Supporting information

Resistive Pulse Analysis of Chiral Amino Acids Utilizing Metal-Amino Acid Crystallization Differences

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1. Experimental Section

Chemicals and Materials. Cadmium chloride (99.99% trace metals basis), L-cystine (≥98% (TLC), crystalline), D-cystine (98%), L-aspartic acid (reagent grade, ≥98% (HPLC)), L-serine (≥99% (HPLC)), D-serine (≥98% (TLC)), and sodium chloride were purchased from Sigma Aldrich. D-Aspartic Acid (≥95%, crystalline) was purchased from Cayman Chemical. Silver wire (0.5mm (0.02in) dia, annealed, 99.9% (metals basis)) was purchased from Thermo Scientific Chemicals. All solutions contained deionized (DI) water (PURELAB, 18.2 MΩ/cm, TOC < 3 ppb) as the solvent.

Nanopipette Fabrication. The nanopipettes were fabricated from a quartz glass capillary (outer diameter = 1.0 mm, inner diameter = 0.7 mm, Sutter) using a CO_2 laser puller (Sutter, P-2000) with the following pulling program was used: Heat=500, Fil=1, Vel=30, Del=145, Pul=175. The opening of nanopipettes is ~200 nm in diameter, which was measured by scanning electrochemical microscopy (FEI Quanta 650) at 5.0 kV. Nanopipettes were adjusted to a micron size by gently cutting the tip with a flexible needle used for filling micropipettes (World Precision Instrument MicroFil Flexible Needle 28 Gauge, 67 mm Length).

Synthesis of Cd/CST microcrystals. 10 mL stock solutions of 0.1 M L-CST, 0.1 M D-CST, 0.1 M $CdCl_2$, and 2.5 M NaOH were made. DI water was the solvent for each stock solution. 1 mL of NaOH was added to the CST solutions to bring the solution pH to 11. Cloudiness quickly disappeared after the addition of NaOH. A 1 mL solution of 0.15 M NaCl, 6 mM CST, and 1 mM $CdCl_2$ was made by first adding 8.77 mg of NaCl to a 1 mL vial. 930 μL of DI water was then added to the vial. 60 μL of 0.1 M CST was the next addition. When a racemic mixture was made, 30 μL of L-CST and 30 μL of D-CST were added. Finally, 10 μL of 0.1 M $CdCl_2$ was added. This addition would instantly cloud the solution as the crystals formed. The vial was hand shaken until the solution was completely cloudy. The solutions were then left undisturbed for 15 minutes for synthesis completion. The same procedure was followed for synthesizing Cd-serine and aspartate crystals.

SEM imaging. Before SEM imaging, the sample solutions were washed with DI water, followed by centrifuging twice to remove NaCl. An SM-7600F field emission SEM was used. The SEM images were analyzed using Nano Measurer.

Electrochemical Measurements. Cyclic voltammetry and chronoamperometry were performed with a CHI 760E potentiostat. Ag/AgCl wire electrodes were prepared by soaking a wire in bleach for 20 seconds. One Ag/AgCl wire electrode was put in the micropipette solution, while the other was in the external solution. For every experiment, 0.15 M NaCl was used as the electrolyte. All experiments were performed in a Faraday cage.

