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ABSTRACT

Droplets are essential for spatially controlling biomolecules in cells. To work properly, cells need to control the emergence and morphology of droplets. On the one hand, driven chemical reactions can affect droplets profoundly. For instance, reactions can control how droplets nucleate and how large they grow. On the other hand, droplets coexist with various organelles and other structures inside cells, which could affect their nucleation and morphology. To understand the interplay of these two aspects, we study a continuous field theory of active phase separation. Our numerical simulations reveal that reactions suppress nucleation while attractive walls enhance it. Intriguingly, these two effects are coupled, leading to shapes that deviate substantially from the spherical caps predicted for passive systems. These distortions result from anisotropic fluxes responding to the boundary conditions dictated by the Young–Dupré equation. Interestingly, an electrostatic analogy of chemical reactions confirms these effects. We thus demonstrate how driven chemical reactions affect the emergence and morphology of droplets, which could be crucial for understanding biological cells and improving technical applications, e.g., in chemical engineering.

I. INTRODUCTION

Droplets comprised of biomolecules, also known as biomolecular condensates, are crucial for organizing biological cells. For example, such droplets separate molecules, control chemical reactions, and exert forces. To fulfill these functions, it is likely that cells control the nucleation, location, size, and shape of droplets. While nucleation can happen spontaneously inside the cytoplasm, most droplets might be nucleated heterogeneously involving other structures as nucleation sites. Indeed, many droplets interact with other structures inside cells, like cytoskeletal elements, membrane-bound organelles, and the plasma membrane. Such interactions of liquid-like droplets with more solid-like structures are known as wetting and directly linked to heterogeneous nucleation. However, most traditional examples of heterogeneous nucleation, e.g., by dust particles in clouds, concern passive systems. In contrast, biological cells use external energy input to control processes actively, but it is unclear how activity affects heterogeneous nucleation and the properties of the subsequently forming droplets attached to the solid surface (sessile droplets).

Driven chemical reactions that affect the droplet material are one crucial example for an active process that controls droplets in cells. If such reactions take place in the entire system, droplet size can be controlled, and homogeneous nucleation is suppressed. Moreover, if reactions are restricted to the boundary, Liese et al. recently demonstrated modified shapes of sessile droplets. However, the generic case of wetting in the presence of bulk chemical reactions has not been considered so far.

To study how boundaries affect the behavior of chemically active droplets, we consider a continuous description of phase separation with driven reactions in the bulk and a passive interaction of the droplet material with a flat wall. Our stochastic simulations and analytical results from an equilibrium surrogate model reveal that reactions generally suppress nucleation while attractive walls enhance it. Intriguingly, these two effects are coupled, leading to shapes that deviate substantially from the spherical caps predicted for passive systems.
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II. MODEL

We consider an isothermal system of fixed volume $V$ filled with an incompressible, binary mixture of droplet and solvent material with equal molecular volume $v$. The state of the fluid is described by the concentration field $c(r,t)$ of the droplet material, whereas the solvent concentration is $v^{-1} - c(r,t)$. We describe the interactions and entropy in the system using free energy comprised of bulk and surface terms given by

$$F = \int_V \left[ f(c) + \frac{\kappa}{2} |\nabla c|^2 \right] dr - \int_{\partial V} g(c) dA, \quad (1)$$

where $f(c)$ is the local free energy density, $\kappa$ penalizes compositional gradients, and $g(c)$ is the contact potential describing the interaction of the fluid with the immobile boundary $\partial V$ of the system. For simplicity, we focus on the linear order of the expansion $g(c) = g_0 + g_1 c + O(c^2)$ since $g_0$ merely shifts the total free energy $F$ but does not affect the behavior. In contrast, we describe the bulk interactions by

$$f(c) = -\frac{a_2}{2} \left( \frac{c - 1}{2\nu} \right)^2 + \frac{a_4}{4} \left( \frac{c - 1}{2\nu} \right)^4 , \quad (2)$$

where $a_2, a_4 > 0$ are phenomenological coefficients. Note that $f(c)$ is symmetric when $c$ is replaced by $v^{-1} - c$.

Equilibrium states minimize the free energy $F$. As a necessary condition, the variation of $F$ with respect to $c$ must vanish, which yields the two conditions,

$$f'(c) - k \nabla^2 c = \text{const.} \quad \text{(in the bulk)}, \quad (3a)$$

$$n \cdot \nabla c = \frac{g_1}{\kappa} \quad \text{(at the boundary)}, \quad (3b)$$

where $n$ denotes the outward normal of the surface $\partial V$. The first equation describes the balance of the exchange chemical potential $\mu = f'(c) - k \nabla^2 c$, where the constant is determined from material conservation. This generically yields a dense phase of concentration $c_m^{(0)} \approx (2v)^{-1} + \sqrt{a_2/a_4}$ that is separated from a dilute phase of concentration $c_m^{(0)} \approx (2v)^{-1} - \sqrt{a_2/a_4}$ by an interface of width $w \approx 2\kappa/\sqrt{a_2}$. The dense phase typically assumes a spherical shape to minimize the surface tension $\gamma_{ds} = 2\sqrt{2\kappa a_2/(3a_4)}$ between the two phases. In contrast, Eq. (3b) describes a boundary condition, which determines the behavior of the system close to the wall. In particular, the droplet material is repelled from the wall if $g_1 < 0$. Since the droplet still maintains its spherical shape, its geometry at the wall is fully quantified by the contact angle $\theta$, which is given by the Young–Dupré equation, cos($\theta$) = ($y_{ds} - y_{sd})/y_{sd},$ where $y_{ds}$, $y_{sd}$, and $y_{dl}$ denote the surface tensions between wall–solvent, wall–droplet, and droplet–solvent, respectively. Since $g(c)$ directly quantifies surface energies, we have $y_{sd} \approx -g_1 c_m^{(0)}$ and $y_{dl} \approx -g_1 c_m^{(0)}$, resulting in

$$\cos(\theta) = \frac{3g_1}{a_2} \frac{\sqrt{a_4/2\kappa}} {a_2/\sqrt{2\kappa}} \quad (4)$$

