



Skin Formation and Phase Separation in Polymer Particle Formation: Drying of Acoustically Levitated HPMC Droplets

PhD in Chemical Engineering

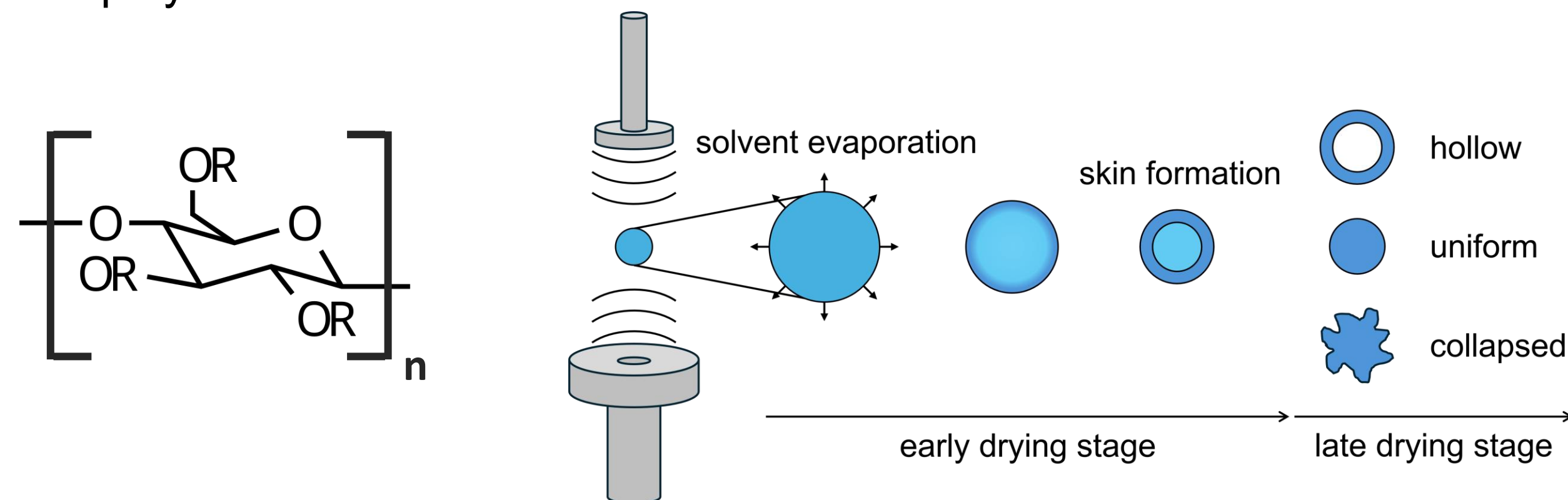
José Santos Pereira (josemariasantospereira@tecnico.ulisboa.pt)

Motivation

The transformation of liquid solution droplets into solid particles by spray drying is a fundamental step in the manufacture of pharmaceuticals, allowing the design and control of particle properties that define their performance [1,2].