2. Supplemental Tables and Figures

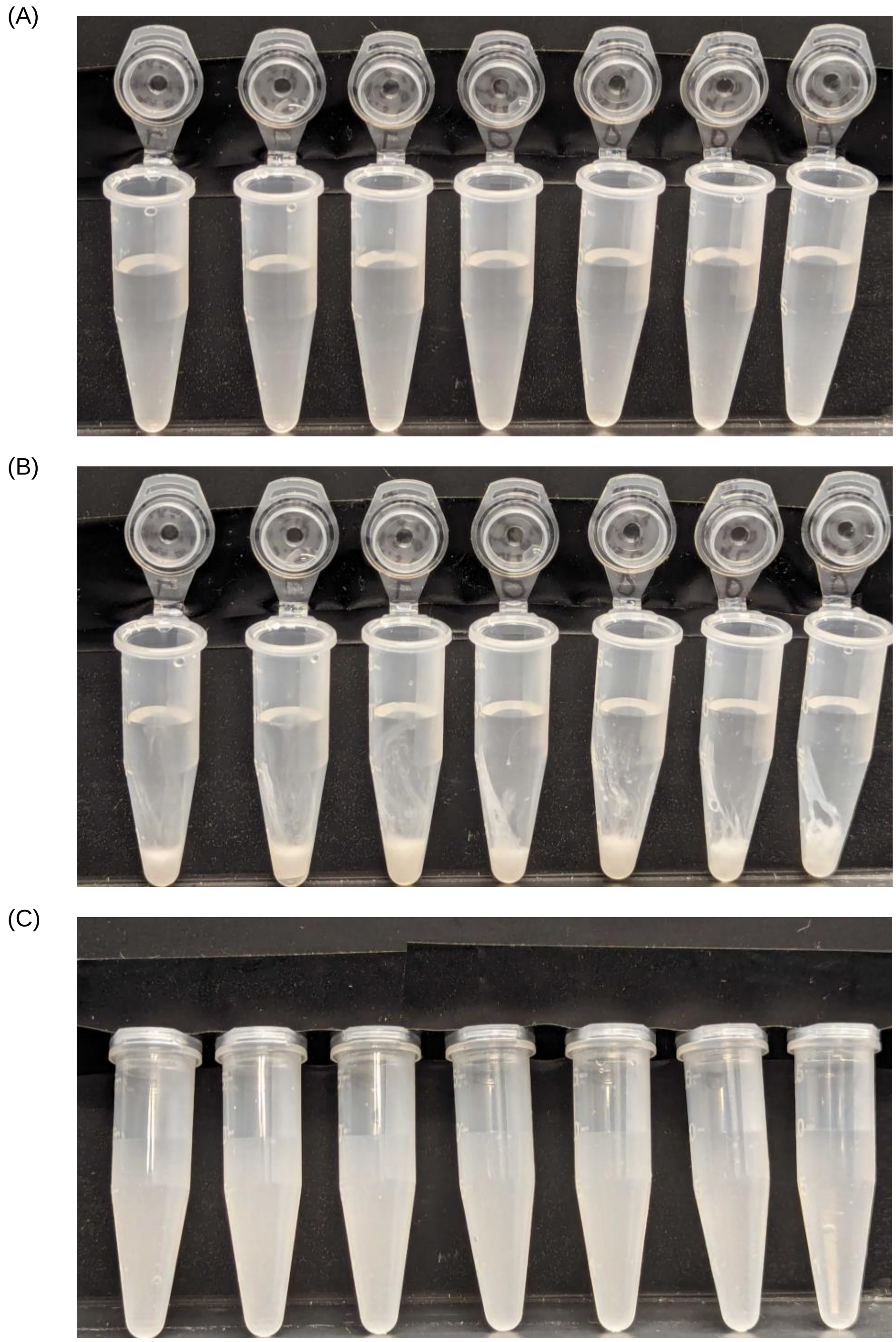


Figure S1. Photographs of CST solutions with various $\mathcal{X}$ of +1, +0.75, +0.5, 0, -0.5, -0.75, and -1 (from left to right) (A) before $CdCl_2$ was added, (B) after $CdCl_2$ was added, and (C) following shaking for complete synthesis.

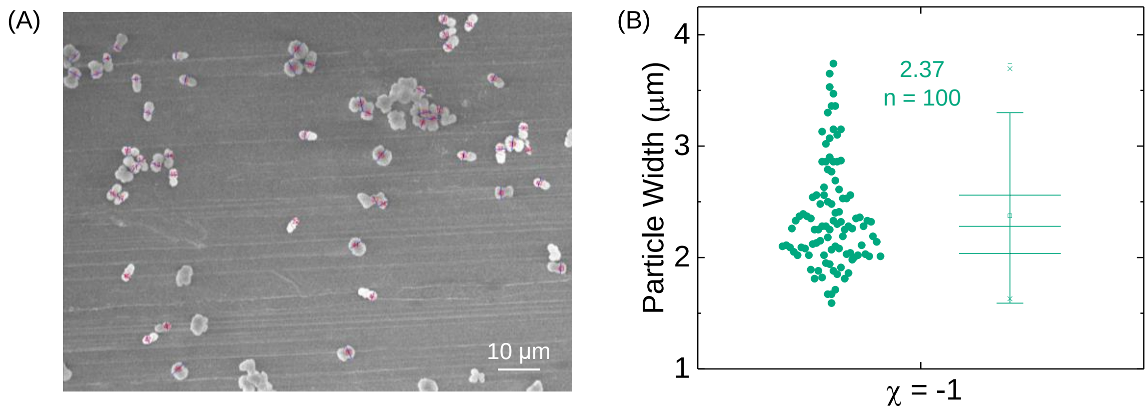


Figure S2. (A) SEM image of bowties. The blue lines show the measured width of $\mathcal{X}$ = -1.0 bowties using Nano Measurer 1.2. (B) Distribution of particle width. The average width was found to be 2.37 ± .47 µm.

Table S1. Zeta potential, mobility, and conductivity of ex-situ synthesized Cd-CST crystals from CST solutions with different $\mathcal{X}$ values.

$\mathcal{X}$	Zeta Potential (mV)	Mobility (10^{-8} m^2/Vs)	Conductivity (mS/cm)
-1.0	-31.3 ± 0.4	-2.586 ± 0.074	18.4 ± 0.35
-0.75	-32.6 ± 2.1	-2.568 ± 0.11	19.1 ± 0.60
-0.50	-33.8 ± 2.0	-2.586 ± 0.17	19.2 ± 0.75
0	-35.1 ± 1.2	-2.754 ± 0.10	18.2 ± 0.50
+0.50	-33.0 ± 2.2	-2.647 ± 0.16	18.8 ± 0.50
+0.75	-32.8 ± 1.4	-2.556 ± 0.16	19.1 ± 0.50
+1.0	-33.0 ± 1.0	-2.455 ± 0.034	19.1 ± 0.51

