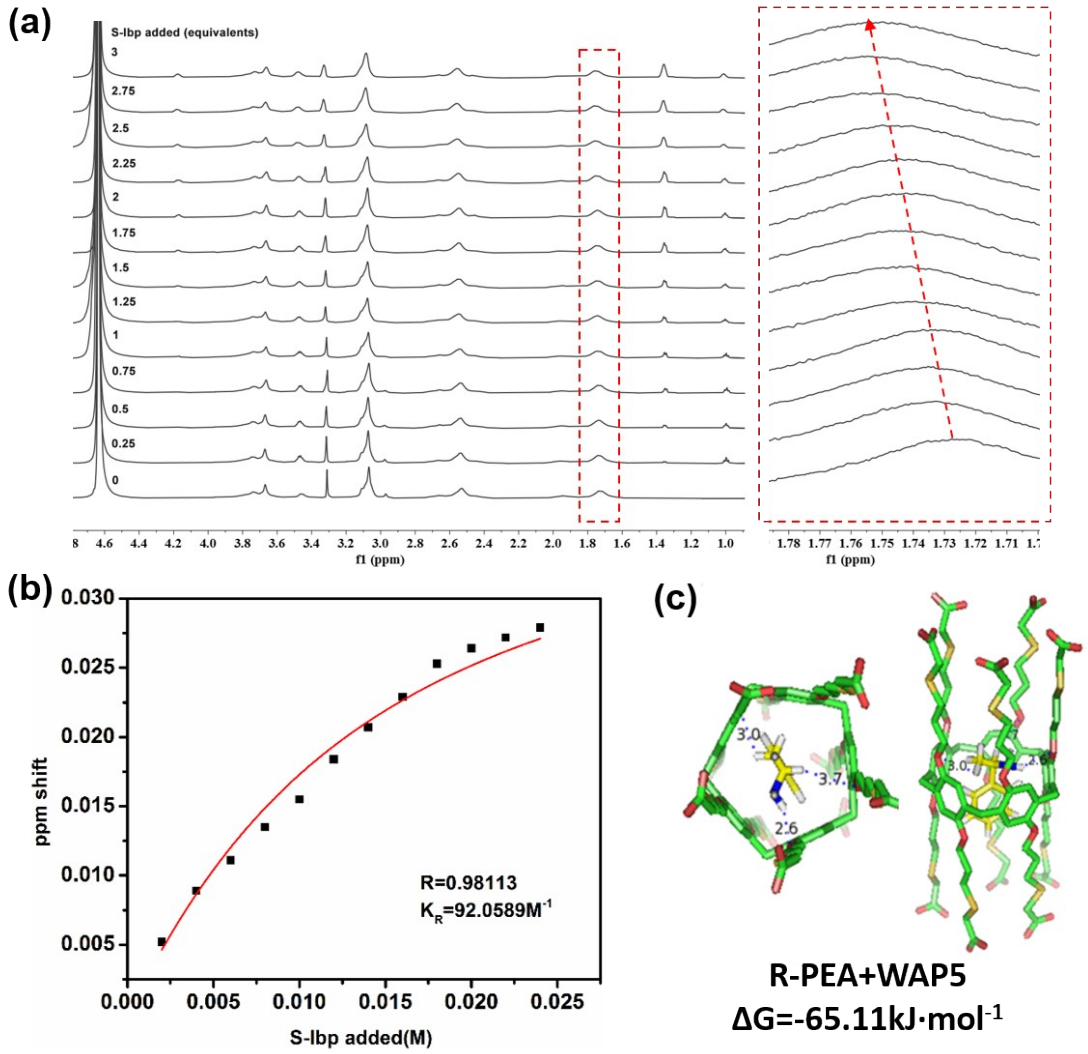

Figure S3. (a) nuclear magnetic titration for host-guest system interaction. (b) The non-linear curve fitting of NMR titrations for the complexation of WAP5 and R-PEA. The association constant (K_R) of WAP5 and R-PEA was calculated to be 92.0589 M^{-1}**.** (c) Gaussian simulation of WAP5 and R-PEA(ΔG=-65.11kJ/mol)**.**

5. Fabrication of nanochannel.

The nanochannels were prepared in a Poly ethylene terephthalate (PET) membrane (Hostaphan RN12 Hoechst, 12μm thick, with 1×10^7 tracks/cm^2) using the ion track etching technique[1,2]. The etching was performed in a conductivity cell at 25 ℃, with the PET membrane separating two-compartments (Figure S4). One side of the cell contained the etchant, (6 M NaOH), while the other side of the cell was filled with a stopping solution (1 M HCOOH+ KCl) that is able to neutralize the etchant as soon as the pore opens, thus significantly slowing down further etching. two compartments of a conductivity cell. For monitoring the etching process, a voltage (1 V) was applied in such a way that the transmembrane ion current can be observed as soon as the nanopores open. The etching process was stopped at a desired current value corresponding to a certain tip diameter. After about 50 min etching, both sides of the membrane were filled with 1 M HCOOH+ KCl solution that stopped the etching process. Finally, the membrane was immersed in MilliQ water (18.2 MΩ) to remove residual salts.

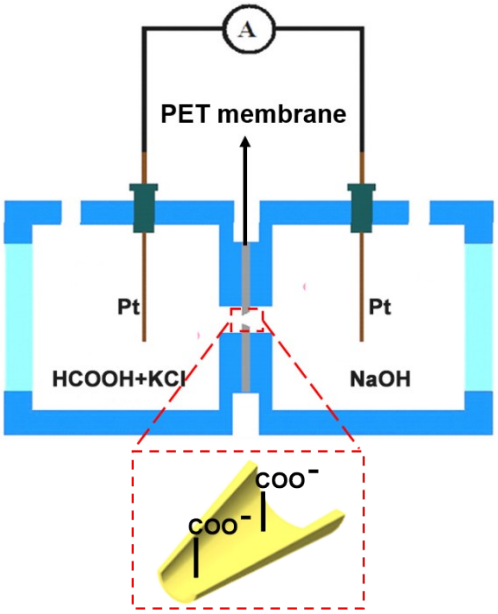

Figure S4. Schematic image for the etching process of nanochannels in a conductivity cell.