This equation can only be solved for $\theta$ if the interactions between the droplet and the wall are weak, $|g_1| < g_s$ with $g_s \approx \sqrt{(2a_2/\kappa)/(9a_4)}$. In contrast, the droplet will be repelled from the wall if $g_1 < -g_s$, and it will fully wet the wall if $g_1 > g_s$. Since the interesting process of heterogeneous nucleation is related to partial wetting where $\theta$ is defined, we concentrate on the case $|g_1| < g_s$. In particular, we consider the case $g_1 > 0$, corresponding to an attractive wall that is the most probable site for nucleation.

To describe nucleation, we next specify the dynamics of the system. We start with the continuity equation,

$$\partial_t c + \nabla \cdot j = s, \quad (5)$$

where $j$ denotes the diffusive exchange flux between droplet material and the solvent, and the source term $s$ describes chemical transitions. The passive diffusive flux $j$ is driven by gradients of the exchange chemical potential, $j = -\Lambda_d \nabla \mu + \eta$, where $\Lambda_d$ is the diffusive mobility and $\eta$ denotes diffusive thermal noise, which obeys $\langle \eta(r,t) \rangle = 0$ and the fluctuation–dissipation theorem $\langle \eta(r,t)\eta(r',t') \rangle = 2k_B T \Lambda_d \delta(t - t') \delta(r - r')$. $k_B T$ is the thermal energy.

The system becomes active when we drive the reactions described by $s$ out of equilibrium. We focus on driven reactions that result in size–controlled droplets, which requires the production of droplet material outside the droplet, while it is degrading inside. This behavior can be captured by the linear expression,

$$s(c) = -k(c - c_0), \quad (6)$$

where $k$ sets the reaction rate and $c_0$ denotes the stationary state of the reaction scheme. We have shown previously that this case faithfully describes homogeneous nucleation in active systems and that the thermal noise associated with the reactions can be neglected since the diffusive noise $\eta$ dominates on the length scales relevant for nucleation. Taken together, our system is described by the stochastic partial differential equation,

$$\partial_t c = \Lambda_d \nabla^2 \mu - k(c - c_0) + \nabla \cdot \eta, \quad (7)$$

augmented by the no–flux boundary condition $n \cdot j = 0$, and Eq. (3b) describing local equilibrium at the boundary. The linear reactions given by Eq. (6) imply that the average concentration $\bar{c} = V^{-1} \int c \, dV$ approaches the stationary value $c_0$ exponentially, $\bar{c}(t) = c_0 + \left[ \bar{c}(0) - c_0 \right] e^{-kt}$. In particular, a system initialized at chemical equilibrium, $\bar{c} = c_0$, will conserve the average composition, despite potential droplet nucleation. We focus on this case for simplicity, omitting the transient dynamics of the chemical relaxation.

III. CHEMICAL REACTIONS SUPPRESS HETEROGENEOUS NUCLEATION

A. Numerical simulations reveal increased nucleation times

To investigate heterogeneous nucleation, we performed numerical simulations of Eq. (7) in a two-dimensional system. Here, we used finite differences to approximate derivatives and an Euler–Maruyama scheme to perform the time stepping. We applied periodic boundary conditions along the $x$-direction and Eq. (3b) on both boundaries in the $y$-directions. Repeating the simulations many times, we observed that the time $t_{\text{Nuc}}$, quantifying when the first droplet nucleates, follows an exponential distribution; see Fig. S1 in the supplementary material. Thus, we define
the nucleation time \( \tau \) as the ensemble average of \( t_{\text{nucl}} \). Figure 1(b) shows that \( \tau \) decreases for stronger droplet-wall attraction (larger \( g_1 \)), as expected for nucleation of passive droplets.\textsuperscript{24} In contrast, larger reaction rates \( k \) lead to longer nucleation times \( \tau \), indicating that active chemical reactions hinder nucleation. This stabilization of the homogeneous state by chemical reactions is consistent with the results for homogeneous nucleation.\textsuperscript{23} These numerical simulations indicate that repulsive walls (small \( g_1 \)) and larger reactions (larger \( k \)) suppress heterogeneous nucleation, but they do not reveal the underlying principles governing the nucleation process.