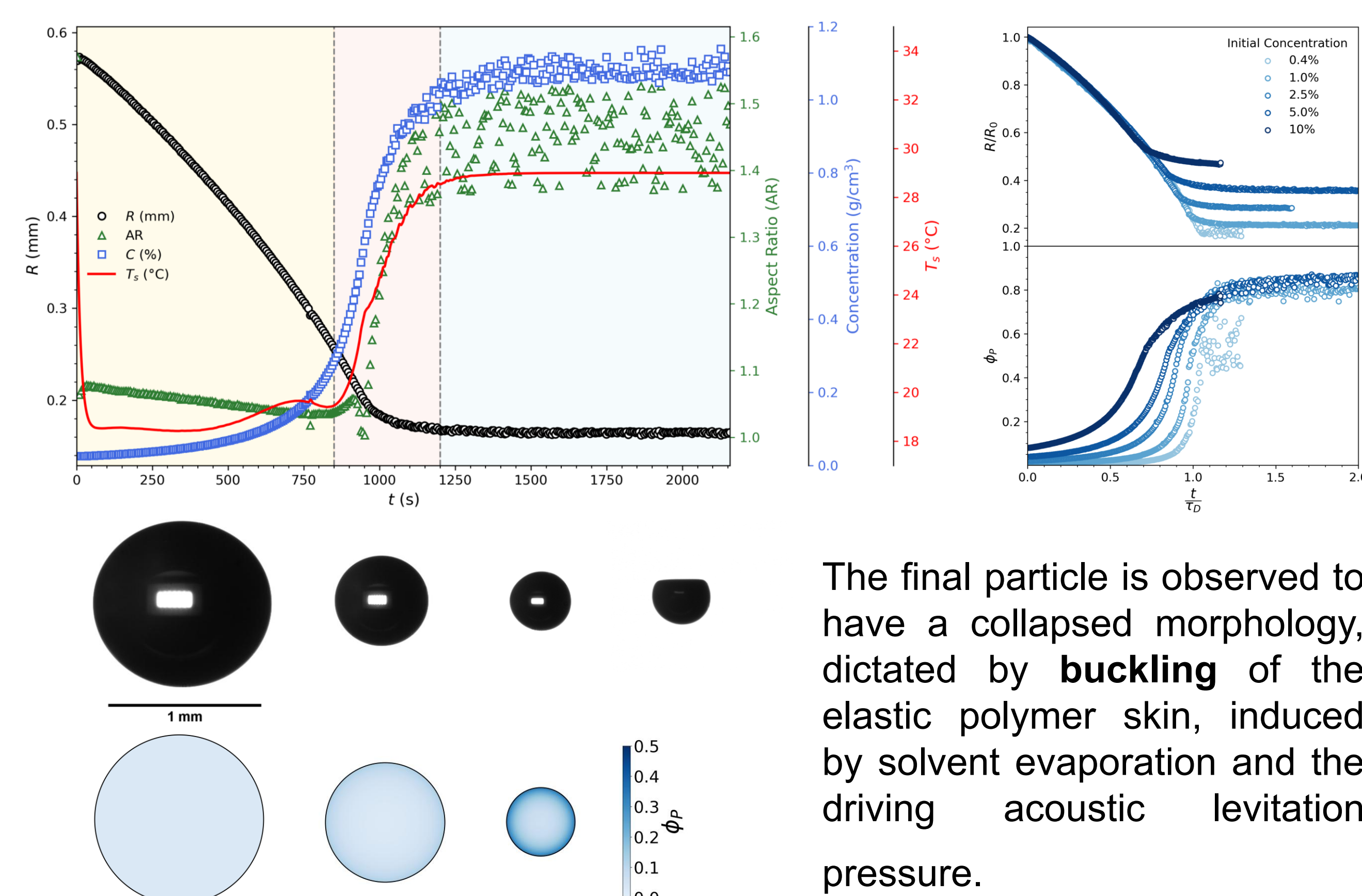
Nonetheless, morphology prediction is challenging due to the interplay of several complex mechanisms [3] (figure 1). This work seeks to address this challenge and **elucidate the fundamental mechanisms underlying particle formation**.

We use **acoustic levitation** to investigate the drying of suspended, isolated polymer droplets. **Hydroxypropyl methylcellulose** (HPMC) and hydroxypropyl methylcellulose acetate succinate (HPMCAS) are chosen as model polymers for this work.



Droplet-to-Particle Transformation

The drying of HPMC aqueous solution droplets was investigated and found to display three main stages: stage I, where **solvent evaporation** dominates and the shrinkage of the droplet takes place; stage II, where a **skin forms** on the surface of the droplet, leading to an abrupt decrease in the drying rate and initiating the solidification process; and, lastly, stage III, where the particle enters **kinetic arrest** and returns to thermal equilibrium.