6. SEM Characterization.

Scanning electron microscopy (SEM) was used to test the aperture characterization of the bionic nanochannel. SEM can be used to visually observe the mouth end of the conical nano-channel, as shown in Fig S5. The mouth end of the nanochannel is about 560±11nm, which cannot be directly measured due to the small diameter of the mouth end.

$$d_{tip} = \frac{4LI}{\pi k(c)UD}$$

Formula.S1

Under the condition of 25 ℃, where L refers to the length of the nano-channel, namely the thickness of the PET membrane, I is the current value, K is the constant 0.11173 $\Omega^{-1}cm^{-1}$, U is the external field voltage, and D is the diameter of the large mouth end of the nano-channel. DTIP is calculated from this, and the relevant data is put into the following formula, and the small mouth end of the nanochannel is about 20nm

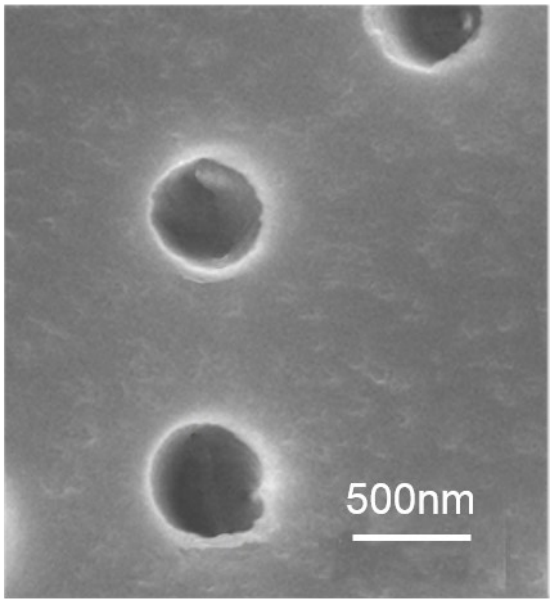

Figure S5. SEM image of the surface of tapered PET membrane.

7. Modification Process.

The host-guest system of WAP5 and R-PEA was introduced into etched nanochannel by two steps. The first step was to modify the etched nanochannel with chiral guest R-PEA, generating the chiral monomolecular functionalized nanochannel (R-PEA channel). The second step was to assembly the achiral macrocyclic host WAP5 on the inner surface of R-PEA channel (Figure S6). First, the etched PET membrane was immersed in 4 mL aqueous solution containing 30 mg 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (EDC) and 6 mg N-hydroxyl-succinimide (NHS) at room temperature for activing the carboxyl groups on the inner surface of etched nanochannel. After 50 minutes, the membrane was rinsed with water and immersed in 1mM R-PEA aqueous solution for 12 hours for chiral modification. Secondly, the R-PEA channel was put into 1mM WAP5 aqueous solution for 3 hours for the self-assemble of host-guest system.

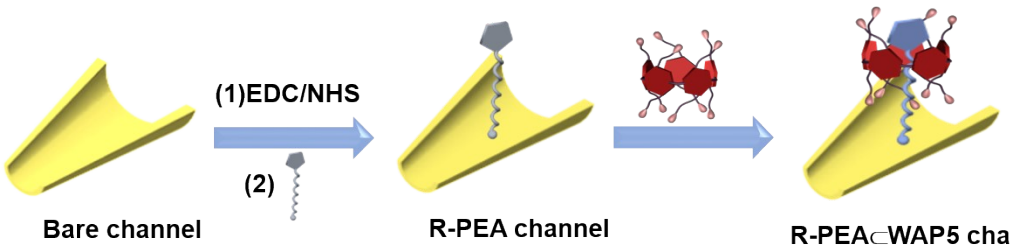

Figure S6. Schematic diagram of the modification method for the R-PEA⊂WAP5 channel.

8. Contact angles and Confocal fluorescence measurements.

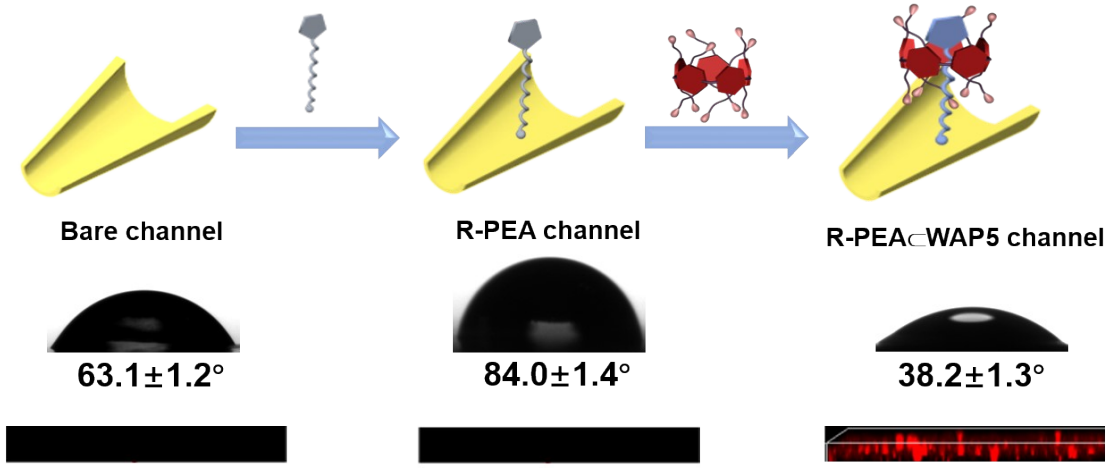

Figure S7. Contact Angle and Confocal fluorescence data of the construction process of R-PEA⊂WP5.

9.XPS characterization.

Before PET membrane was modified, there was no nitrogen element, but after R-PEA was modified, it contained nitrogen element, so the appearance of nitrogen signal peak in PET membrane indicated that the modification of R-PEA was successful. Based on this, WAP5 was continued to be assembled, because WAP5 contained sulfur element. Therefore, the appearance of sulfur signal peak proves the successful assembly of R-PEA⊂WP5 membrane.

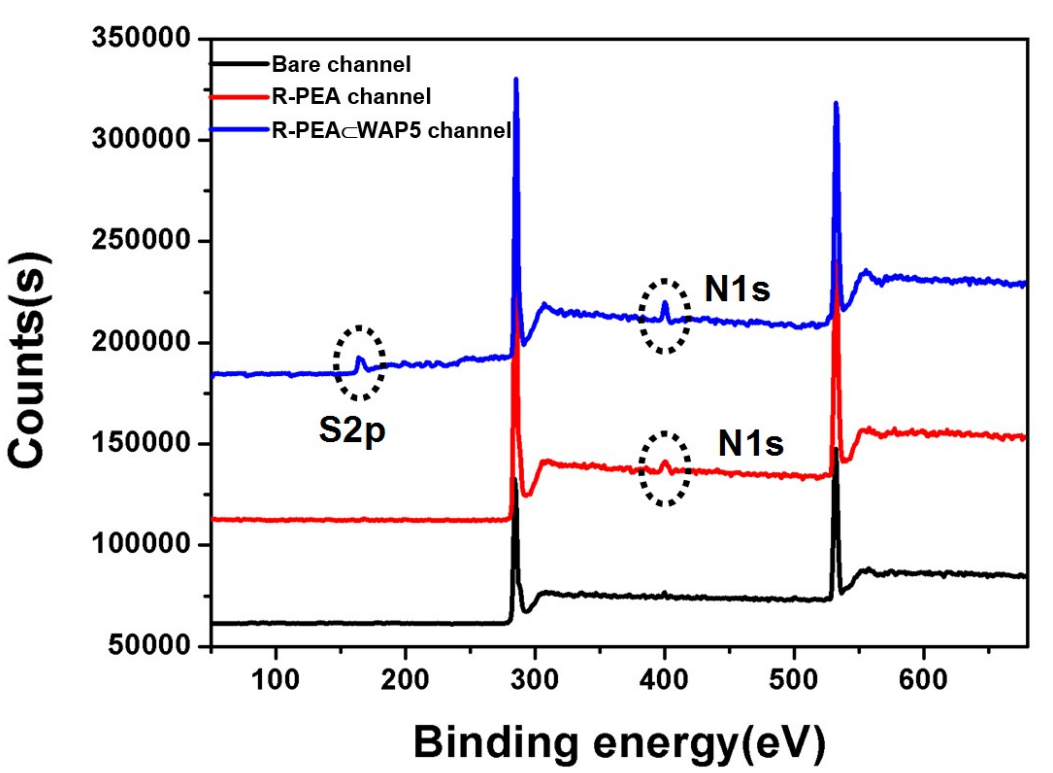

Figure S8. XPS of PET membrane before and after functionalization.