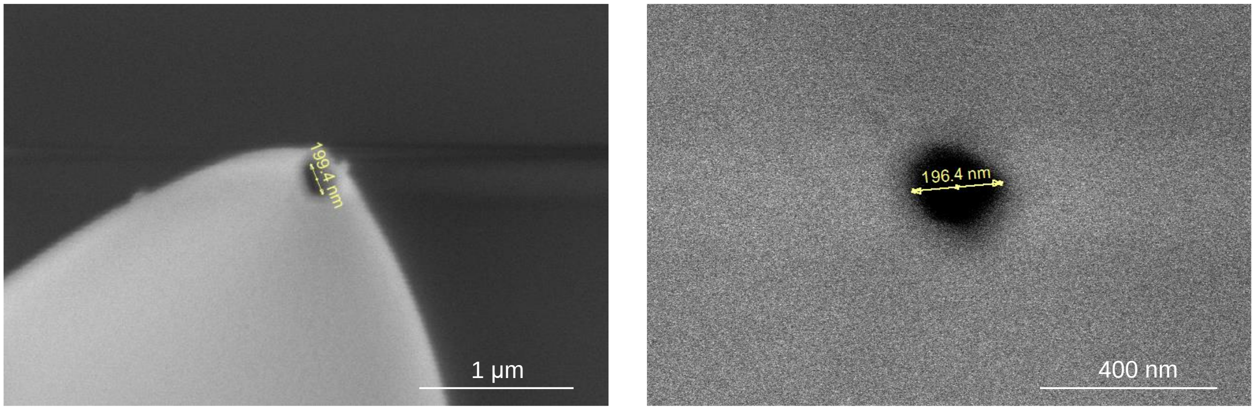


Figure S3. SEM images of an as-prepared nanopipette.

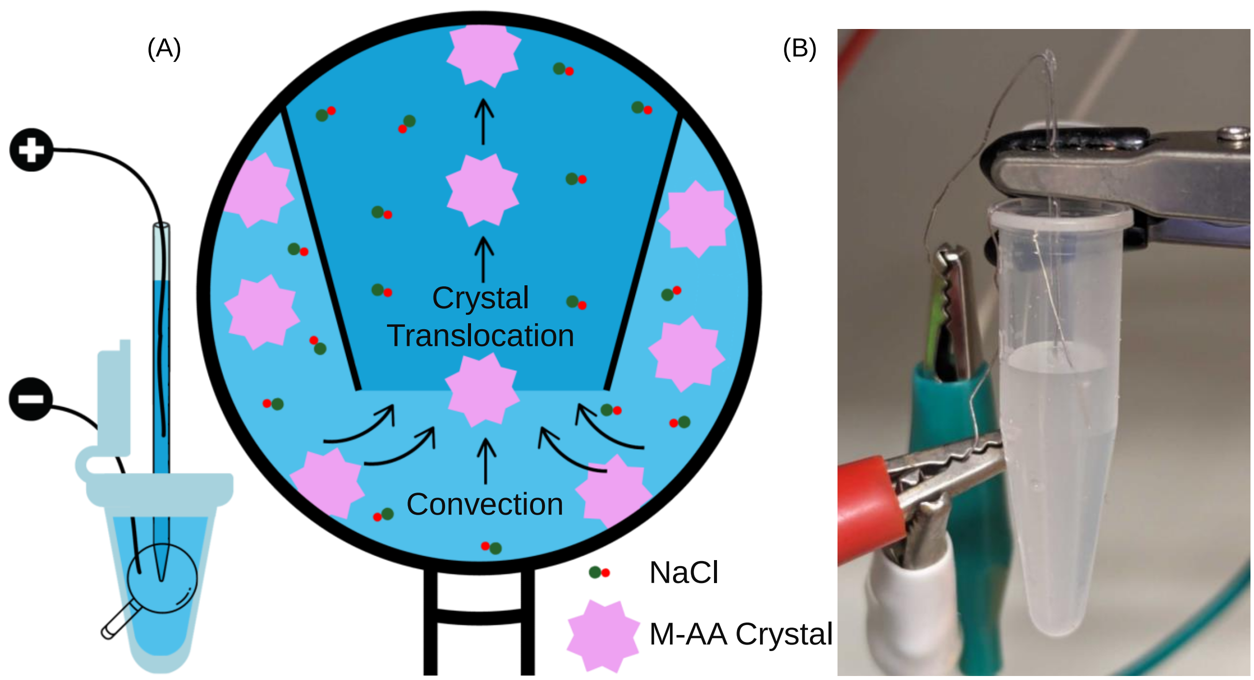


Figure S4. (A) Schematic of pulse resistive analysis of ex-situ formed M-AA crystals. (B) Photograph of the experimental setup.