References

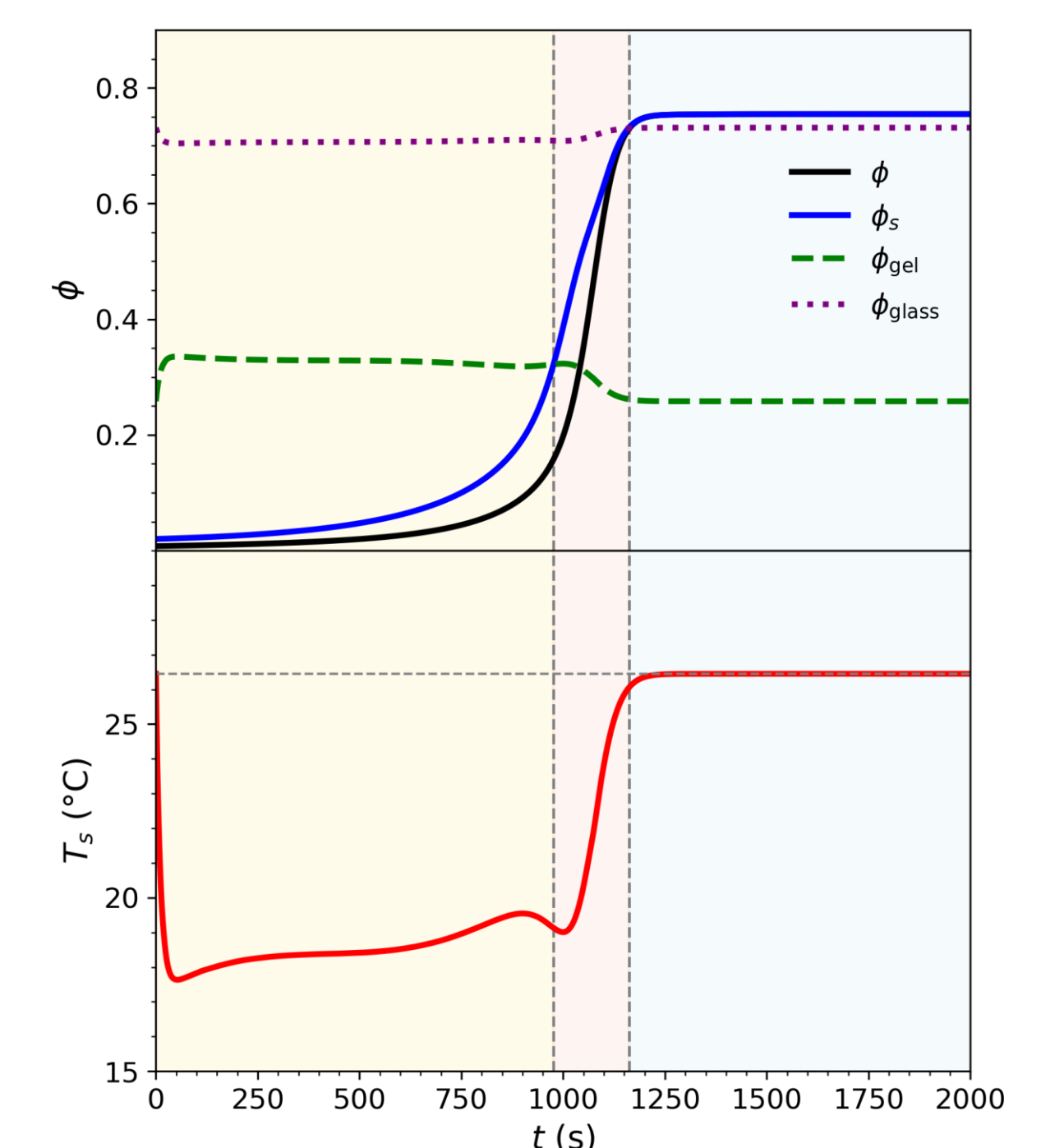
[1] K. J. Ploeger et al (2019) Chemical Engineering in the Pharmaceutical Industry. 2nd ed, John Wiley & Sons. pp. 267-292. [2] R. Vehring (2007) Pharm. Res. 25: 999-1022. [3] R. A. O'Connell et al (2023) Phys. Rev. Lett. 131:218101.

Skin Formation and Kinetic Arrest

The skin formation stage is crucial as it defines the final particles properties and morphology.