Table S1. XPS data of unmodified PET membrane

Name	Start BE	Peak BE	End BE	Height Counts	Atomic%
C1s	291.32	283.8	281.0	57908.62	75.24
O1s	536.84	534.1	519.8	45715.31	24.76

Table S2. XPS data of modified R-PEA PET membrane

Name	Start BE	Peak BE	End BE	Height Counts	Atomic%

C1s	292.42	285.81	283.42	13287.15	74.12
O1s	535.85	532.63	527.64	9942.8	23.25
N1s	406.01	398.92	397.50	285.42	2.63

Table S3. XPS data of modified WAP5 PET membrane

Name	Start BE	Peak BE	End BE	Height Counts	Atomic%
C1s	292.12	279.68	280.78	13710.12	73.04
O1s	540.28	530.93	529.90	9826.65	22.76
N1s	402.99	398.90	395.80	515.66	2.42
S2p	173.12	164.01	161.23	765.23	1.78

10. I-V curves for NPX recognition using only R-PEA and the R-PEA⊂WP5 membrane.

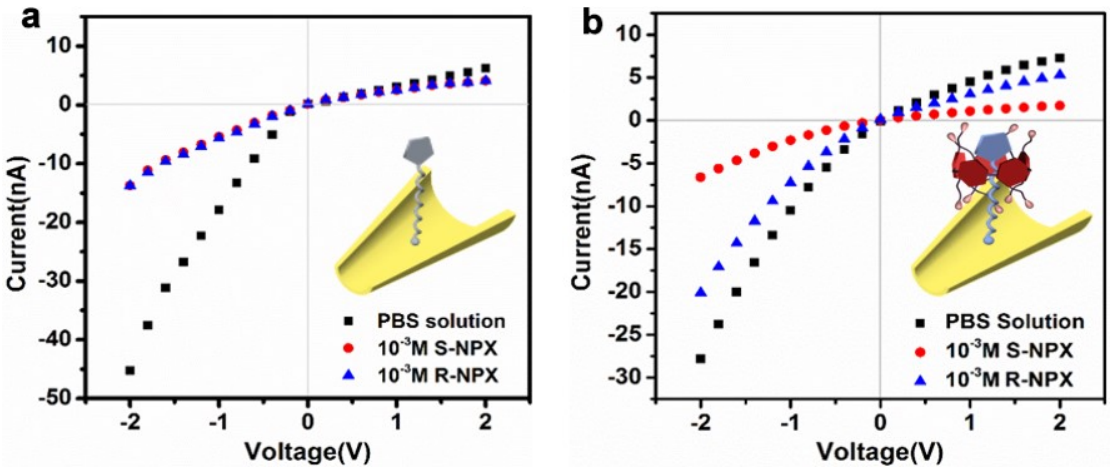

Figure S9. (a)(b) Selective recognition I-V representation of chiral NPX in the R-PEA channel and R-PEA⊂WAP5 host-guest channel.

11. Current-Voltage (I-V) curves in response to different concentrations of R/S-Ibp.

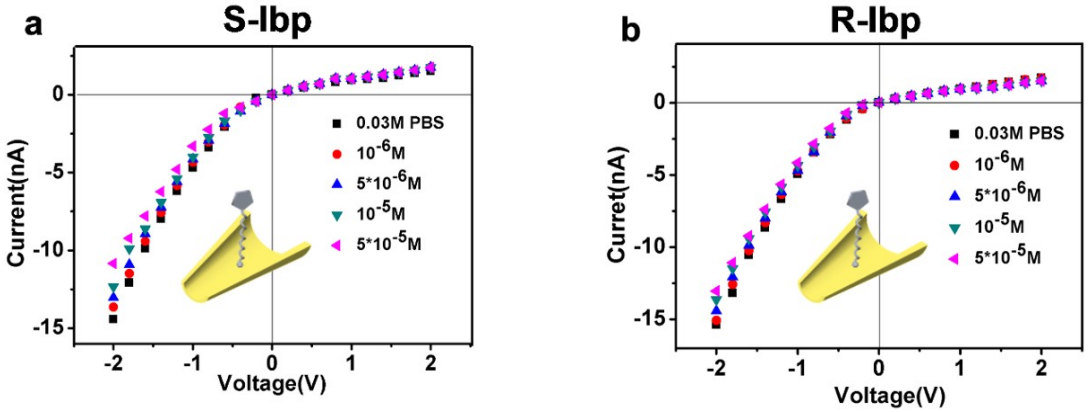

Figure S10. The selective response of the enantiomers of ibuprofen in the bionic nanochannel of R-PEA.

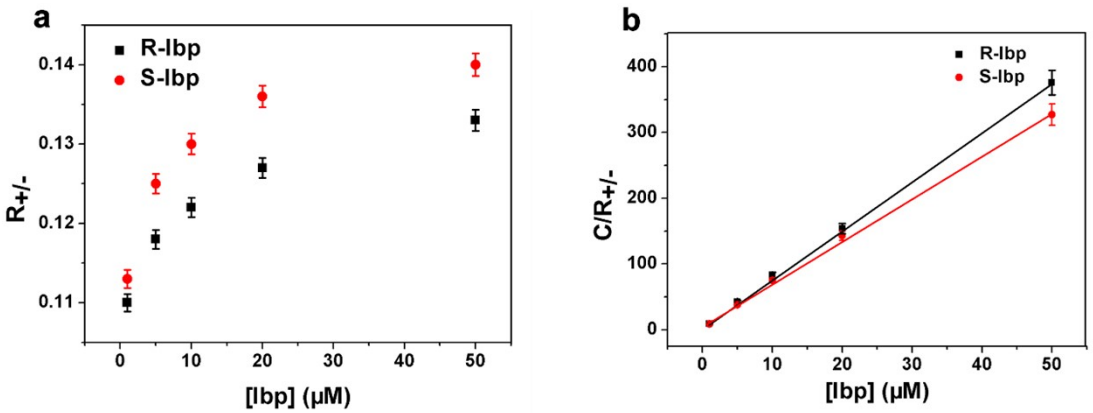

Figure S11. (a) Ionic rectification ratio of I-V curve in R-PEA modified nanochannels at different concentrations of R/ S-ibuprofen. (b) A linear fitting diagram of C/ $R_{+/-}$ and C.