**B. Equilibrium surrogate model reveals trade-off between wall affinity and chemical reactions**

To understand the nucleation path in detail, we next map the active system onto a surrogate equilibrium system with long-ranged interactions described by the potential \( \Psi \). This mapping is possible for the special case of the linear reactions that we consider, where the average composition \( \bar{c}(t) \) is conserved for systems initialized with \( \bar{c} = c_0 \). In this case, we can re-write the dynamics given by Eq. (7) as

\[
\dot{c} = \Lambda_\text{d} \nabla^2 \Psi[c] / \bar{c} + \nabla \cdot \eta
\]

when we use the augmented free energy functional,

\[
F[c] = F[c] + F_{\text{react}}[c],
\]

where

\[
F_{\text{react}}[c] = \frac{k}{2\Lambda_\text{d}} \int \left[ c(r) - c_0 \right] \Psi(r) \, dr
\]

captures the energy associated with reactions.\textsuperscript{35–37} Here, \( \Psi \) is the solution to the Poisson equation \( \nabla^2 \Psi = \bar{c} - c(r) \) and describes the long-ranged interactions, which originate from the interplay of chemical reactions and diffusion in the original model. Since the surrogate model requires mass conservation, we solve for \( \Psi \) employing Neumann boundary conditions, \( n \cdot \nabla \Psi = 0 \).

We used the free energy of the surrogate model, given by Eq. (8), to map out the minimal energy path connecting the homogeneous state with the state where a droplet wets the wall. To do this, we used constrained optimization to obtain concentration profiles at successively larger values of a nucleation coordinate \( X \); see Sec. II in the supplementary material. We chose \( X \) such that it measures the amount of material inside the droplet, but these details do not affect the energies of the minima and the saddle point in between. Figure 2(a) shows example profiles of minimal energy for successive \( X \), which together form a minimal energy path. These initial data already indicate that the maximal concentration inside the droplet increases alongside its size.

The minimal energy path allows us to determine the saddle point in the energy landscape, which is the transition state of the nucleation process with associated critical energy and critical nucleus. Figure 2(b) shows that chemical reactions generally increase the energy \( \tilde{F} \) along the minimal energy path, potentially explaining why reactions suppress nucleation. However, reactions also increase \( \tilde{F} \) of the homogeneous state when the wall is attractive (\( g_1 > 0 \)). This is because the boundary condition given by Eq. (3b) perturbs the homogeneous state in a layer with a thickness of roughly the interfacial width \( \nu \), leading to local reactive fluxes. To see how chemical reactions affect nucleation, we thus evaluated the energy difference \( \Delta \tilde{F} \) between the transition state and the homogeneous initial state, which is the energy of the nucleation barrier. Figure 2(c) shows that \( \Delta \tilde{F} \) increases with the reaction rate \( k \), while it decreases with more attractive walls (larger \( g_1 \)), which is expected.\textsuperscript{23,34}

To see how the nucleation barrier \( \Delta \tilde{F} \) depends on the chemical reactions and the wall affinity, we decompose \( \Delta \tilde{F} \) into different terms,

\[
\Delta \tilde{F}(g_1, k) = \Delta \tilde{F}_{\text{pas}}(g_1) + \Delta \tilde{F}_{\text{react}}(k) + \Delta \tilde{F}_{\text{coupl}}(g_1, k),
\]

where \( \Delta \tilde{F}_{\text{pas}} = \Delta \tilde{F}(g_1, k = 0) \) quantifies the barrier for passive heterogeneous nucleation, \( \Delta \tilde{F}_{\text{react}} = \Delta \tilde{F}(g_1 = 0, k) \) is the energy barrier of chemically driven droplets at a neutral wall, and \( \Delta \tilde{F}_{\text{coupl}}(g_1, k) \) denotes the energy due to the interaction of the two effects. Since we directly determined \( \Delta \tilde{F}(g_1, k) \), \( \Delta \tilde{F}_{\text{pas}}(g_1) \), and \( \Delta \tilde{F}_{\text{react}}(k) \), we can infer \( \Delta \tilde{F}_{\text{coupl}}(g_1, k) \) from Eq. (10). The data shown in Fig. 2(d) indicate a significant negative coupling between the wall affinity and the reactions, i.e., strong affinity to the wall can decrease the relative effect of chemical reactions.

The coupling between the wall affinity \( g_1 \) and the reaction rate \( k \) is also apparent in the contour lines of equal \( \Delta \tilde{F} \), where reactions and wall affinity compensate each other; see Fig. 2(c). We show in Sec. IV of the supplementary material that concave contour lines would be expected without coupling (\( \Delta \tilde{F}_{\text{coupl}} = 0 \)) so that the slight convex shape of the observed lines is a strong indication for coupling. To analyze these contour lines in more detail, we approximate the coupling by a bilinear function, \( \Delta \tilde{F}_{\text{coupl}}(g_1, k) \approx h g_1 k \) with pre-factor \( h \), motivated by Fig. 2(d). Moreover, we use a linear approximation...
FIG. 2. Reactions raise energy barrier of nucleation. (a) Cuts through concentration profile $c(x, y)$ along the two axes (top) and shape of droplet interface (bottom) along the nucleation path (colors) for $k/k_0 = 0.01$ and $g_1 w/a_2 = 0.05$. The shape of the critical nucleus is indicated in red. (b) Energy $\tilde{F}$ of the surrogate model as a function of the nucleation coordinate $X$ for various reaction rates $k$ for a neutral wall ($g_1 = 0$) and an attractive wall ($g_1 = 0.05a_2/w$). (c) Energy barrier $\Delta\tilde{F}$ as a function of $g_1$ and $k$. (d) Energy $F_{\text{coupl}}$ following from Eq. (10) as a function of $g_1$ and $k$. (a)–(d) Model parameters are as in Fig. 1.