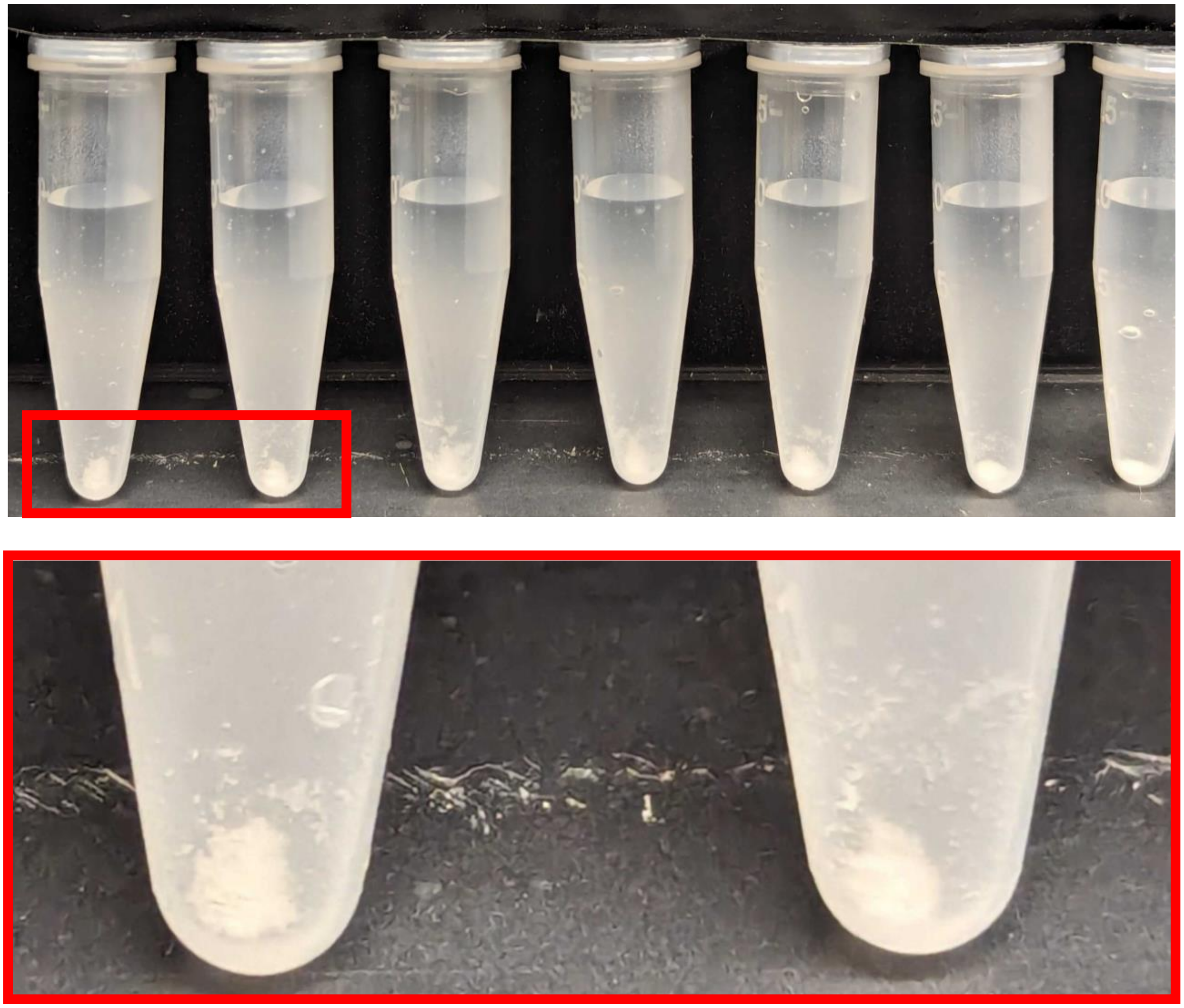


Figure S5. Photographs showing particles immediately settled down at the bottom of the vials.