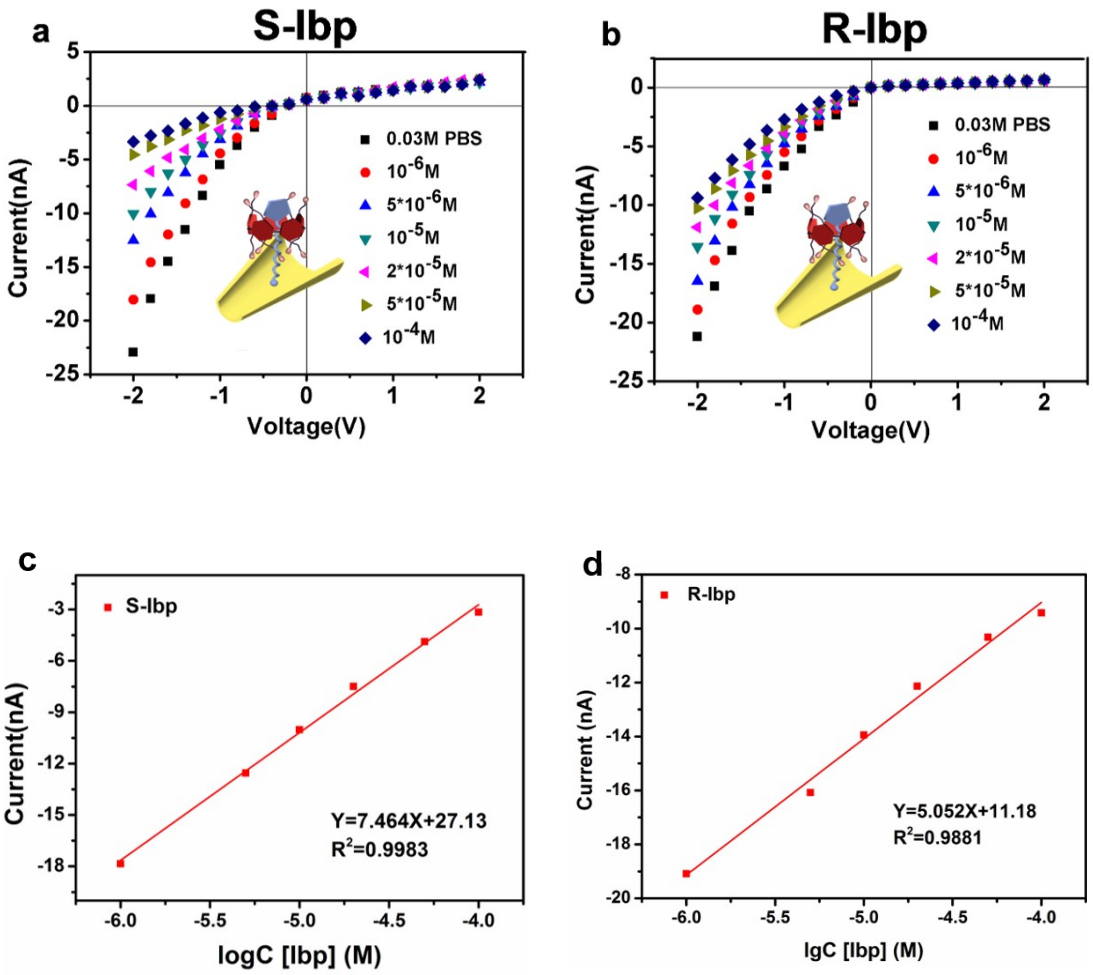

Figure S12. The selective response of the enantiomers of (a) S-ibuprofen and (b) R-ibuprofen in the bionic nanochannel of R-PEA⊂WAP5. A linear fitting diagram of Current-lg c (concentration of (c) S-Ibp and (d) R-Ibp).

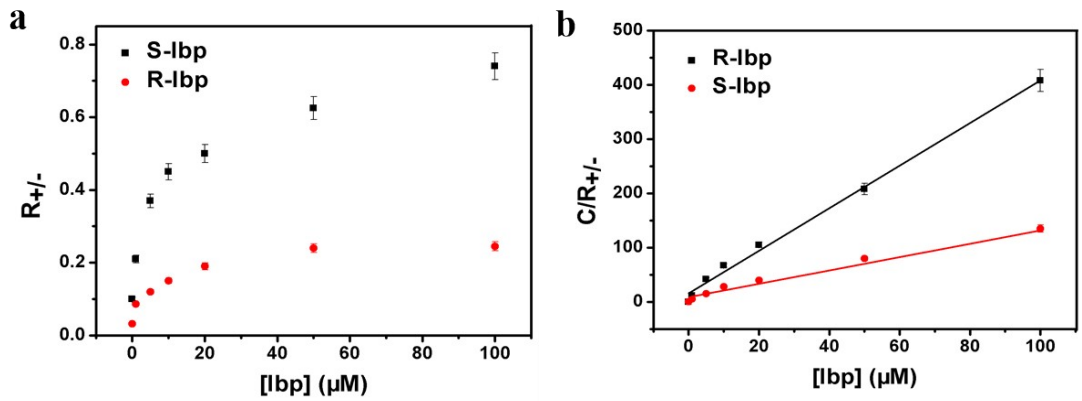

Figure S13. (a) Ionic rectification ratio of I-V curve in R-PEA⊂WAP5 modified nanochannels at different concentrations of R/S-ibuprofen. (b) A linear fitting diagram of C/ $R_{+/-}$ and C.