for the reactive energy, $\Delta F_{\text{react}} = mk$, and we express the energy associated with the passive case as $\Delta F_{\text{pas}}(g_1) = \gamma ds \Delta f[2\varphi(g_1) - \sin(2\varphi(g_1))]$, Eq. (11), where $\Delta f = f(c_0) - f(c_{\text{eq}}^n) + f'(c_0)(c_{\text{eq}}^n - c_0)$ and $\varphi$ is given by Eq. (4). Taken together, the contour line associated with energy $\Delta\tilde{F}_{\text{cont}}$ then satisfies

$$k = \frac{1}{m + hg_1} [\Delta F_{\text{cont}} - \Delta F_{\text{pas}}(g_1)].$$

(12)

We show in Sec. IV of the supplementary material that the curvature of these contour lines is typically negative ($\partial^2 k/\partial g_1^2 > 0$), consistent with the observed convex shape.

To explore the observed coupling further, we next ask how the energy $F_{\text{react}}$, defined by Eq. (9), changes with the wall affinity $g_1$. Thus, we initialized droplets of fixed volume for various affinities $g_1$ and numerically calculated $F_{\text{react}}$ inside the droplet; see Sec. IV D in the supplementary material. Figure S3 in the supplementary material shows that $F_{\text{react}}$ indeed decreases with larger $g_1$, consistent with the negative effect we found above. However, this analysis only probes how different contact angles affect the reactions, whereas the reactions potentially also change the entire droplet shape away from a spherical cap.

IV. SESSILE ACTIVE DROPLETS SPREAD ALONG WALLS

A. Droplets deviate from spherical cap shape after nucleation

The minimal energy paths that we obtained from the surrogate model not only provide energy barriers for nucleation but also the most likely droplet shape along the nucleation path. Figure 2(a) shows that small droplets are shaped like a disk segment, which corroborates the sampled critical droplet shapes shown in Fig. 1(c). However, Fig. 2(a) also shows that larger droplets can deviate significantly from this equilibrium shape.

The droplet shape originates from a minimization of the free energy $\tilde{F}$ of the surrogate equilibrium model. If reactions are absent, surface tension $\gamma_{\text{th}}$ minimizes the interface between droplet and solvent material, resulting in a circular shape with constant mean curvature. At the boundary of the system, the shape must be compatible with the contact angle $\varphi$ controlled by the energy balance that led to Eq. (4), which implies that attractive walls result in flatter disk segment. The situation is more complicated with chemical reactions. The long-ranged interaction described by Eq. (9) leads to a repulsion...
of the droplet material, analogously to the electrostatic repulsion of charged material. Consequently, different parts of the droplet repel each other, which can induce spontaneous splitting for large bulk droplets and explains why active droplets spread along the wall.

B. Interplay of reactions and wall affinity can deform macroscopic droplets

To understand how the interplay between wall affinity and driven chemical reaction influences the droplet shape, we next study the equilibrium shapes of sessile droplets numerically. We initialized droplets at the wall and simulated their time evolution for different reaction rates and wall affinities until steady states were reached. To get an initial understanding, we first quantified droplet size, which is an area in our two-dimensional simulations. If droplet size is controlled by the reaction-diffusion length scale $L_{\text{rd}} = (D/k)^{1/2}$, with some diffusivity $D$, we expect the droplet size to scale with $k^{-1}$. Figure 3(a) indeed reveals such a scaling, at least for large reaction rates. In contrast, for intermediate rates, we observe significant deviations, which increase with the wall affinity. The snapshots shown in Fig. 3(b) suggest that intermediate reaction rates lead to strongly deformed droplets, which could explain the observed size-dependence.

We next quantified droplet shapes by analyzing the curve describing the interface, defined as the iso-contour at $\nu_c = 0.5$. First, we determined the aspect ratio $\alpha$, obtained as the quotient of the droplet height at the center and the width of the droplet Fig. 3(c). Second, we quantified the curvature $K$ of the interface (see Sec. III in the supplementary material) and determined its variation along the interface [see Fig. 3(d)] as well as the curvature at the center.
of the interface [see Fig. 3(c)]. All three quantities shown reveal the same fundamental dependence: Droplets are essentially disk segments when reactions are absent \((k = 0)\), consistent with expectations. Moreover, droplets are circular for neutral walls \((g = 0)\), even when reactions are strong because all fields are radially symmetric in this symmetric case. Interestingly, droplets also exhibit a disk segment shape for large reaction rates likely because strong reactions reduce the droplet size and so interfacial effects dominate. Between these extreme values, we observe strong deviations from a circular shape, both in the snapshots [Fig. 3(b)] and in the quantities [Figs. 3(c)–3(e)]. In fact, for a given wall attraction \(g_1\), we empirically find an intermediate rate \(k\) for which the deformation is maximally, and this rate increases with \(g_1\). Taken together, these quantities reveal an interplay between wall attraction and reactions, which leads to macroscopic deformations of sessile droplets.

