How to manipulate the phase separation of charged polymers

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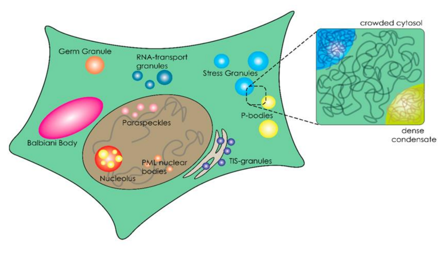
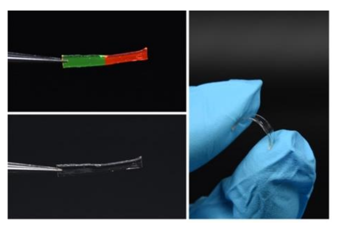
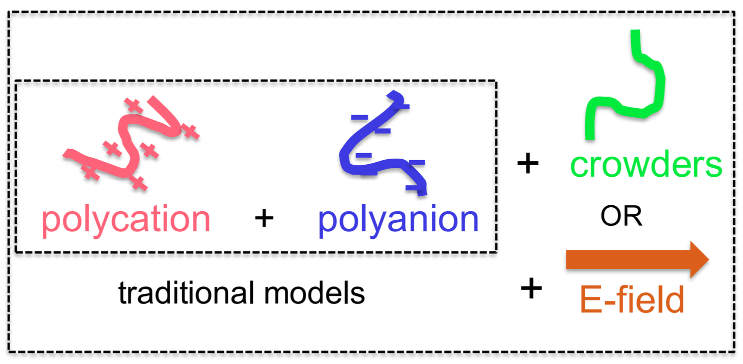
Motivation: phase separation environment is often ignored



Biomolecular condensates in cells[1]



Photoresponsive hydrogel for sensors[2]

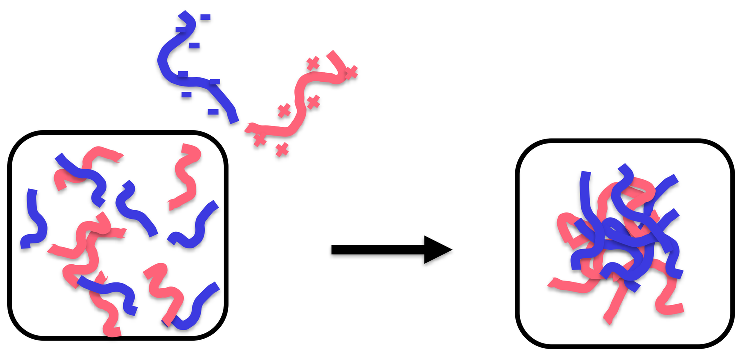


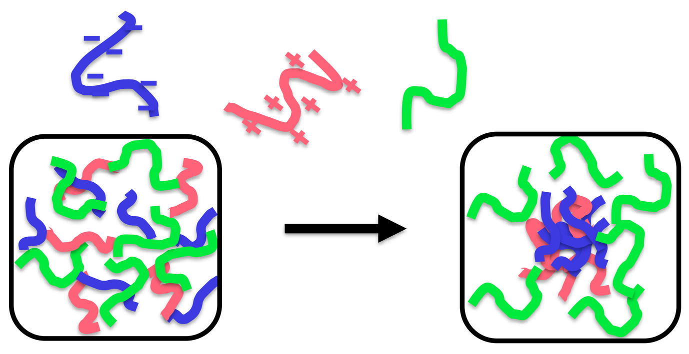
Our model

Oppositely charged polymers show phase separation in water due to Coulomb attraction. Nature has long evolved to harness the power of this electrostatic phase separation[1] to fine-tune macro-molecular assembly; now we can use it for sensors, conductive gels, and more[2,3].

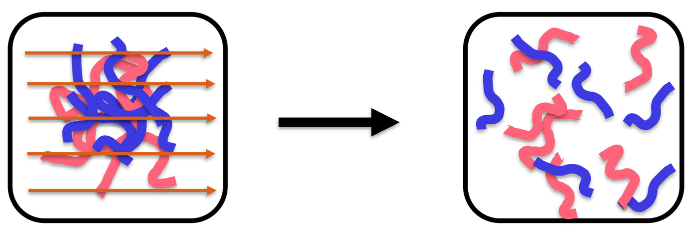
Traditional models ignore the local environment of phase separation[4], which is almost always crowded by other *inert* molecules. And experiments use electric field to manipulate the coacervate.

