# There and Back Again: The Story of Elastic Microphase Separation

1. **Liquid demixing in elastic networks: Cavitation, permeation, or size selection?**
   Authors: P Ronceray, S Mao, A Košmrlj, MP Haataja
   Europhysics Letters 137 (6), 67001 31 (2022)

2. **Nonlocal Elasticity Yields Equilibrium Patterns in Phase Separating Systems**
   Authors: Y Qiang, C Luo, D Zwicker
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Phase separation processes touches our lives daily. Ice melts in a glass, water boils in a kettle, and salad dressings that are oil-water mixtures demix over time [1]. About fifteen years ago Brangwynne, *et al.* [2] discovered the existence of membraneless organelles - biological assemblages that are formed via phase separation processes. A non-vanishing interfacial tension leads to the formation of spherical drops, and manifests in the formation of a sharp interface between the demixed phases in a cellular soup. This discovery ignited significant interest within the physics and biology communities, leading to a rapidly expanding body of research on phase separation processes. These processes span vast ranges of length and time scales [3] and are linked to various human pathologies [4, 5]. It has long been known, however, that the cytoplasm is a complex mileu of biomacromolecules and thereby a viscoelastic fluid [6, 7]. Consequently, the role of viscoelasticity in modifying phase separation processes has been thoroughly investigated [8, 9]. Relatively less importance has been placed on the role of elastic effects in modifying phase separation both in synthetic as well as biologically reticulated networks and gels and is the subject of this commentary.

Pioneering experiments in this connection were carried out by the Dufresne group [10]. They considered the growth of phase-separated droplets (fluorinated oil) inside of a cross-linked polymer network (silicone gel - consisting of a cross-linked silicone polymer network in silicone oil) and conclusively proved the existence of a stable highly uniform microdroplet

phase. The droplet size was tunable and dependent on the cross-link density, quench rate, and loading of the minority fluid. This work sparked our interest in the subject as we had been considering elastic effects on phase separation in the context of complex industrial mixtures [11, 12]. Among the many theoretical formulations that exist [13, 14] in predicting a microdroplet phase in networked systems, we find the paper by Ronceray *et al.* (the first recommended paper, referred to as *PR*, henceforth) most appealing and elegant on account of its simplicity.

Ronceray *et al.*'s calculations employ a scaling theory backed by analytical arguments and perturbation analysis of swollen network models. Coarsening processes that drive phase separation lead to the growth of droplets inside an elastic matrix. The free energy penalty $\Delta g$ per droplet volume, compared to an infinite droplet of phase separated liquid in the absence of an elastic network has three distinct contributions: (i) the elastic energy stored in the network, (ii) the interfacial tension, and (iii) the wetting energy of the filaments comprising the network by the liquid. The mathematically non-trivial aspect lies in the evaluation of the elastic energy resulting from the network deformation induced by the droplet, a dynamic version of the classic Eshelby problem in continuum mechanics [15–17]. The elastic deformation energy of the network outside the droplet of size $r_d$ to grow in a spherically symmetric infinite medium is written as a functional $W(\lambda_1, \lambda_2, \lambda_3)$, where $\lambda_i$'s are the principal stretches. The authors consider two different scenarios, depending on whether the impregnating fluid wets or is excluded from the polymer network.

Consider an initial spherical inclusion of radius $\xi$, and a phase separated drop of radius $r_d = r(\xi)$ that stretches the pore by a factor $\lambda_d = r_d/\xi$ (see Fig.1 of the *SI* of the *PR* paper). The elastic energy outside this droplet that is stored in the network is therefore given by

$$E_{el,out} = \int_\xi^\infty W\left(\frac{dr}{dR}, \frac{r}{R}, \frac{r}{R}\right) R^2 dR. \tag{1}$$

Rescaling the energies by $u = R/\xi$ and introducing the variables $s = dr/dR$ and $t = r/R$ for the radial and hoop stretches the elastic energy per unit volume is given by

$$\frac{E_{el,out}}{v_d} = \frac{3}{\lambda_d^3} \int_1^\infty W\left(s(u), t(u), t(u)\right) u^2 du \equiv f_{out}(\lambda_d), \tag{2}$$

where $v_d = \left(\frac{4\pi}{3}\right) r_d^3$ the droplet volume.