The macroscopic deformations induced by the reactions affect the entire interface and could thus also impact the contact angle \(\vartheta\). To test this, we evaluated the slope \(-\partial_c \vartheta / \partial_c R\) along the implicit curve \(c(x_1, y_1) = 0.5\) and measured the associated \(\vartheta\) at the boundary. The inset in Fig. 4(a) shows that \(\vartheta\) decreases with increasing wall affinity \(g_1\), consistent with the prediction from Eq. (4). However, the data in Fig. 4(a) also indicate that \(\vartheta\) decreases for larger reaction rates \(k\), indicating an effect of the reactions. For attractive walls \((g > 0)\), the contact angle first declines sharply for increasing \(k\) although this decline becomes weaker for larger \(k\) and there is even a brief non-monotonic behavior, observed, depends on \(g_1\), and coincides with the maximal shape deformation of the droplets [compare Figs. 3(a) and 4(b)]. Chemically active sessile droplets, thus, exhibit changes in apparent contact angle concomitantly with global shape deformations.

C. Anisotropic fluxes cause droplet deformation

To gain further insights into shape deformations, we next analyze how reactions disturb the spherical cap shapes expected for passive droplets. We consider a spherical cap described by a radius \(R\) and contact angle \(\vartheta\) in the half-space \(y < 0\). To describe the droplet shape explicitly, we use an effective droplet model,\(^{28}\) assuming a thin interface \((w \ll R)\); thus, we can expand the chemical potential \(\mu\) and approximate the dynamics of the concentration fields \(c_i\) by reaction–diffusion equations,

\[
\partial_t c_i \approx D \nabla^2 c_i - k(c_i - c_0),
\]

inside \((i = \text{in})\) and outside \((i = \text{out})\) the droplet; see Sec. V in the supplementary material. Here, we linearized Eq. (7) without noise around the concentrations \(c^{(0)}_\text{in}\) and \(c^{(0)}_\text{out}\), thus, the diffusivity is given by \(D = \Lambda_d f''(c^{(0)}_\text{in}) = \Lambda_d f''(c^{(0)}_\text{out})\) for our choice of a symmetric free energy.\(^{27}\) To solve the reaction–diffusion problem, we employ polar coordinates \((r, \varphi)\) centered at the circle describing the disk segment. We impose \(\partial_c c\big|_{r=0} = 0\) and \(\partial_c c\big|_{r=\infty} = 0\) at the system boundary. The conditions at the droplet interface are governed by the local phase equilibrium and read \(c_i(R) = c_i^{(0)} + \beta_i y_\text{int}/R\), where \(\beta_i = 2 \left[ (c^{(0)}_\text{in} - c^{(0)}_\text{out}) f''(c^{(0)}_i) \right]\) quantifies surface tension effects for \(i = \text{in, out}\).\(^{28}\) For simplicity, we consider the quasi-stationary situation where the concentration fields equilibrate faster than the interfacial shape. The resulting stationary state solutions to Eq. (13) then depend on the reaction–diffusion length scale \(L = \sqrt{D/k}\), the average concentration \(c_0\), and the boundary conditions. The general solution of this Helmholtz equation reads

\[
c_i(r, \varphi) = c_0 + \sum_{n=1}^{\infty} \left[ A_n I_n \left( r / \Lambda_n \right) + B_n K_n \left( r / \Lambda_n \right) \right] \cos \left( \Lambda_n (\varphi - \vartheta) \right),
\]

where \(I_n(z)\) and \(K_n(z)\) are the modified Bessel functions of first and second kinds. Here, the wavelength \(\Lambda_n = \pi \vartheta / \beta_i\) of the polar coordinate is quantized by the boundary conditions, which can also be used to determine the series coefficients \(A_n\) and \(B_n\) as described in Sec. V of the supplementary material. Taken together, this approach provides approximate solutions for the concentration profiles inside and outside the droplet.

The concentration fields imply fluxes \(\mathbf{j}_i = -D \nabla c_i\), which can affect droplet shapes. Indeed, the interface speed \(v_n\) normal to the interface reads\(^{27}\)

\[
v_n(\varphi) = \frac{\mathbf{j}_\text{in}(r, \varphi) - j_\text{out}(r, \varphi)}{c^{(0)}_\text{in} - c^{(0)}_\text{out}} \cdot \mathbf{n},
\]

FIG. 4. Reactions affect contact angles. (a) and (b) Deviation of contact angle \(\vartheta\) from passive case \((k = 0)\) as a function of reaction rate \(k\) for various wall affinities \(g_i\). The inset shows \(\vartheta\) as a function of \(g_1\) for \(k = 0\). Model parameters are given in Fig. 1.
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droplets can only grow spontaneously when $R_{\text{zeroth mode}}$ is negative, indicating an unstable size. Consequently, $R$ captures the behavior we observed so far: For very small radii, the droplet shapes. The dependence of these modes on the droplet radius become important for larger droplet sizes, indicating non-circular wall \[ \text{shapes}. \] The zeroth mode is essentially unchanged for an attractive wall \[ g \neq 0, \] whereas \[ A \] might be related to the steady state size of reactive droplets. Larger reaction rates $k$ first cause \[ |C_1| \] to increase, but \[ |C_1| \] then decreases beyond a critical value of $k$. This non-monotonic behavior is qualitatively consistent with the shape deformations shown in Fig. 3 and might be related to the steady state size of reactive droplets: Higher reaction rates $k$ reduce the droplet size [see Fig. 3(a) and Ref. 22], leading to smaller magnitudes of the droplet deforming modes; see Fig. 3(b). In summary, chemical reactions combined with symmetry breaking by an attractive wall lead to non-isotropic flows that cause droplet deformation.