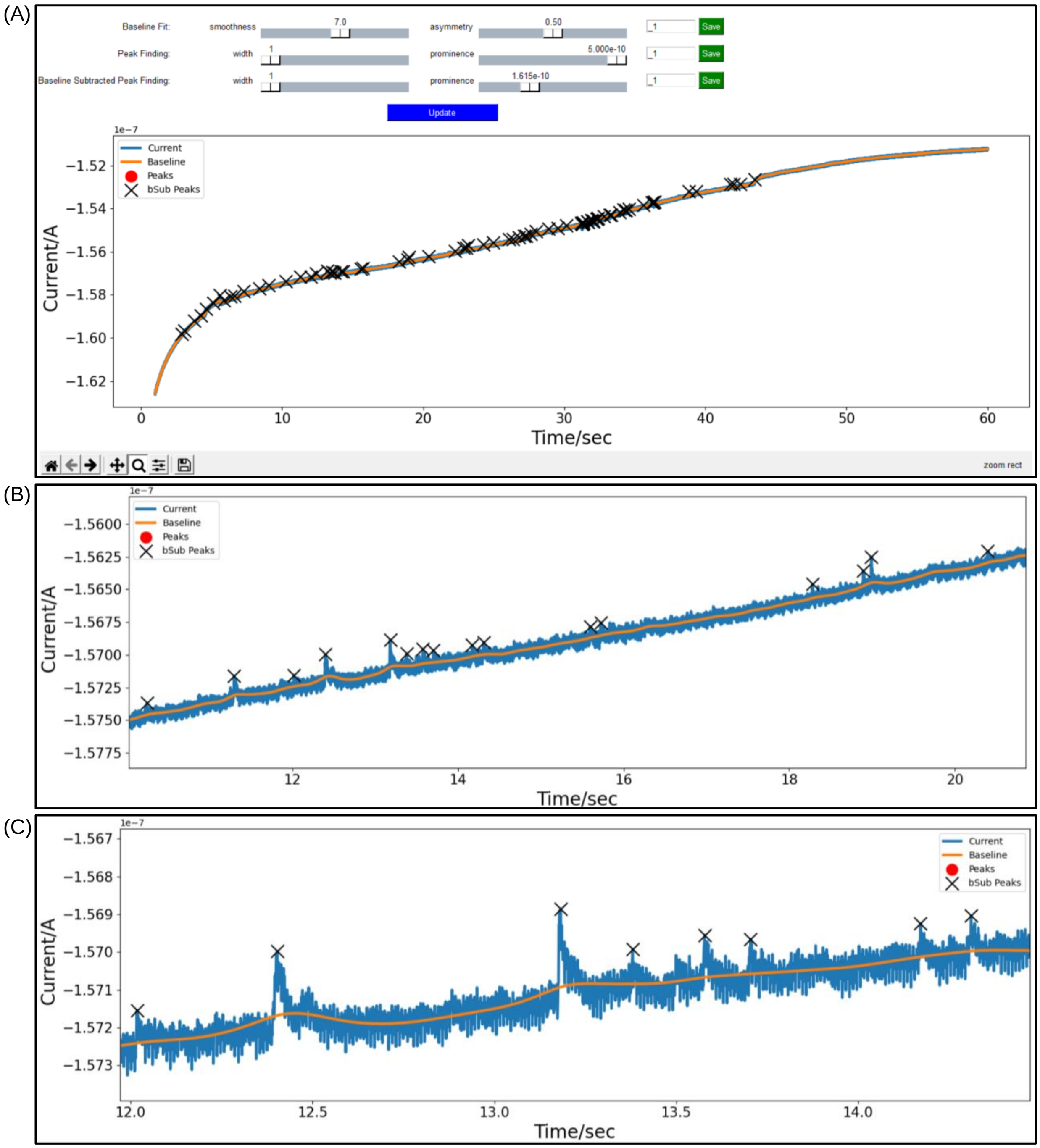


Figure S6. (A)A Python-based peak finder user interface visualizes all the found peaks with customizable baseline fitting. (B-C) Zoomed-in views of the peaks for $\mathcal{X}$ = 0 sample are shown.

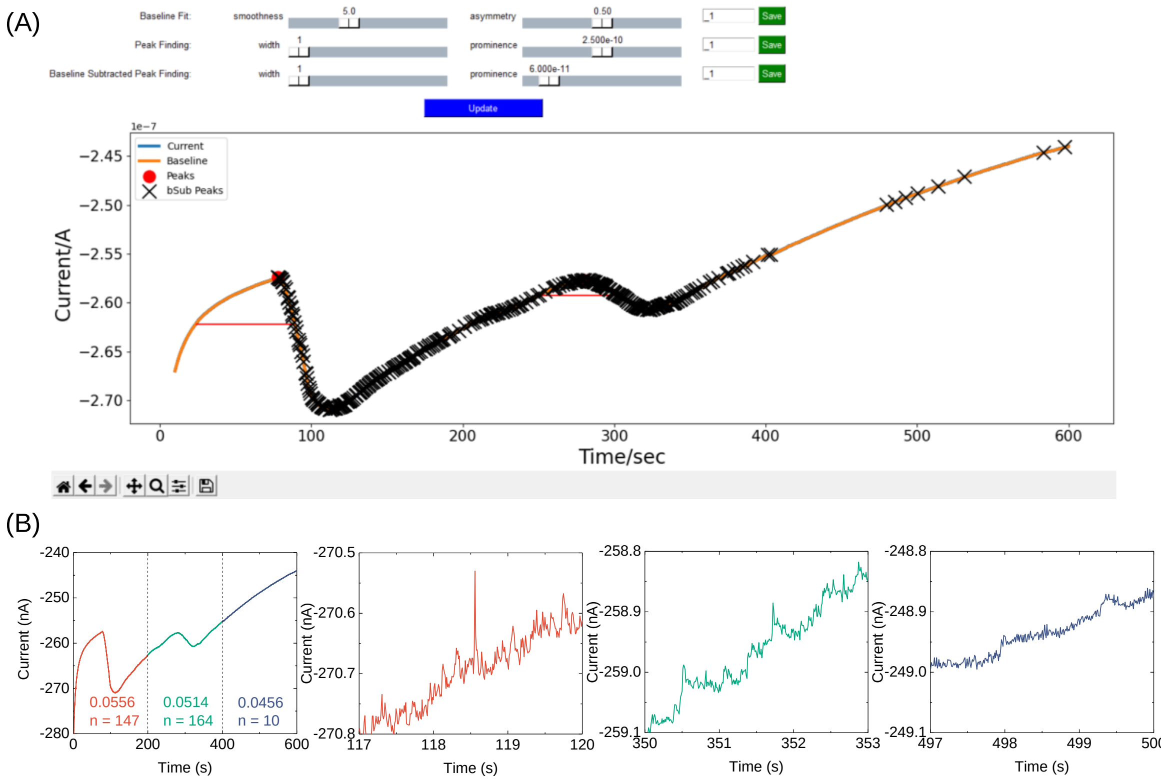
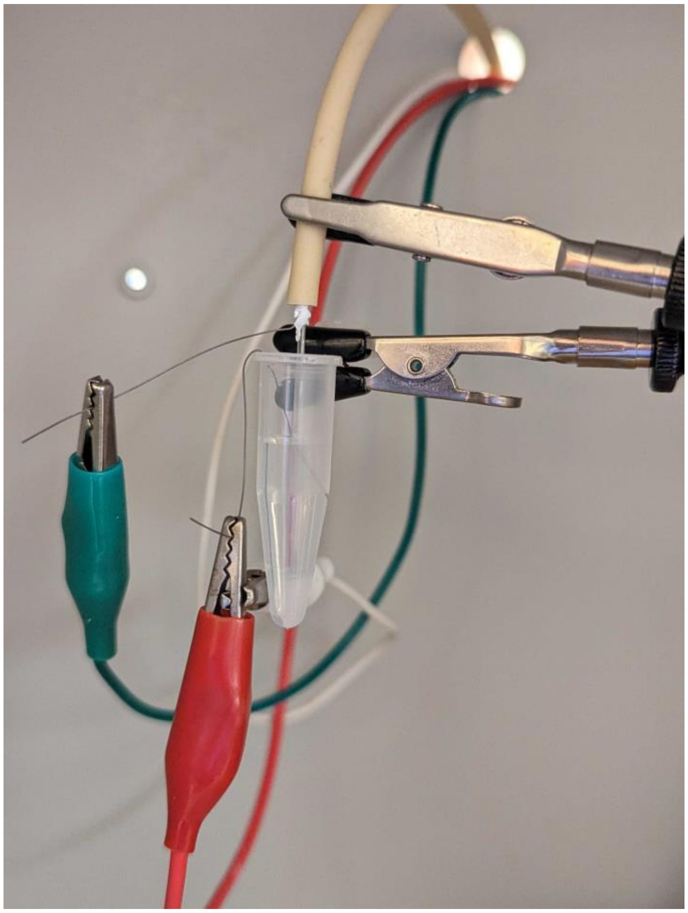