For a permeating droplet the elastic energy has two contributions, the elastic energy inside and outside the drop. The elastic energy inside the drop assuming a homogeneous and isotropic deformation of stretch $\lambda_i$ the total elastic energy is given by

$$E_{el} = \frac{4\pi}{3}\left(\frac{r_d}{\lambda_i}\right)^3 W(\lambda_i, \lambda_i, \lambda_i) + 4\pi \int_{r_d/\lambda_i}^\infty W\left(\frac{dr}{dR}, \frac{r}{R}, \frac{r}{R}\right) R^2 dR, \tag{3}$$

which leads to

$$\frac{E_{el}}{v_d} = \frac{1}{\lambda_i^3} W(\lambda_i, \lambda_i, \lambda_i) + f_{out}(\lambda_i). \tag{4}$$

Thus the elastic energy of the droplet per unit volume $\frac{E_{el}}{v_d} \sim \alpha G$, where $\alpha$ is a material dependent constant and $G$ is the shear modulus of the network (proportional to the local cross-link density). The phase boundary, *i.e.* the line demarcating regions of parameter space between a micro-droplet phase and a droplet that extrudes all the network filaments forming a cavity, is given by a balance of the elastic deformation and interfacial energies. The interfacial energy of a microdroplet of radius $r \sim \xi$ is given by $E_{surf} \sim 4\pi\xi^2\gamma$, where $\gamma$ denotes the surface tension between the two liquids. The surface free energy per droplet volume is thus given by $\frac{E_{surf}}{v_d} \sim \frac{3\gamma}{\xi}$. The ratio of the elastic and surface energy per unit volume defines a dimensionless parameter, the *elasto-capillary number*

$$ h \equiv \frac{3\gamma}{\xi G}. \tag{5} $$

Thus, for $h < \alpha$, *i.e.*, for low surface tensions, or large values of shear modulus $G$ the thermodynamic stable phase is one composed of several pore-sized microdroplets. The choice of the first recommended $PR$ paper for this commentary is based on the simplicity and elegance of the analysis leading to this significant result. A mean-field calculation that describes the phase boundary in this regime accounting for the free energies of mixing, interfacial tension and droplet deformation was developed subsequently [18].

The other interesting regime concerns the liquid wetting the network. An additional energy cost for wetting the network

$$ E_{wet} = \frac{4\pi r^3}{3}(1 - \varphi)\sigma_p, \tag{6} $$

where $\sigma_p$ is the permeation stress and $\varphi$ denotes the fraction of the network that is expelled from the droplet $\varphi = 1 - \lambda_i^3$ ($\lambda_i$ is the homogeneous, isotropic deformation stretch factor introduced earlier). The ratio of the wetting and deformation energies per unit volume of a droplet leads to another dimensionless number, the *permeo-elastic number*

$$ p \equiv \frac{\sigma_p}{G}, \tag{7} $$

which measures the degree of network deformation induced by the permeation stress. Thus for $p > \alpha$ the fluid-network repulsion is strong enough to cause cavitation, while for $p < \alpha$ the filaments wet the fluid. These two dimensionless parameters $h$, and $p$ completely determine the morphology of droplets in networked systems as shown in Fig. 1.

We now address a crucial question about the phase-separated microdroplet phase previously discussed: the equilibrium thermodynamics of concentrated microdroplets within an elastic network. Existing models [10, 13, 14, 18] (including the first recommended $PR$ paper), utilize local elastic theories to calculate the morphology of droplets undergoing phase separation in polymer networks. These calculations consider a dilute concentration of droplets where the deformation field induced by a droplet does not affect the thermodynamics and growth kinetics of another one nearby. This notion is challenged in the recent study by the Zwicker group (the second recommended paper referred to as $DZ$ henceforth). Their argument stems from identification of length-scales in a phenomenological free energy that
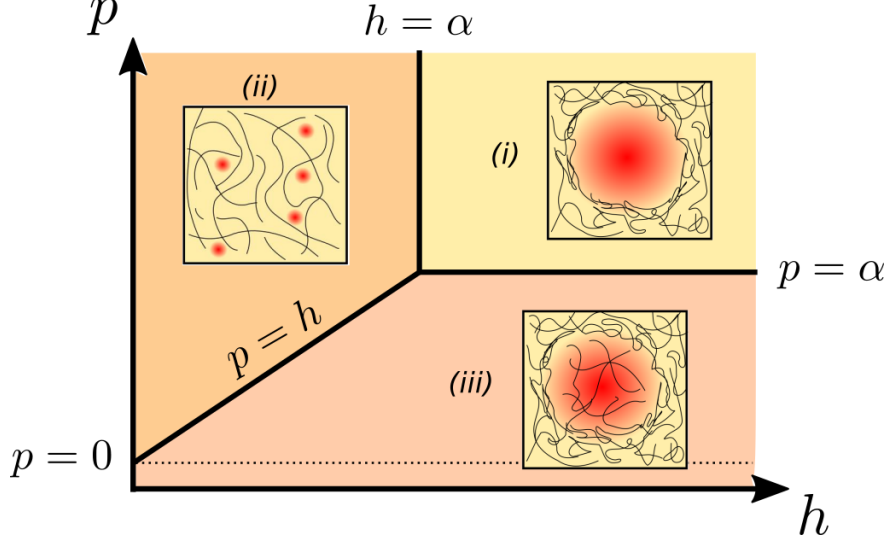
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Figure 1: Phase diagram of droplets undergoing liquid-liquid phase separation (LLPS) in elastic networks from scaling arguments (Fig. 2 of the first recommended *PR* paper, reproduced with permission). The two dimensionless numbers $h$, the *elastocapillary number* (a ratio of the surface and elastic deformation energies per-unit volume), and $p$, the *permeo-elastic number* (the ratio of the wetting and elastic deformation energies per unit volume) determine the thermodynamically stable phases, (i) the cavitated, (ii) the microdroplet, and (iii) the permeated.