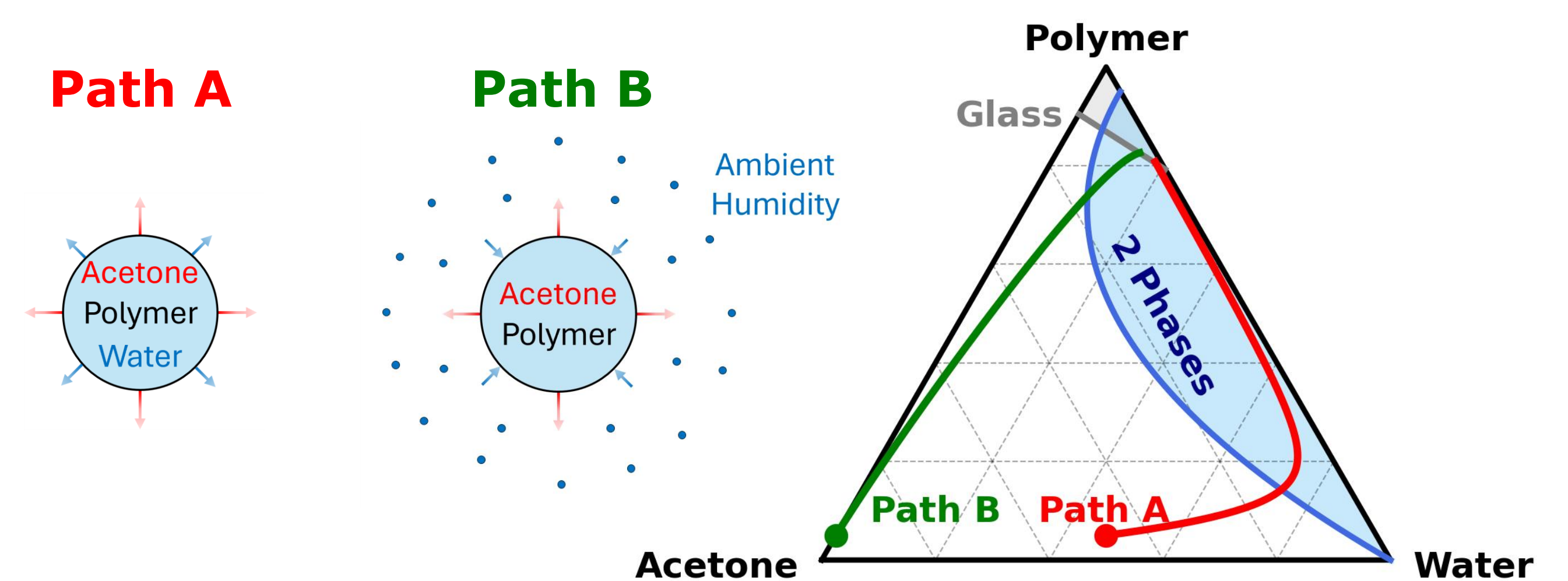
We observe that skin formation initiates when the **surface of the droplet reaches the gel point**. Kinetic arrest, on the other hand, occurs when the concentration crosses the **glass transition**.

Furthermore, the temperature gradient established by evaporative cooling is relaxed into thermal equilibrium upon droplet solidification.

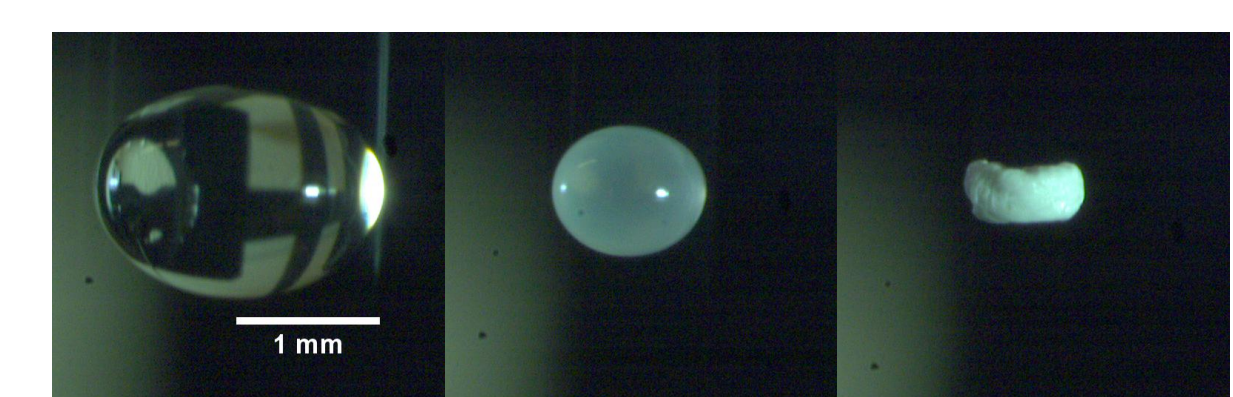


Phase Separation

Exploring the role of phase separation in particle formation, we use HPMCAS in acetone/water mixtures to template morphology.



In Path A, the droplet starts with a solvent mixture that becomes richer in water as evaporation occurs. In Path B, no water is present in the initial droplet but rather **condenses from ambient humidity to drive phase separation**.



Future Work

How does polymer molecular weight and substitution influence particle formation?

Can we relate mechanical and rheological properties to particle morphology?

How does the surface of phase separated particles look at the microscale?

Acknowledgments

This work was financially supported by Hovione Farmaciência S.A. [DIBP/BDE/24].