Figure S7. (A) Current-time trace in the peak analyzer user interface for a 10-minute analysis of ex-situ synthesized $\mathcal{X}$ = -1.0 Cd-CST microcrystals. Each identified peak is labeled by an X symbol. (B) In the first 200 seconds (red), the peak height average is 0.0556 ± 0.025 nA, n = 147. The next 200 seconds (green) show an average peak height of 0.0514 ± 0.015 nA, n = 164. The final 200 seconds (blue) shows an average peak height of 0.0456 ± 0.0076 nA, n =10.

(A)



(B)

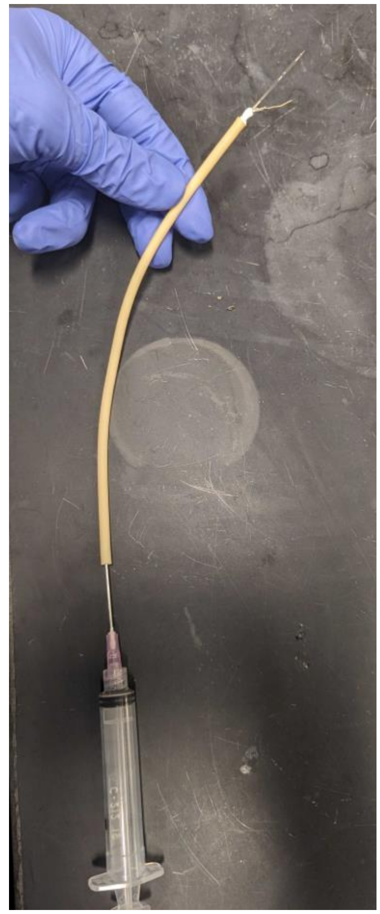


Figure S8. (A) Photograph of the experimental setup for resistive pulse analysis of in situ formed Cd-amino acid crystals. (B) A micropipette is connected to a rubber tubing to apply a negative pressure to drive the sample solution inside the micropipette.