At the critical size, the higher modes shown in the right two panels in Fig. 5(b) are vanishingly small, consistent with the circular shape of critical nuclei observed in Fig. 1(c). Droplets larger than the critical size grow until they reach a stationary state, marked by the second root of $C_0(R)$ in Fig. 5(b); see also Ref. 22. At this stationary state, the zeroth mode does not contribute to the dynamics, but higher order modes, which are connected to shape deformations, do. Indeed, Fig. 5(c) shows that the interface speed of a stationary droplet with radius $R^*$, chosen such that $C_0(R^*) = 0$, is such that the droplet flattens and spreads along the walls. Taken together, the analysis of the first mode of a droplet with a stationary size indicates that fluxes caused by the driven reactions deform the droplet.

To understand droplet deformations in detail, we next focus on the first mode ($n = 1$). Figure 5(d) shows that its magnitude \[ |C_1| \] vanishes when reactions are absent ($k = 0$), consistent with the expected circular shape of passive droplets. Larger reaction rates $k$ first cause \[ |C_1| \] to increase, but \[ |C_1| \] then decreases beyond a critical value of $k$. This non-monotonic behavior is qualitatively consistent with the shape deformations shown in Fig. 3 and might be related to the steady state size of reactive droplets: Higher reaction rates $k$ reduce the droplet size [see Fig. 3(a) and Ref. 22], leading to smaller magnitudes of the droplet deforming modes; see Fig. 3(b). In summary, chemical reactions combined with symmetry breaking by an attractive wall lead to non-isotropic flows that cause droplet deformation.

where $n$ is the normal vector of the interface. Using Eq. (14), we find

$$v_n = \frac{1}{c_{\text{in}}(0) - c_{\text{out}}(0)} \sum_{n=0}^{\infty} C_n(R, L, \theta) \cos(n\phi),$$

(16)

with

$$C_n(R, L, \theta) = \left( D_{\text{out}} A_{n\text{out}} - D_{\text{in}} A_{n\text{in}} \right) \frac{R}{L} + \left( D_{\text{out}} B_{n\text{out}} - D_{\text{in}} B_{n\text{in}} \right) K_n \left( \frac{R}{L} \right).$$

(17)

This interfacial speed $v_n$ quantifies how chemical reactions would disturb the circular shape.

We start by examining the shape of a droplet on a neutral wall ($g_1 = 0$). Figure 5(a) shows that only the $n = 0$ mode contributes, whereas $A_{n\text{in}} = B_{n\text{in}} = 0$ for $n \geq 1$, consistent with the observed circular shapes. The zeroth mode is essentially unchanged for an attractive wall ($g_1 > 0, \theta < \pi/2, \text{Fig. 5(b)}$); however, the first and second modes become important for larger droplet sizes, indicating non-circular droplet shapes. The dependence of these modes on the droplet radius $R$ captures the behavior we observed so far: For very small radii, the zeroth mode is negative, indicating an unstable size. Consequently, droplets can only grow spontaneously when $R$ exceeds the first root of $C_0(R)$, which, thus, corresponds to the size of the critical nucleus.

**FIG. 5.** Reactions cause non-isotropic interface speeds. (a) Series coefficients $C_n$ as a function of droplet size $R$ for $n = 0, 1, 2$ at a neutral wall ($g_1 = 0$, contact angle $\theta = 90^\circ$) for $k = 0.0025$. (b) $C_n$ as a function of $R$ for an attractive wall ($\theta = 60^\circ$). (c) Interface velocity $v_n$ (red arrows) predicted from Eq. (16) using the first three modes for a disk segment of $R/w = 7$ for $\theta = 60^\circ$ (black line). (d) $|C_1|$ as a function of the reaction rate $k$ for $\theta = 60^\circ$. (a)–(d) Additional parameters are derived from values given in Fig. 1.
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V. ELECTROSTATIC ANALOGY EXPLAINS EFFECTS OF DRIVEN REACTIONS

D. Reactions deform sessile 3D droplets

So far, we analyzed deformed droplets only in two spatial dimensions. To check whether the observed effects persist in three dimensions, we performed a simulation for the parameter regime where droplets are deformed. Figure S5 of the supplementary material shows that such droplets are circular in the xy-plane and are deformed only in the z-direction. Consequently, simulations using cylindrical symmetry are suitable to describe the problem. Figure 6 shows that we find spherical cap shapes for small and large reaction rates $k$ and strongly deformed droplets between these extremes, consistent with our results for attractive walls in two-dimensional systems. Taken together, we, thus, expect that our results translate directly to three-dimensional systems.

The reaction–diffusion length scale $L = \sqrt{D/k}$ controls the extent of the cloud and the reaction rate $k$ determines the magnitude of the electrostatic interaction. Even though the sessile droplet in Fig. 7(a) looks as if it would form a dipole with the surrounding negative charges, this is not the case since image charges restore the symmetry. Distant droplets thus hardly interact with each other.

To be more quantitative, we next calculate the total energy of a single sessile droplet in the limit of a thin interface, also known as a capillary approximation; see Sec. VII in the supplementary material. The approximate expressions for small droplets in two and three dimensions read:

\[
F^{\text{2D}} \approx 0.029 + 0.32 \log \left( L V^{-1/2D} \right) \left( \frac{c^{(o)} - c_0}{\Lambda_d} \right)^2 k V^{1/2D}_2 - \Delta f V^{2D}_2 + y_d A^{2D}, \tag{18a}
\]

\[
F^{\text{3D}} \approx 0.039 \left( \frac{c^{(o)} - c_0}{\Lambda_d} \right)^2 k V^{1/3D}_3 - \Delta f V^{3D}_3 + y_d A^{3D}, \tag{18b}
\]

FIG. 6. Reactions deform sessile 3D droplets. Concentration profiles $c(x,y,z)$ of 3D droplets in a stationary state for various reaction rates $k$ at an attractive wall ($g_1 = 0.05a_2/w$). Simulations were performed in cylindrical symmetry using the parameters $r_{\text{max}}/w = 64$, $dr/w = 1$, $z_{\text{max}}/w = 32$, and $dz/w = 0.25$. Additional parameters can be found in Fig. 1.