describes phase separation in an elastic network, with $\phi$ being the volume fraction of the network as in Flory-Huggin's theory.

$$F_{local}[\mathbf{F}, \phi] = \frac{k_B T}{\nu} \int \left[ f_{el}(\mathbf{F}) + f_0(\phi) + \kappa |\nabla \phi|^2 \right] d\mathbf{x}. \tag{8}$$

Here, $\mathbf{F}$ is the deformation tensor, $f_{el}(\mathbf{F})$ the elastic deformation energy, while $f_0(\phi)$ corresponds to the mean-field mixing free-energies that leads to phase separation. The third term that accounts for energetic penalty for variations of the $\phi$ field and hence models the interfacial tension [19]. Zwicker's arguments stem from the existence of a single length scale in the problem dependant on $\kappa$ and the need for an additional length-scale to explain the bicontinuous phases observed in elastic systems recently [20]. Their solution is in assuming the network as a linear elastic solid and adding a non-local contribution to the elastic energy of the form

$$F_{nonlocal}[\phi] = \frac{1}{2} \int \epsilon(X) \sigma_{nonlocal}(X) dX, \tag{9}$$

where the nonlocal stress $\sigma_{nonlocal}(X)$ is given by

$$\sigma_{nonlocal}(X) = E \int \epsilon(X') g_\xi(X' - X) dX' \tag{10}$$

with $\epsilon(X) = \frac{\phi_0}{\phi(X)} - 1$ corresponding to the strain in the network, with

$$g_\xi(X) = \sqrt{\frac{2}{\pi\xi^2}} \exp\left(-\frac{2X^2}{\xi^2}\right). \tag{11}$$

Thus, a second characteristic length $\xi$ (not to be confused with the variable introduced earlier in the first recommended $PR$ paper) that quantifies the non-locality of the mesh is introduced. The interplay between the elastocapillary length $h$ and that governing non-local heterogeneities $\xi$ qualitatively matches the experimental results.

What is the microscopic origin of this emergent length scale in networked systems? How does it depend on the material parameters? Does this have a role in dictating the biology of cellular condensates? These are fundamental questions that need answering and the developments outlined here offer exciting possibilities. It is the view of the author that a throwback at the past on statistical mechanics of phase transitions applied to magnetic systems and alloys can offer helpful insights. For example, can one get a regular arrangement of droplets in a cross-linked network? If after all elastic interactions are important, it would indeed influence the underlying microstructure of the droplets. This is a classic problem first considered in context of magnetic systems undergoing phase transitions on compressible cubic lattices [21]. Another important question relates to the ordering kinetics of phase separated droplets in a medium where elastic interactions are important [22, 23]. This has also been investigated in the past in context of metallic alloys undergoing phase separation [24, 25]. Biological systems are however active materials driven far from equilibrium and the theories of phase ordering kinetics developed need to be reviewed carefully for systems where a long-time Boltzmannian probability distribution $P[\phi] \sim e^{-\beta F[\phi]}$ is not the equilibrium state. Synergistic experiment-theory collaboration on specific systems would pave the way forward. The gauntlet has been cast, and the future of elastic microphase separation is certainly looking bright.

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