We show how these environments affects charged phase separation using coarse-grained molecular dynamics.



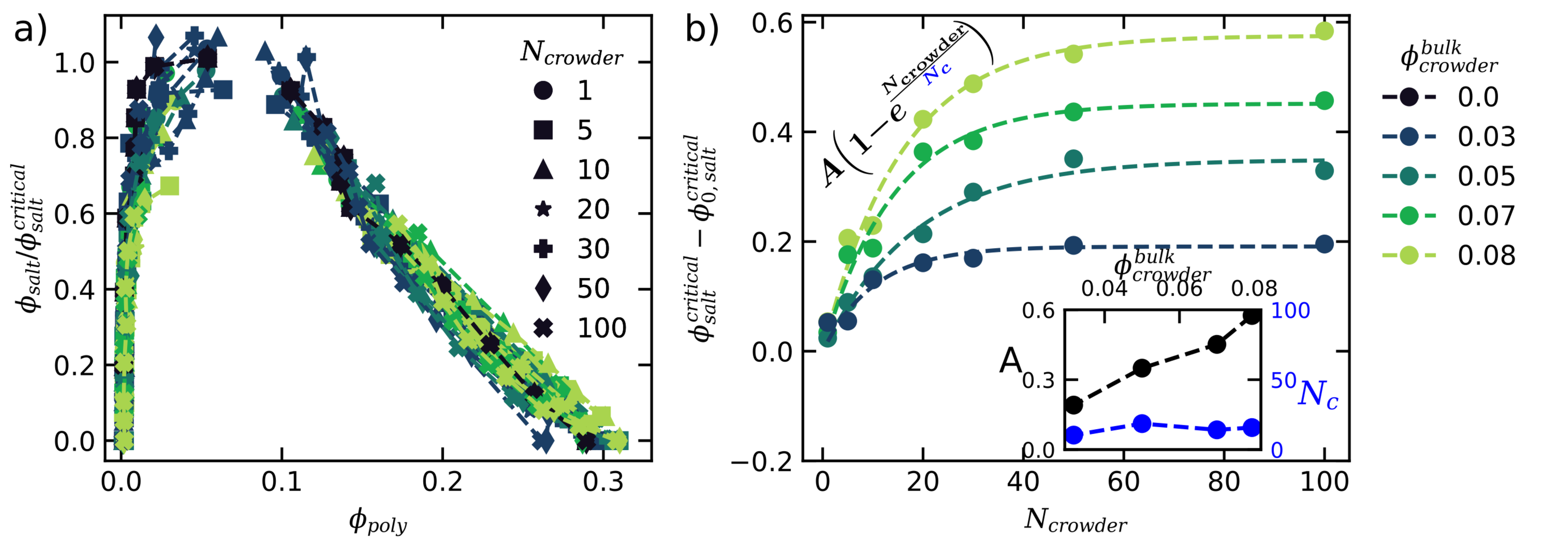


crowders



Electric field

Higher crowder concentration leads to stronger phase separation



Long crowders
(50 monomers)

- promote phase separation
- do not mix with the dense phase
- shift the phase diagram more with increasing concentration