FIG. 7. Electrostatic analogy explains nucleation behavior. (a) Effective charge density $c(r) - c_0$ of a sessile droplet for reaction rate $k/k_0 = 0.005$. (b) and (c) Energy $\bar{F}$ of the surrogate model as a function of the volume $V$ in 2D [ (b) $k/k_0 = 0.001$ and 3D (c) $k/k_0 = 0.001$] for various thin-interface approximations: The solutions (blue solid lines), see Eqs. (S64) and (S78) that are compared to the further approximations given in Eq. (18) (dashed lines) and the expression for $k = 0$ (black lines). The contact angle is $\theta = 80^\circ$. (d) Nucleation barrier $\Delta F_m = \max V^{1/2D} \bar{F}(V) - \bar{F}(0)$ given by Eq. (18a) as a function of $g_1$ and $k$ for the 2D system. (a) (d) Additional parameters are given in Fig. 1.
where the bulk energy proportional to \( \Delta f = f(c_0) - f(c_{in}) + f'(c_0)(c_{in} - c_0) \) scales with the droplet volume \( V \), whereas the surface energy proportional to \( \gamma \) scales with the effective size of the interface, which depends on the contact angle \( \Theta \): \( \Delta E_2D = [2V_{2D}(2\rho - \sin(2\rho))]^2 \) and \( \Delta E_3D = 4\pi(3V_{3D}/[\pi(2 + \cos(\rho))(1 - \cos((\frac{\rho}{2}))^3)])^2(2 + \cos(\rho)) \). For simplicity, we neglect the influence of \( \Theta \) on the electrostatic energies associated with the charge distribution given by the respective first terms proportional to \( k \). Instead, we use the expression for one-half of a spherical droplet on a wall as an approximation; see Sec. VII in the supplementary material. Neglecting logarithmic corrections, we, thus, find that reactive energies scale as \( R^2 \), bulk energies as \( R^4 \), and surface energies as \( R^3 \), when droplets are small and \( d \) is the space dimension.

We first use the approximate energies to investigate nucleation. The surface energy dominates for small droplets, explaining why nucleated droplets close to the critical size are spherical; see Fig. 1(c). Equation (18) also shows that chemical reactions raise the nucleation barrier [see Figs. 7(b) and 7(c)], consistent with suppressed nucleation. The associated energy barrier \( \Delta F \) shown in Fig. 7(d) exhibits a very similar dependence on the reaction rate \( k \) and the wall affinity \( g_1 \) compared to the numerically determined barriers shown in Fig. 2(c). However, since we do not consider the contact angle \( \Theta \) in the simplified electrostatic energy given in Eq. (18), this approximation cannot capture the coupling between \( k \) and \( g_1 \) as we revealed above. Moreover, the capillary approximation used here is known to overestimate the energy barrier for droplet formation since it assumes a well-defined separation of the droplet and the surrounding dilute phase during nucleation. Yet, we can conclude that the electrostatics do not affect the shape of small droplets, but they oppose their formation, thus lowering nucleation rates.

To discuss shape deformations and splitting of droplets, we next approximate these two situations by considering two sessile droplets with total volume \( V_{tot} \) that either touch each other or are well-separated; see Fig. 8(a). If \( F(V_{tot}) \) denotes the energy of the single droplet of volume \( V_{tot} \), the two well-separated droplets have a total energy of \( 2F(V_{tot}) \). In addition, the two connected droplets exhibit an electrostatic repulsion, which we approximate as the repulsion between two point charges; see Sec. VII in the supplementary material. Since the approximations given in Eq. (18) only hold for small droplets, we here obtain \( F(V) \) from Eqs. (S64) and (S78) in the supplementary material. Taken together, we can, thus, compare the energies of the two droplets at different separations to the energy of a single droplet in 2D and 3D for various \( V_{tot} \); see Figs. 8(b) and 8(c). Without reactions (\( k = 0 \)), the energy of two droplets is always higher than that of a single droplet, consistent with a minimization of surface energies and absent droplet deformations. Moreover, \( F(V) \) decreases monotonously beyond the critical size, implying that droplets grow until they are limited by system size. The picture changes qualitatively when reactions are enabled (and droplets become charged in the electrostatic picture): Even for arbitrarily small \( k \), \( F(V) \) develops a minimum at a finite size \( V \) and the electrostatic energy makes larger droplets unfavorable; see Figs. 8(b) and 8(c). Since the minimal energy is negative (implying that the droplet is favored over the homogeneous state), we observe that the states with two droplets (orange curves) have lower minima than the one-droplet states (blue curves), which implies that a large system would prefer to have many droplets. A large droplet count could emerge either from nucleating additional droplets or from splitting existing droplets.

