Supporting Information

Molecular synchronization enhances molecular interactions: An explanatory note of pressure effects

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1. General:

Micro-mixer (a static type reactor made of SUS316) was purchased from YMC *(Kyoto, Japan)* as a ready-made microreactor. The channel depth and width of this reactor were both 200 μm. The mixing volume of the channel was 20 μL.

2. Plots of aggregation ratio against pressure:

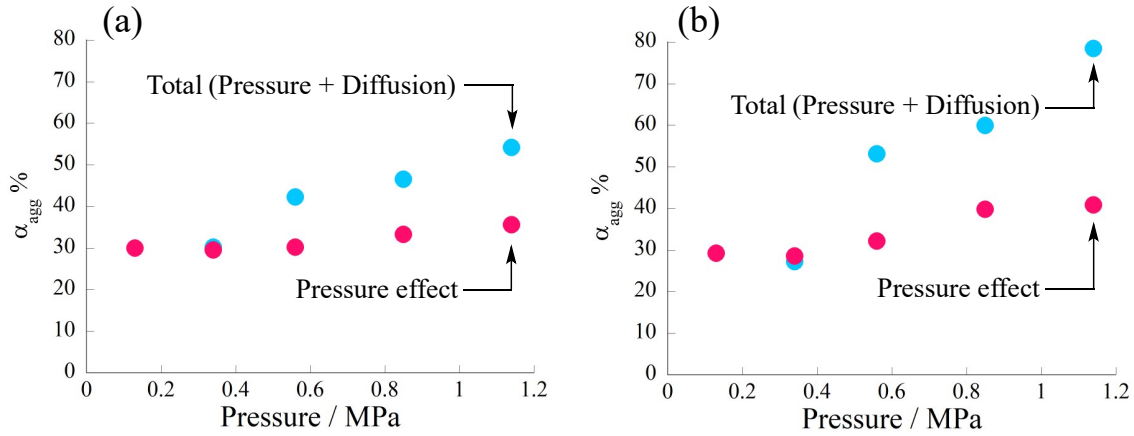

Figure S1. Total aggregation efficiency upon changing the flow rate (including both pressure and diffusion effects; blue dots) and extracted pressure effects under constant proton diffusion effect at 10 μL/min (red dots); (a) pH 5; (b) pH 3.

3. UV–Vis spectral changes at flow rates of 25 and 50 μL/min (pH 5):

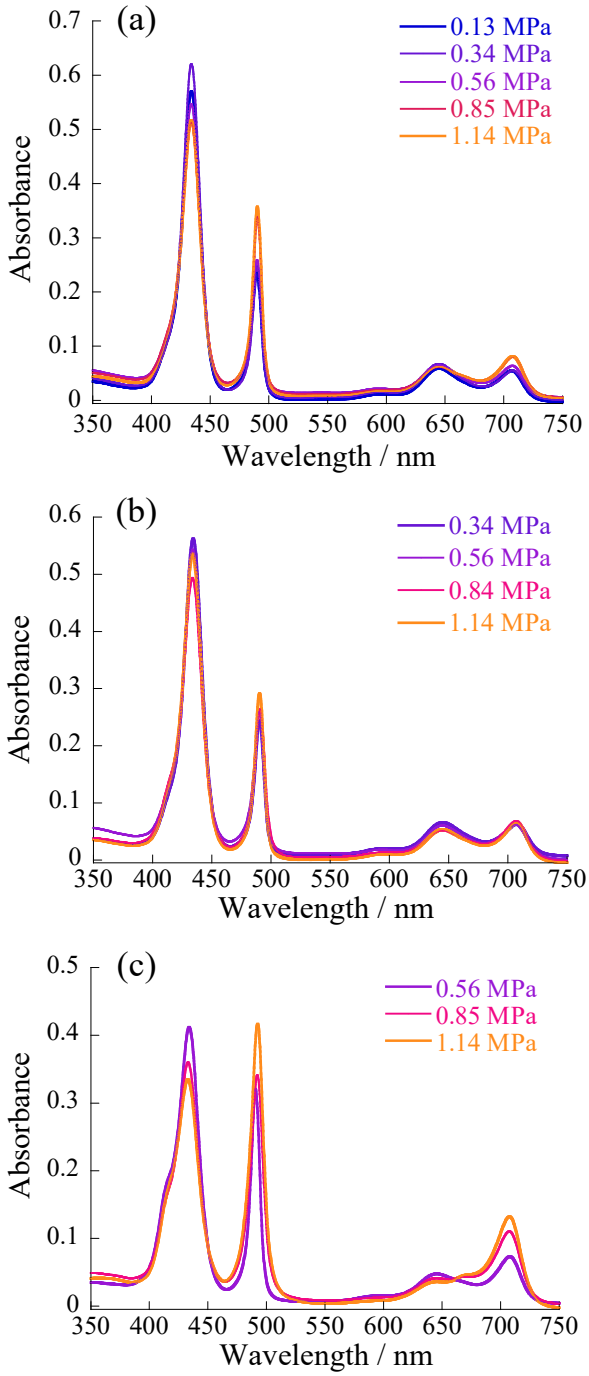

Figure S2. UV–Vis spectral changes of TPPS upon changing the pressure inside the channel at pH 5; v = (a) 10, (b) 25, and (c) 50 μL/min. 0.1 mm cell, r.t.

4. Summary of aggregation efficiencies at flow rates of 25 and 50 µL/min:

Pressure (MPa)	0.13	0.29	0.57	0.84	1.14
Flow rate : 25 µL min^{-1}					
Solution Width (µm)	n.d.	Fixed at 25.9 µm			
Diffusion Time (ms)	n.d.	Fixed at 14.2 ms			
α_{agg} (pH = 5)	n.d.	29.7	32.4	34.5	35.2
Flow rate : 50 µL min^{-1}					
Solution Width (µm)	n.d.	n.d.	Fixed at 19.9 µm		
Diffusion Time (ms)	n.d.	n.d.	Fixed at 8.4 ms		
α_{agg} (pH = 5)	n.d.	n.d.	41.3	46.4	52.9

Figure S3. Effects of proton diffusion time on aggregation efficiency upon changing the back-pressure inside the channel; summary of extracted pressure effects on aggregation efficiency.

The solution width w of the central flow containing TPPS molecules was determined from fluorescence microscopy images, using Image-J. The diffusion time of protons was calculated using a two-dimensional model, as follows:

$$t_{diff} = \frac{w^2}{4D}$$

where D is the diffusion constant of a proton (11.8×10^{-9} m^2/sec at 298 K at pH 4.1) and w is the width of the central flow [1,2].

5. Effects of rapid proton diffusion in a micromixer:

Flow rate (μL min^{-1})	10	25	50	75	100
Pressure (MPa)	0.01	0.01	0.01	0.01	0.01
α_{agg} (pH = 5)	41.6	43.7	43.8	41.5	43.9

Figure S4. Effects of proton diffusion time on aggregation efficiency in turbulent flow.

6. References

1. R. Karnik, F. Gu, P. Basto, C. Cannizzaro, L. Dean, W. Kyei-Manu, R. Langer, O. C. Farokhzad, *Nano Lett*. **2008**, *8*, 2906–2912.
2. J. Choi, N. Hirota, M. Terazima, *J. Phys. Chem. A* **2001**, *105*, 12–18.