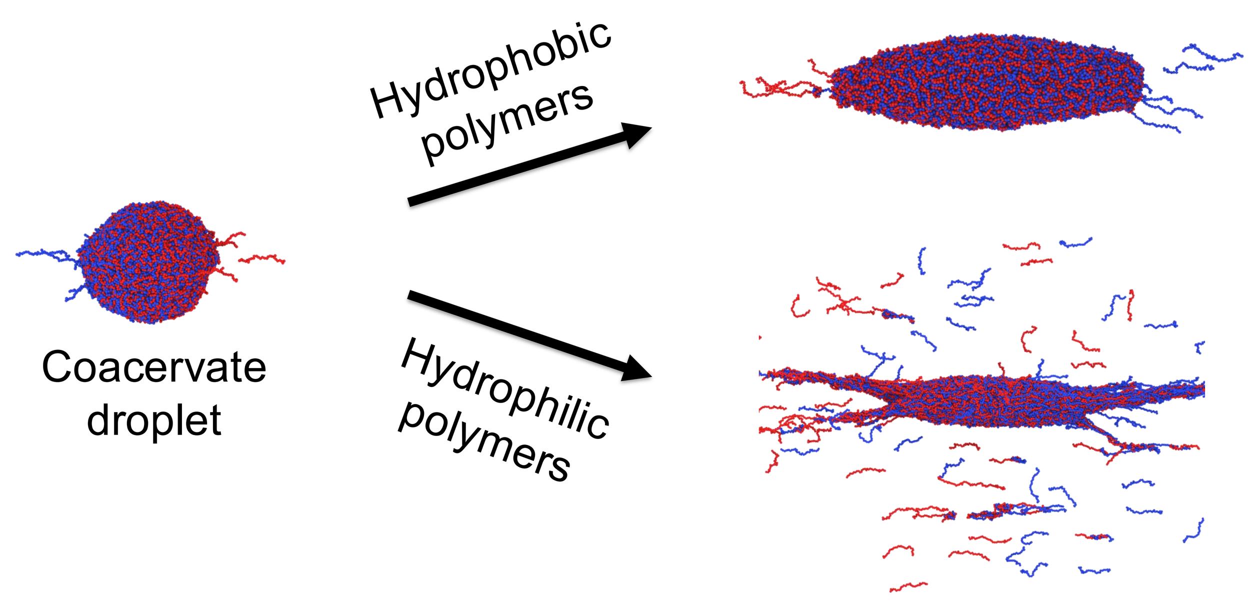
Short crowders
(1 monomer)

- do not affect phase separation
- mix with the dense phase
- do not shift the phase diagram more with increasing concentration

Long polymers do not mix well because mixing offers minimal entropy gain. This results in long crowders staying out of the dense phase. The higher osmotic pressure of longer crowders makes dissolving the dense phase harder.

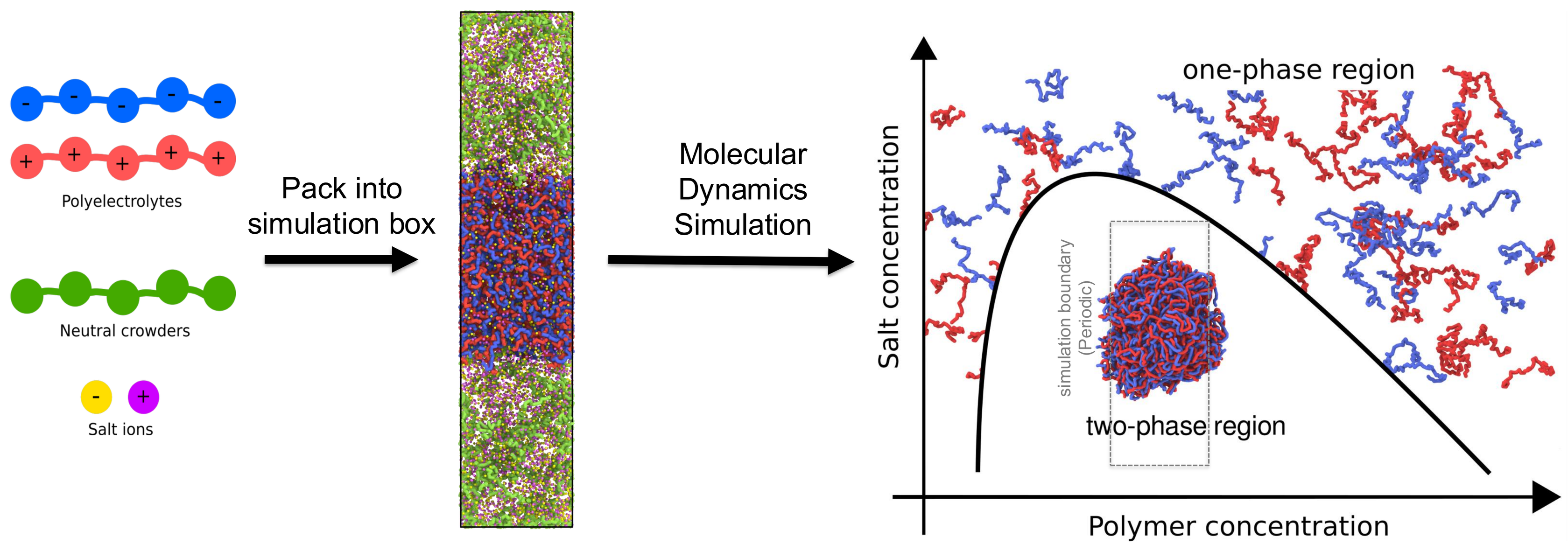
All crowders longer than a critical length (approximately 20 monomers in this model) are completely immiscible with the dense phase. Therefore, increasing crowder length beyond this limit has no additional effect on the phase separation.