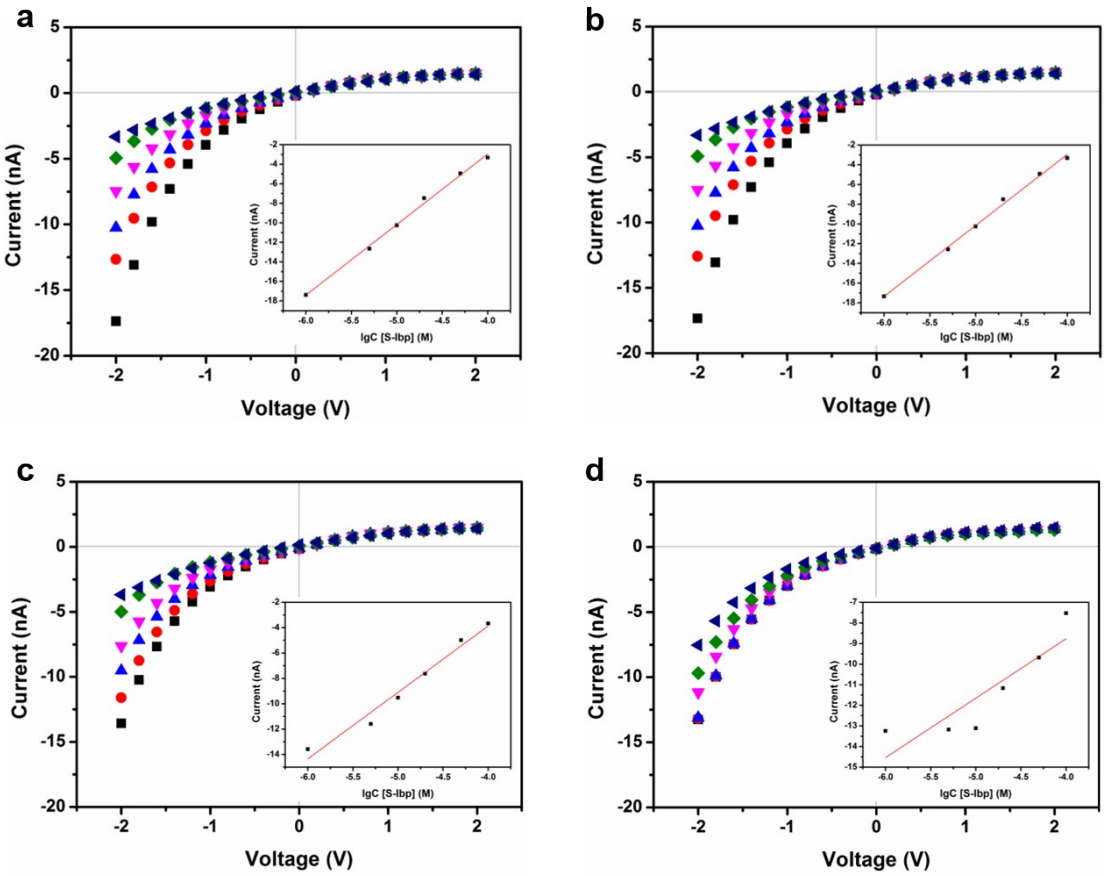

Figure S14. Current of mixed solutions with different concentrations of S-Ibp and the linear fitting diagram of Current-lg C containing (a) 10^{-6} M (b) 5×10^{-6} M (c) 10^{-5} M (d) 2×10^{-5} M R-Ibp

Table S4. the standard curves of mixed solutions containing different concentration of R-Ibp.

Concentration of R-Ibp (M)	Linear fitting equation	R^2
0	Y=7.464X+27.13	0.9983
10^{-6}	Y=7.222X+25.94	0.9949
5×10^{-6}	Y=7.200X+25.85	0.9956
10^{-5}	Y=5.240X+17.10	0.9482
2×10^{-5}	Y=2.885X+2.773	0.7307

12. Current-Voltage (I-V) curves in response to different concentrations of R/S-NPX.

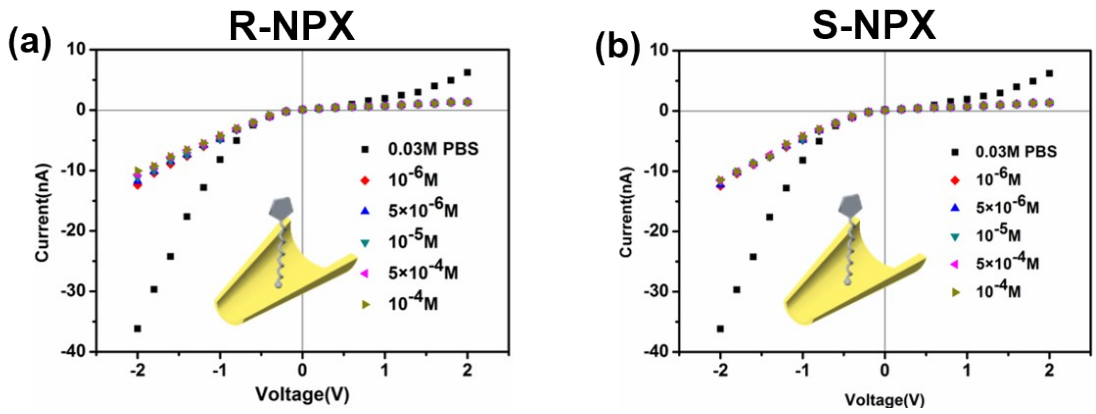

Figure S15. The selective response of the enantiomers of naproxen in the bionic nanochannel of R-PEA.

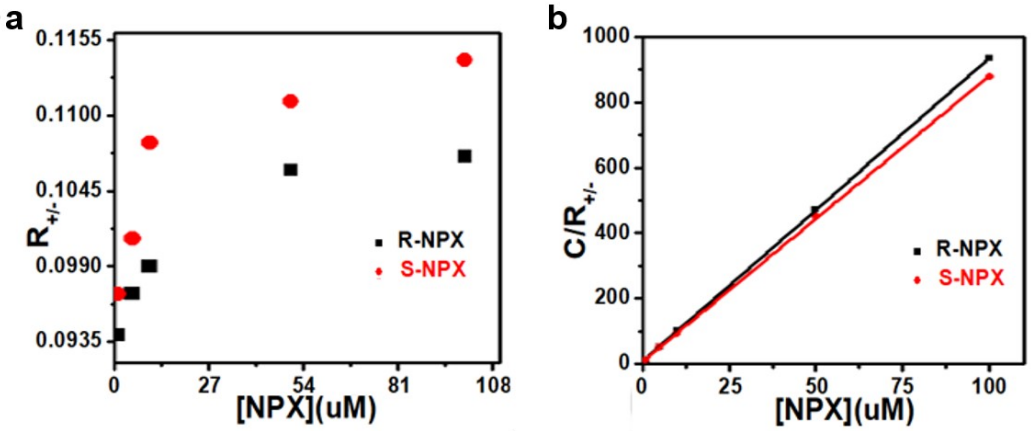

Figure S16. (a) Ionic rectification ratio of I-V curve in R-PEA modified nanochannels at different concentrations of R/S-naproxen. (b) A linear fitting diagram of C/ $R_{+/-}$ and C.

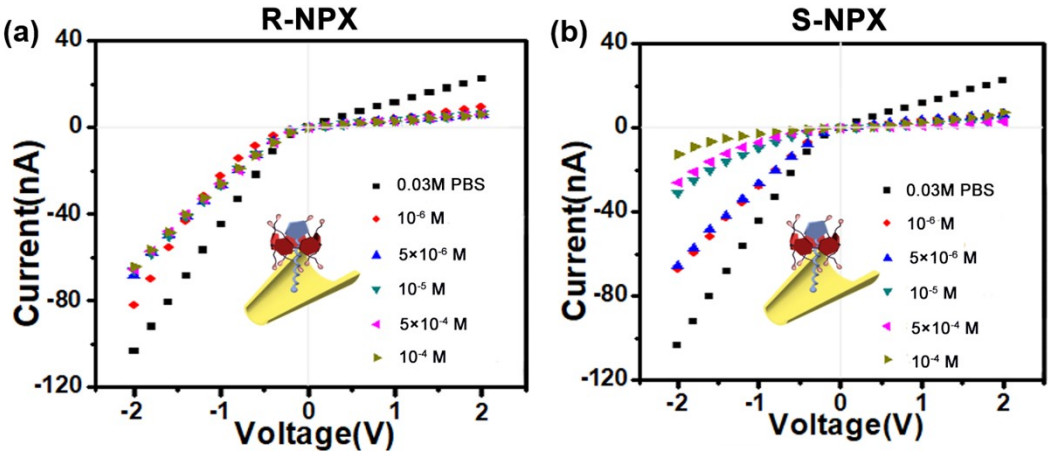

Figure S17. The selective response of the enantiomers of naproxen in the bionic nanochannel of R-PEA⊂WAP5.