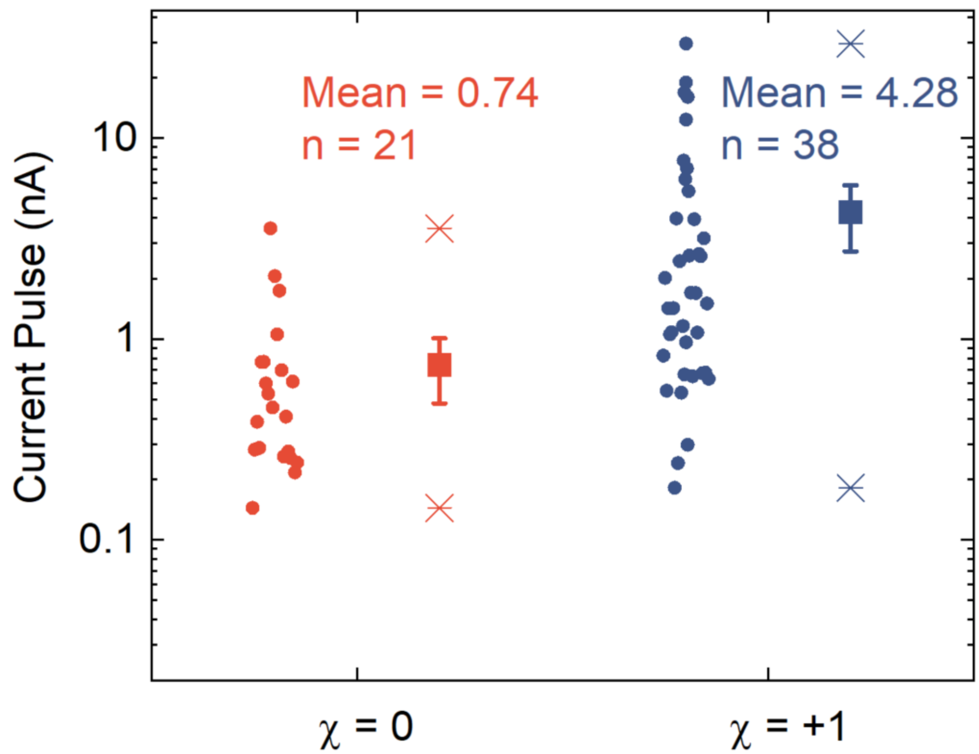


Figure S9. Current pulse size distributions for χ =0 and +1 from a reproduced experiment of Figure 4H. The crosses show the minimum and maximum data points, the solid squares show the mean, and the error bars show the standard error.

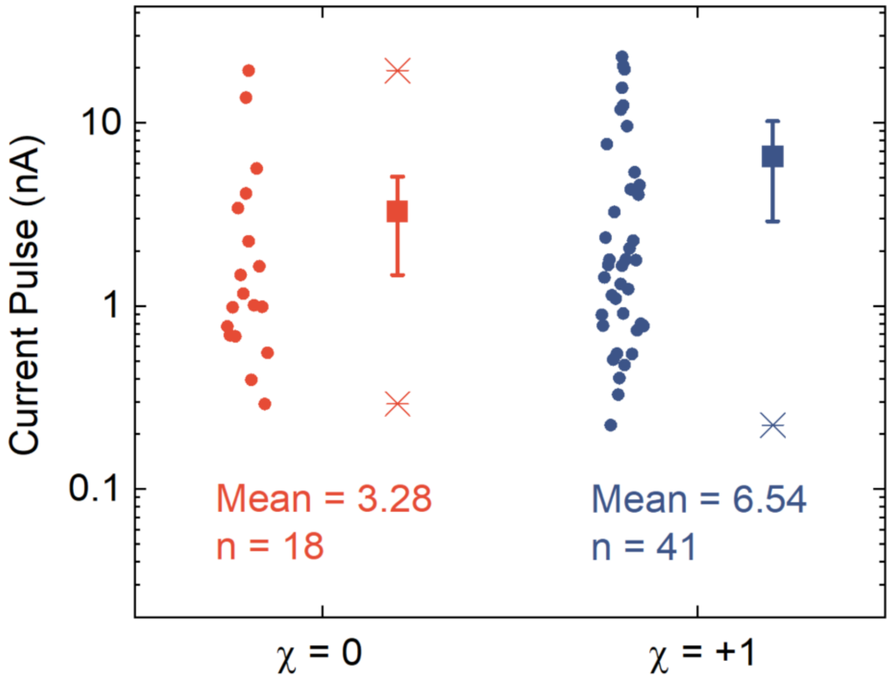


Figure S10. Current pulse size distributions for χ =0 and +1 when 6 mM amino acid in 0.15 M NaCl solution was placed inside the pipette and 1 mM Cd^{2+} in 0.15 M NaCl solution was placed outside. The crosses show the minimum and maximum data points, the solid squares show the mean, and the error bars show the standard error.