E-field pulls the coacervate apart



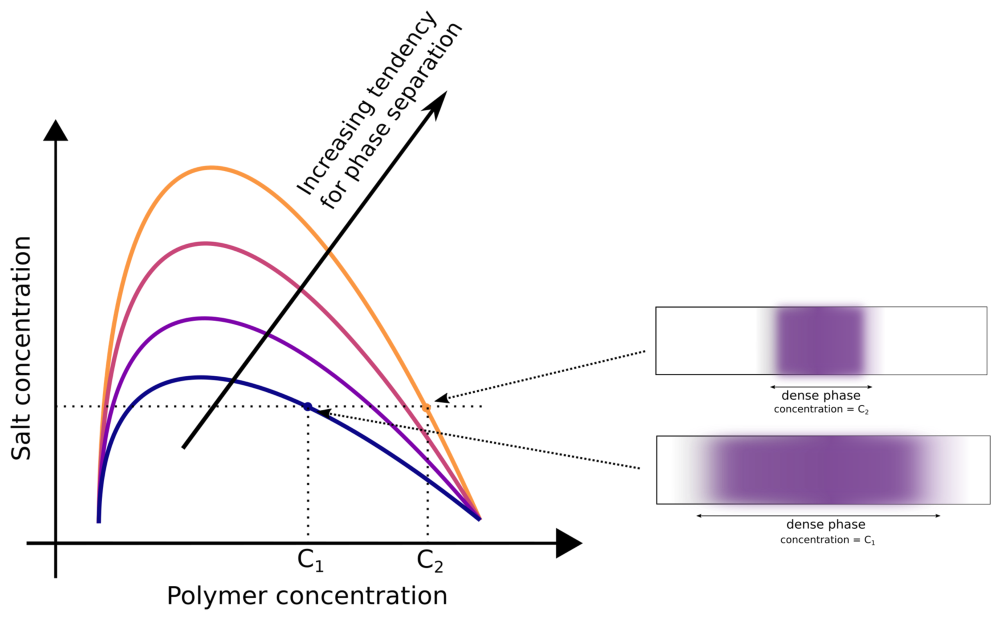
The oppositely charged polyelectrolytes in the coacervate droplet experiance the E-field force in opposite directions. This makes the coacervate droplet unstable and lowers the salt resistance.

Methods & theory: phase diagrams from MD simulations



Oppositely charged polymers phase separate due to their mutual attraction. This creates one phase with high polymer density and another phase with low polymer density.

Introducing oppositely charged ions (salt) replaces polymer-polymer interactions with polymer-ion interactions and partially dissolves the high-density phase. Above a critical concentration of salt ions, the high-density phase is completely dissolved and forms a single uniform phase. Phase diagram shows the boundary between these two states.



All points inside the phase boundary will show phase separation. A larger phase boundary indicates a higher tendency for phase separation. The concentration of the dense phase increases with the size of the phase diagram.

Conclusions

- Phase separation of charged polymers is prevalent in nature.
- Our model accounts for the complex environment of the phase separation.
- The degree of coacervation is proportional to crowder concentration and length.
- Quantifying the effect of crowders helps design better experiments and can open new avenues in guided polymer self-assembly.[5]
- E-field destabilizes the coacervate droplet and can be used to tune its properties.

References:

1. André, Alain AM, and Evan Spruijt. "Liquid–liquid phase separation in crowded environments." *International Journal of Molecular Sciences* 21.16 (2020): 5908.
2. Wang, Jiahua, et al. "Processable and luminescent supramolecular hydrogels from complex coacervation of polycations with lanthanide coordination polyanions." *Macromolecules* 52.22 (2019): 8643-8650
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4. Perry, Sarah L. "Phase separation: Bridging polymer physics and biology." *Current Opinion in Colloid & Interface Science* 39 (2019): 86-97.
5. Bäumer, Nils, et al. "Bioinspired crowding directs supramolecular polymerisation." *Nature Communications* 14.1 (2023): 1084.

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