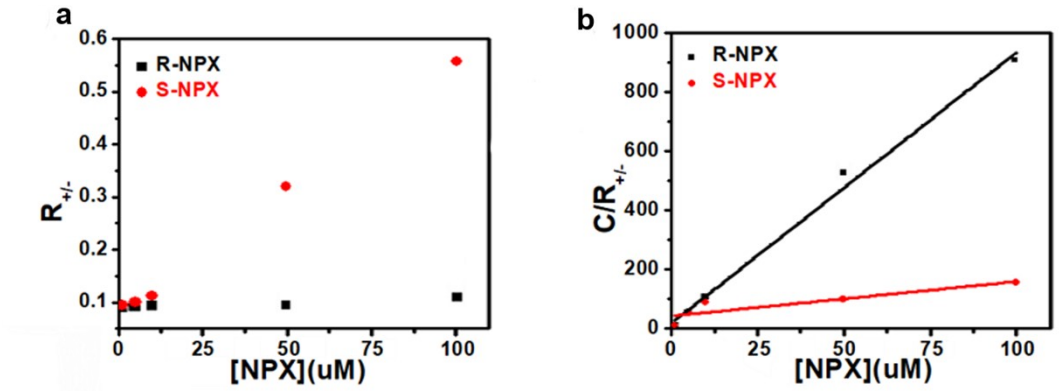

Figure S18. (a) Ionic rectification ratio of I-V curve in R-PEA⊂WAP5 modified nanochannels at different concentrations of R/S-naproxen. (b) A linear fitting diagram of C/ $R_{+/-}$ and C.

13. Standard recovery calculation

Table S5. Detected concentration of S-Ibp using the linear fitting diagram.

Add (M)	Found (M)	Relative recovery (%)	Average recover (%)
10^{-4}	0.9297×10^{-4}	92.97	101.2
	0.9472×10^{-4}	94.72	
	0.9634×10^{-4}	96.34	
10^{-5}	1.024×10^{-5}	95.31	
	1.099×10^{-5}	102.4	
	0.9531×10^{-5}	109.9	
10^{-6}	1.015×10^{-6}	101.5	
	1.071×10^{-6}	107.1	
	1.104×10^{-6}	110.4	

14. Fluorescence titration experiment of R-PEA and R/S-Ibuprofen.

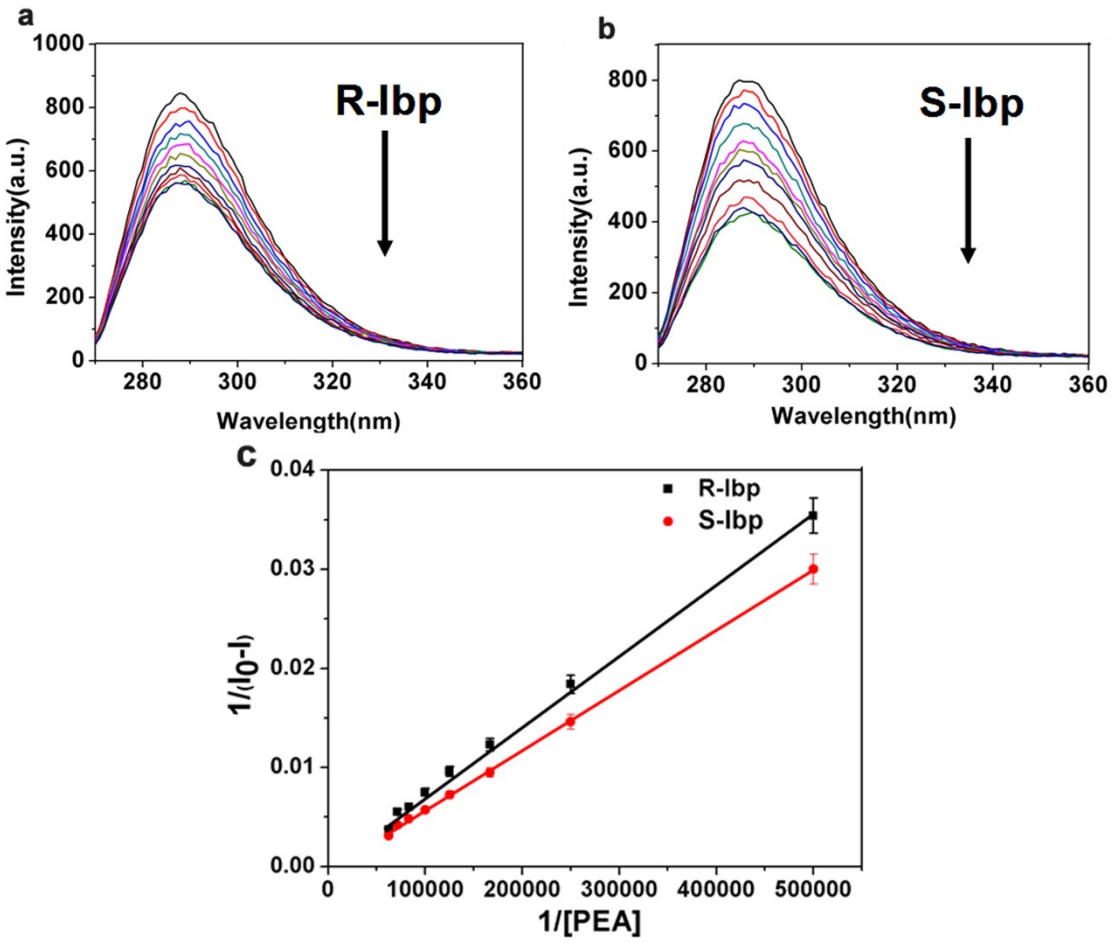

Figure S19. (a) Fluorescence titration of R-PEA with R-Ibp. (c) Fluorescence titration of R-PEA with S-Ibp. (c) Linear fitting diagrams of R-PEA with R-Ibp and S-Ibp.