To investigate droplet splitting, we compare the minimal energy of a single droplet with the energy of the two-droplet states at the corresponding total volume \( V_{tot} \). Figure 8(b) shows that the two-droplet states can have lower energy for small reaction rates \( k \), suggesting that a droplet with this volume might deform spontaneously. In contrast, the right panel shows that a single droplet has lower energy for large reaction rates \( k \), suggesting that the single droplet is stable. The transition between these cases marks the onset of droplet deformation, which depends on the reaction rate \( k \) and the wall affinity \( g_1 \). Figure 8(d) suggests that droplets deform if reactions are not too strong and larger \( g_1 \) favor deformations; similar to Figs. 3(c)–3(e). However, in contrast to Figs. 3(c)–3(e), the simple scaling theory predicts that the deformed droplets (mimicked by the two adjacent droplets) are favored even when \( g_1 = 0 \). It is likely that
deformations are kinetically suppressed, i.e., that small deformations are energetically unfavorable, and thus, we do not observe them.

The predicted transition from a single to a deformed and then split droplet can be understood as a competition between surface energies (favoring compact droplets) and effective electrostatic repulsion (favoring elongated droplets) in conjunction with the favored finite droplet size due to reactions. Droplets are spherical at large reaction rates $k$ since large $k$ implies small droplets where surface energies dominate. Smaller reactions imply larger droplets, where the electrostatic effects are stronger and eventually favor deformed droplets that can also split. However, if reactions are absent, we again observe spherical droplets since there are no electrostatic effects.

In summary, interpreting the reactions using electrostatics explains the delayed nucleation and droplet deformation. Nucleation is suppressed since electrostatics disfavor an accumulation of charges, but the critical droplets are still spherical since surface energies dominate. In contrast, larger droplets can minimize the total energy by deforming, which enlarges the average distance between charges and, thus, lowers the electrostatic energy at the expense of a larger surface energy. In this case, the deformed droplets can also grow beyond the volume predicted for spherical shapes, consistent with Fig. 3(a).

VI. DISCUSSION

We showed that nucleation is accelerated by attractive walls and suppressed by active chemical reactions, consistent with our previous results. However, we also found an intricate interplay between the two processes, likely stemming from shape modifications in sessile droplets. While the shape of critical nuclei is in agreement with a disk segment, consistent with passive scenarios, we found massive deformations for larger droplets at intermediate reaction rates. These deformations originate from anisotropic diffusive fluxes generated by an interplay of the chemical reactions and the symmetry breaking due to the presence of the wall. Within the surrogate model, the elongated droplets can also be interpreted as a tradeoff between surface tension and effective electrostatic repulsion, which demonstrates that the active chemical reactions mediate a repulsive long-ranged interaction.

Our study of sessile active droplets provides the first step toward understanding the interplay of chemically active droplets with other structures. For simplicity, we focused on a two-component mixture, whereas cells exhibit a staggering complexity involving thousands of different components, which could be described by a multicomponent extension of our theory. Furthermore, we considered reactions that depend linearly on composition, but realistic, thermodynamically consistent reactions are more complex. While our previous work suggests that linear reactions capture nucleation quantitatively, more complex reactions might change the shape of macroscopic droplets drastically. Droplet shapes also depend on where the reactions happen. For example, localized reactions, whose effect can be captured by localized electric dipoles, can cause pancake or mushroom shapes, particularly in three dimensions. We focused on two dimensions to accelerate the nucleation simulations, but our analytical results and explorative simulations suggest that similar effects persist in three dimensions. Finally, we only studied flat walls, but boundaries in cells are typically curved and deformable. Incorporating these aspects will likely require more advanced computational methods (such as Ref. 44), but we expect the general behavior that we unveiled here to persist.

Active control of phase separation is a challenge in cells. Our work suggests that cells could use chemical reactions to fine-tune the rate of heterogeneous nucleation as well as the shape of sessile droplets. Such deformed droplets may offer better control of wall deformations by condensation, e.g., by using less material than a spherical cap to achieve the same deformation. Such a regulation process would be a fascinating example, combining control via active chemistry and a membrane surface. Moreover, our model serves as an intriguing example of boundary effects in active field theories, inviting comparisons with other active field theories.

SUPPLEMENTARY MATERIAL

The supplementary material offers insight into the numerical methods employed to sample the nucleation times, the constrained optimization utilized to extract the minimal energy pathways, and the curvature calculation for the macroscopic droplets. Furthermore, it details the coupled effect of the reaction rate and wall affinity on the energy barrier. Additionally, the supplementary material contains details on the expansion of reactive and diffusive fluxes and the calculation of the coefficients. We provide a full 3D simulation in Cartesian coordinates to verify the symmetry used in the main text. Finally, we present details on how the electrostatic picture explains the effects of driven reactions by calculating the static energy for different geometries in 2D and 3D.

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AUTHOR DECLARATIONS

Conflict of Interest

The authors have no conflicts to disclose.

Author Contributions

N.Z. performed the numerical simulations, did the formal analysis, and wrote the first draft of the manuscript. All authors conceived the project, analyzed the data, and edited the manuscript.

Noah Ziethen: Conceptualization (equal); Formal analysis (equal); Investigation (equal); Methodology (equal); Software (equal); Validation (equal); Visualization (lead); Writing – original draft (equal); Writing – review & editing (equal). David Zwicker: Conceptualization (equal); Formal analysis (equal); Funding acquisition (lead);
The data that support the findings of this study are available from the corresponding author upon reasonable request.

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