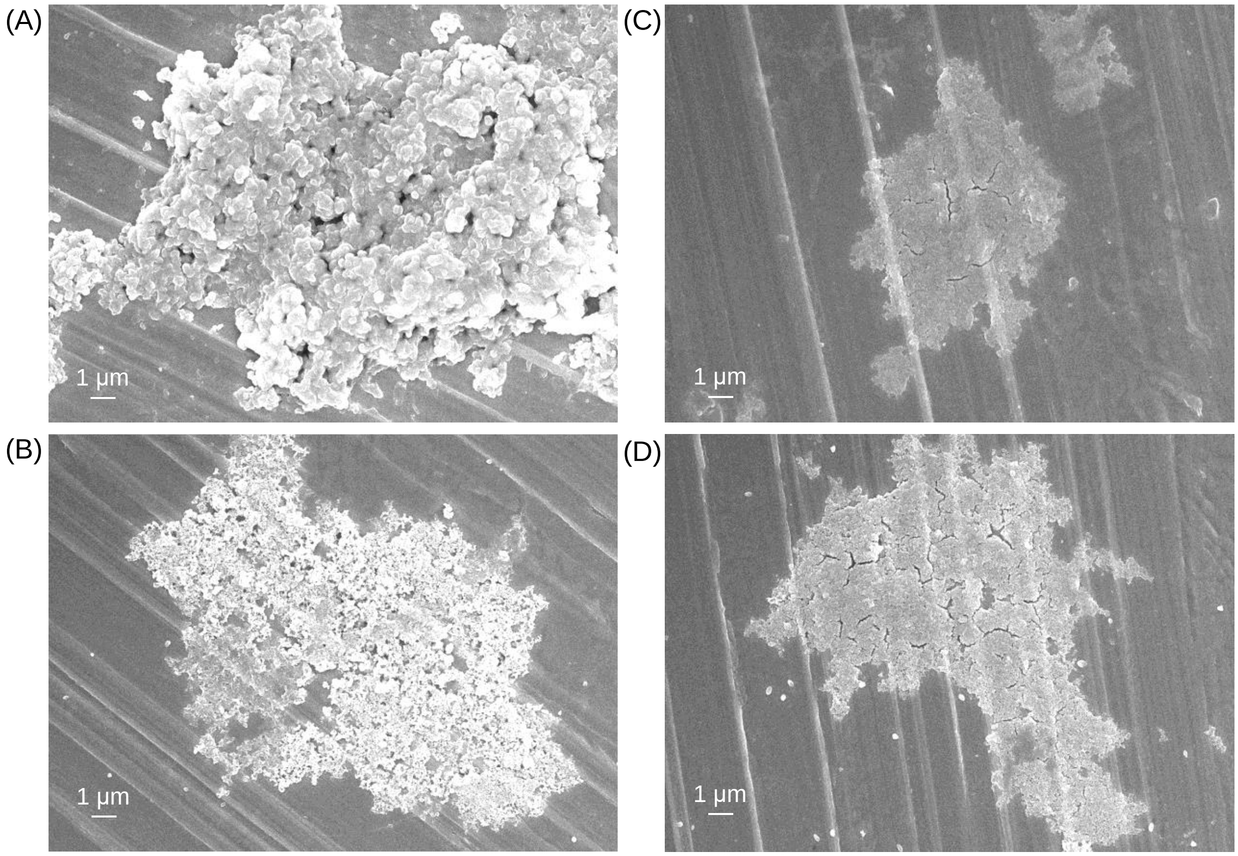


Figure S11. (A) SEM images of $\mathcal{X}$ = +1.0 Cd-Ser microcrystals (B) SEM images of $\mathcal{X}$ = 0 Cd-Ser microcrystals (C) SEM images of $\mathcal{X}$ = +1.0 Cd-Asp microcrystals (D) SEM images of $\mathcal{X}$ = 0 Cd-Asp microcrystals.

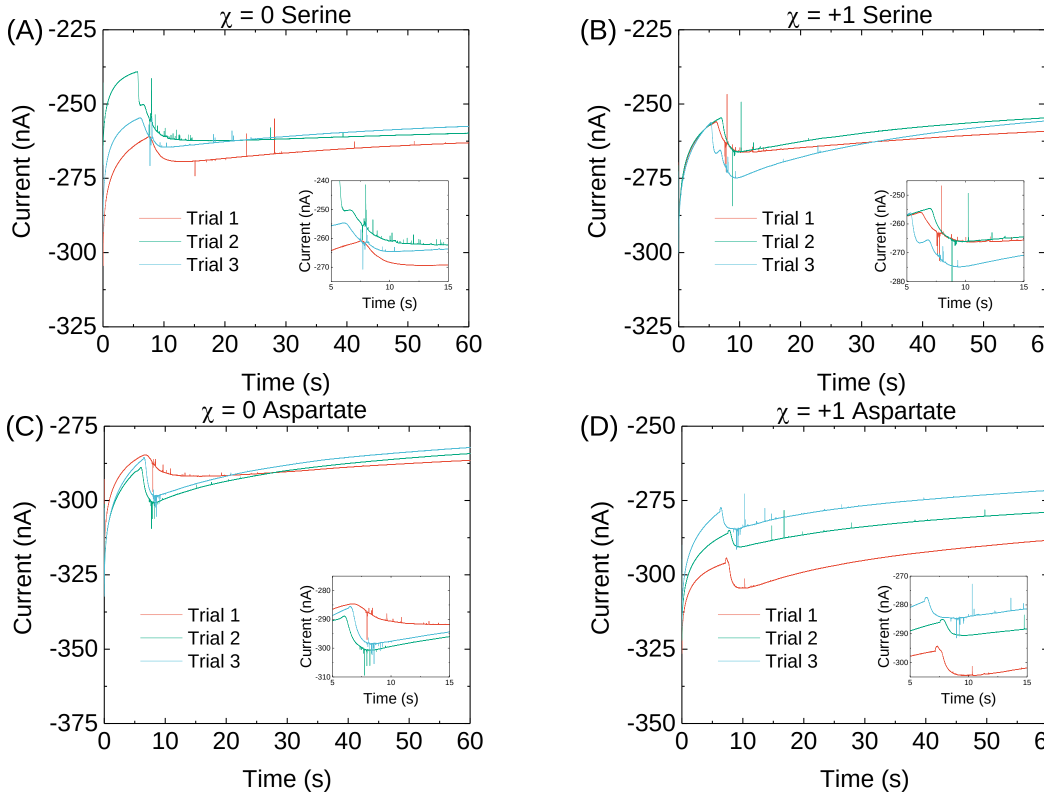


Figure S12. (A) In-situ trials of χ = 0 Cd-Ser microcrystals. (B) In-situ trials of χ = +1 Cd-Ser microcrystals. (C) In-situ trials of χ = 0 Cd-Asp microcrystals. (D) In-situ trials of χ = +1 Cd-Asp microcrystals. Ser: serine and Asp: aspartate.