15. Fluorescence titration experiment of R-PEA⊂WAP5 and R/S-Ibuprofen.

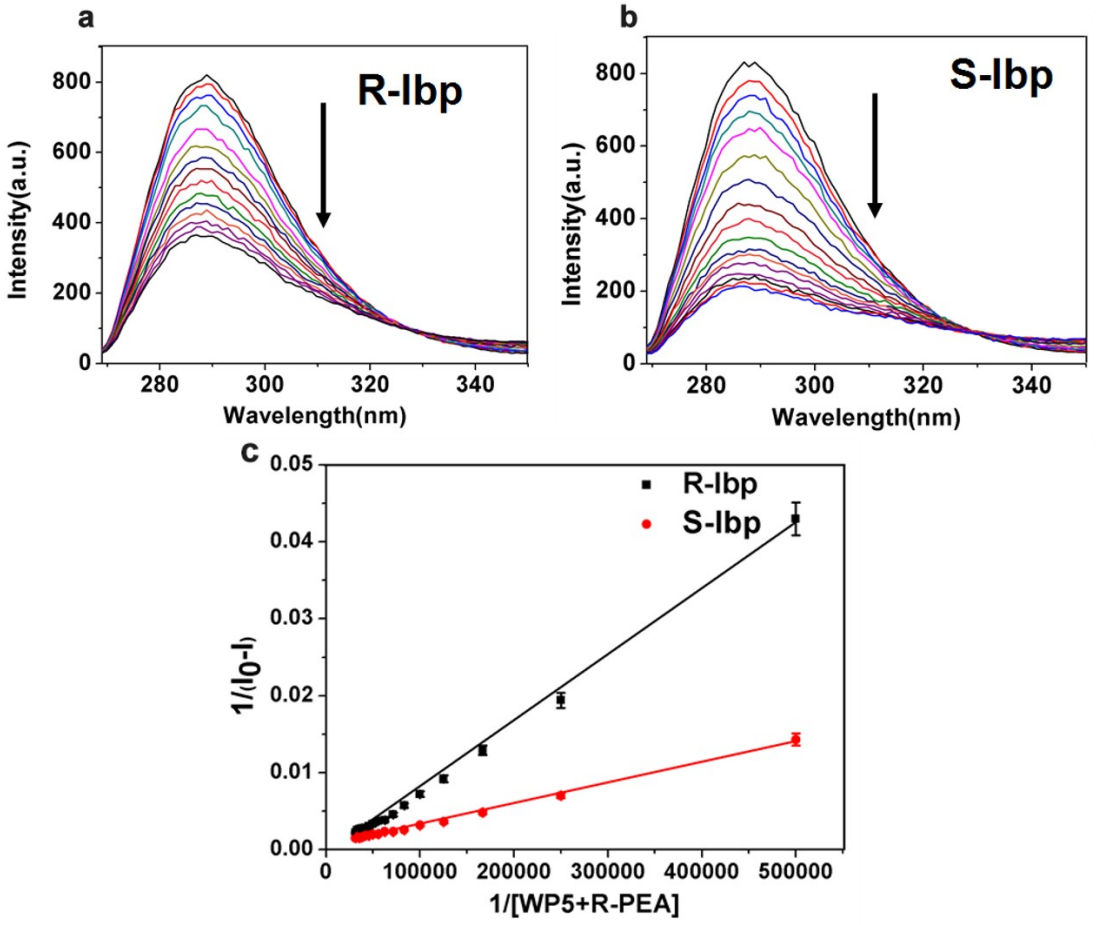

Figure S20. (a) Fluorescence titration of R-PEA⊂WAP5 with R-Ibp. (c) Fluorescence titration of R-PEA⊂WAP5 with S-Ibp. (c) Linear fitting diagrams of R-PEA⊂WAP5 with R-Ibp and S-Ibp.

In the blank experiment, R-Ibp and S-Ibp solutions of 4×10^{-4}M were dissolved in 0.03M PBS (pH=7.4) as the main solution, followed by 10^{-2}M R-PEA solution as the guest solution, and the fluorescence titration was carried out until the fluorescence intensity of ibuprofen was almost unchanged. In the control group, the host solution remained unchanged, and the supramolecular assembly formed by 10^{-2}M R-PEA⊂WAP5 was used as the guest solution until the fluorescence intensity of S/R-Ibp did not change.

16. Gaussian simulation data.

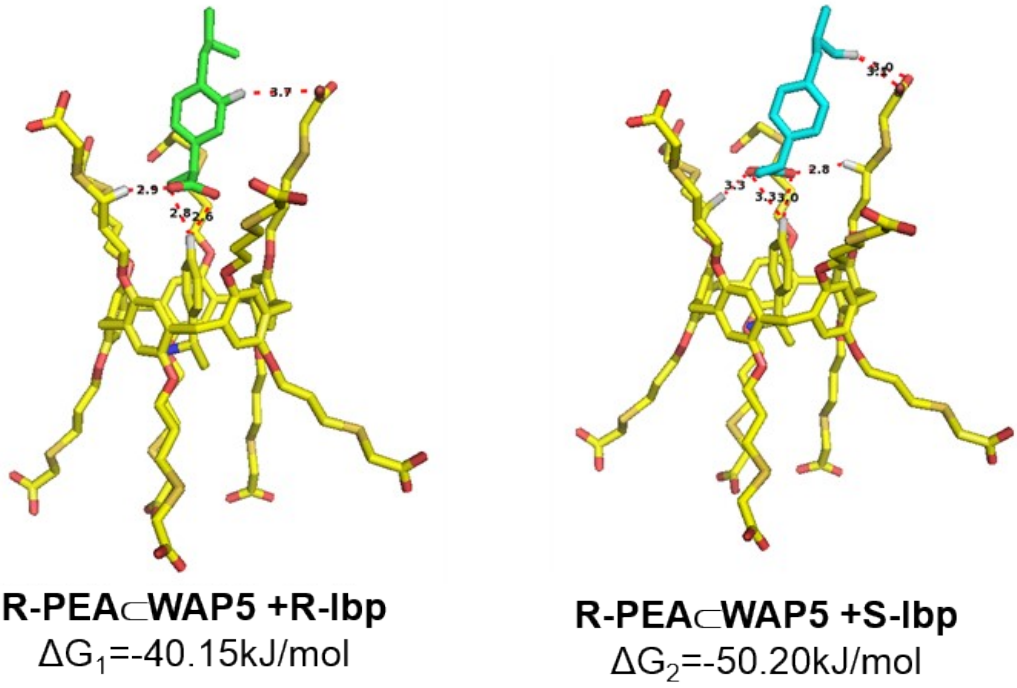

Figure S21. Gaussian simulation results of the interaction between ibuprofen enantiomers and R-PEA⊂WAP5 system. The result shows that S-Ibp is more suitable for combining with R-PEA⊂WAP5 system.

17. Electroosmotic Flow (EOF) experiments for charge calculation of nanochannels.

In the EOF experiments of the three hour-glass shaped nanochannels, the diagram related to phenol transport versus time can be plotted by periodical measurement of fluorescence intensity of the phenol in the permeate solution at 30 min intervals. The 30 min transport cycles were repeated for five times, and the total time we applied was 150 min. The permeability experiments of phenol in the absence of applied voltage were carried out to determine the rate of diffusion (N_{diff}). After that the transport experiments of phenol at -2 V were completed to calculate Ni (the rate of transport with applied voltage). Thus, the enhancement factor (E) can be obtained by the following equation:

$$E = N_i / N_{diff} \quad \text{Formula.S2}$$

$$E = Pe/(1 - e^{-Pe}) \quad \text{Formula.S3}$$

$$V_{eof} = D * \frac{Pe}{L} = -\varepsilon\zeta J_{app}/\eta \quad \text{Formula.S4}$$

$$J_{app} = I_{-2V}/S \quad \text{Formula.S5}$$

$$\sigma = -(V_{eof}\eta)/(J_{app}\rho K^{-1}) \quad \text{Formula.S6}$$

N_{diff} rate of phenol diffusion and N_i rate of phenol transport in the applied voltage can be obtained through this process using Formula S2. Peclet number (Pe) can be determined using Formula S3, the relationship between Pe and V_{eof} is determined using Formula S4, where D is the diffusion coefficient for phenol (D = 8.9 × 10^{-6} cm^2 s^{-1}) and L is the membrane thickness (L = 12 um). The ζ potential of the nanochannel walls can also be determined, where ε is the permittivity of the solution; the constant applied current density (J_{app}) can be determined using Formula S5. The σ surface charge density of the nanochannels can be determined using Formula S6, (η is the viscosity of the solution, η = 0.89 cp; ρ is the resistivity of the electrolyte within the nanochannel, ρ = 2.23 KΩ), K^{-1} is the effective thickness of the electrical double layer,

$K^{-1} = (9.61\times10^{-9})(z^2c)^{-1/2}$). Hence, the surface charge density can be calculated from above formulas. The data details of EOF experiments are as follows:

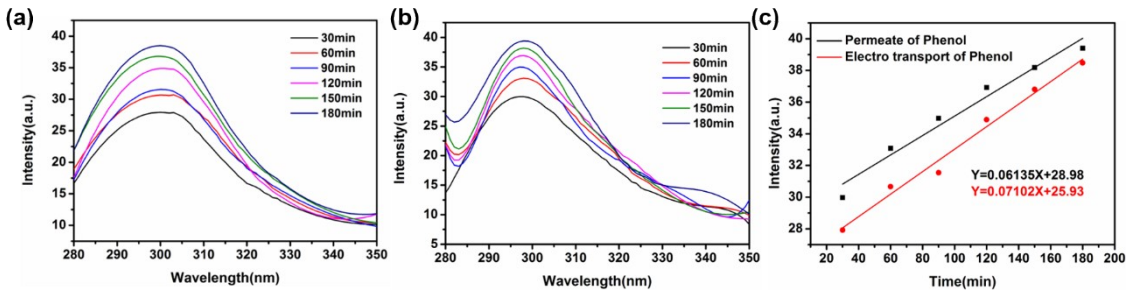

Figure S22. Fluorescence spectra of transmitted phenol for R-PEA channel at (a) DC = 0V and (b) DC = -2V. (c) Flux of phenol transport over time in R-PEA channel.

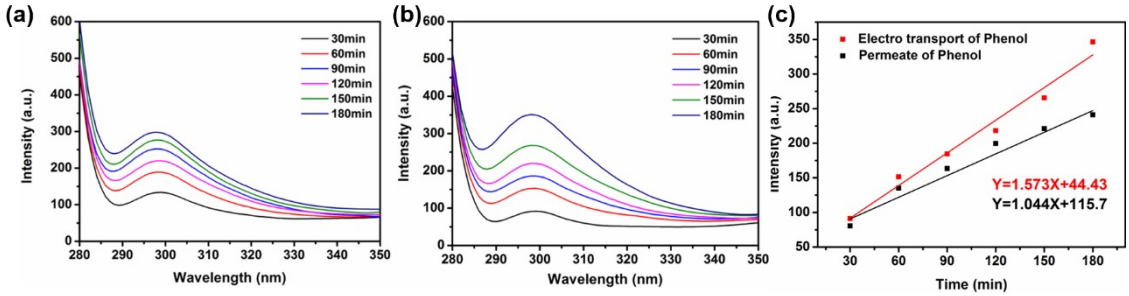

Figure S23. Fluorescence spectra of transmitted phenol for R-PEA⊂WAP5 channel at (a) DC = 0V and (b) DC = -2V. (c) Flux of phenol transport over time in R-PEA⊂WAP5 channel.

18. Simulation of potential of R-PEA and R-PEA⊂WAP5 channel.

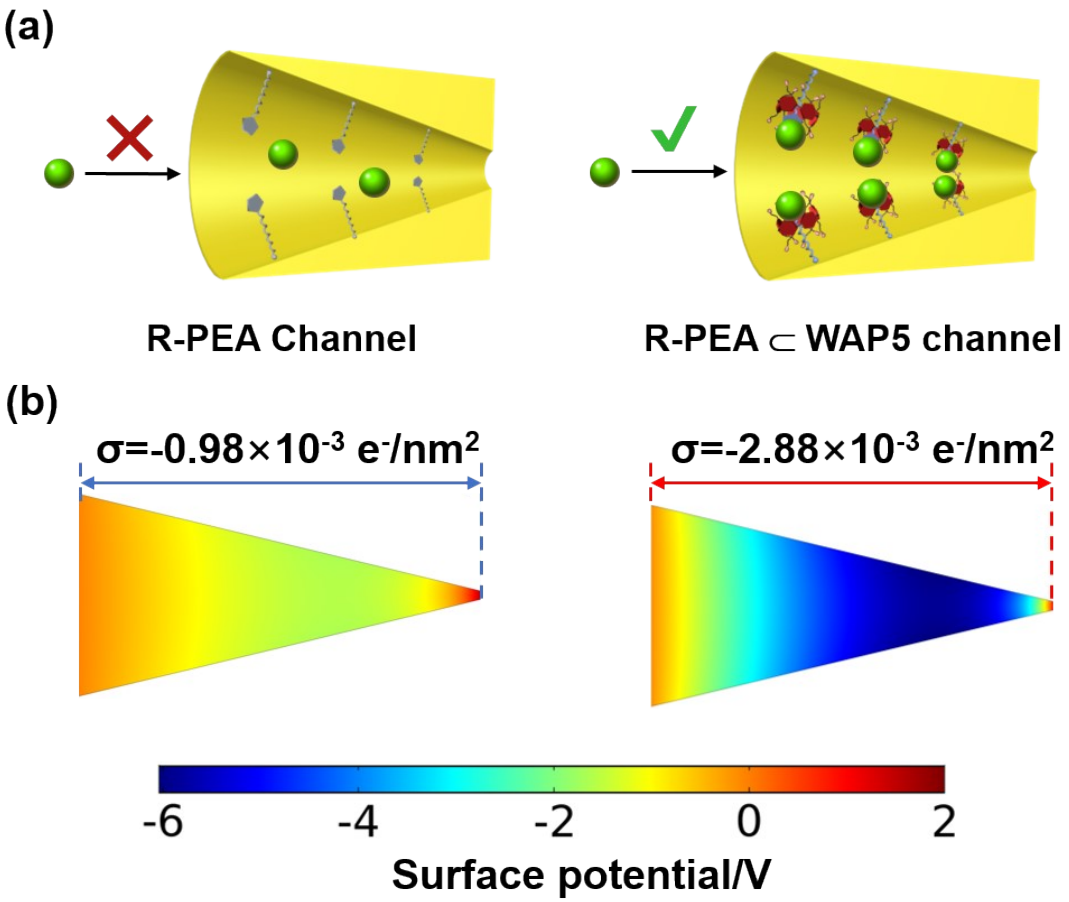

Figure S24. (a) Schematic diagram of enantioselective recognition of S -Ibp in the R-PEA channel and R-PEA⊂WAP5 channel. (b) Comsol simulation of surface potential for R-PEA channel and R-PEA⊂WAP5 channel.

References

[1] Z. Siwy, P.Apel, D. Dobrev, R. Neumann, R. Spohr, C. Trautmann, K. Voss, *Nucl. Instrum. Methods Phys. Res. B*. 2003, **208**, 143–148.

[2] P. Apel, *Radiat. Meas*. 2001, **34**, 559–566.