Kinetics of liquid transport during fish-eye formation and mitigation: Particle- and imbibition-scale imaging

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Background - Fish-eye formation at Particle and Imbibition scales

A key rate-limiting step of numerous processes, both in manufacturing and consumer use contexts, is the formation of gelled aggregates during powder solvation and dissolution. These aggregates, termed 'fish-eyes' because of their gelled exterior and solid dry core, can have numerous costly consequences including longer batch cycle times, incomplete product solvation and mixing, and consumer dissatisfaction. The formation of fish-eyes plagues almost all industries that process or produce powders, with pharmaceutical, cleaning, and food products affected.

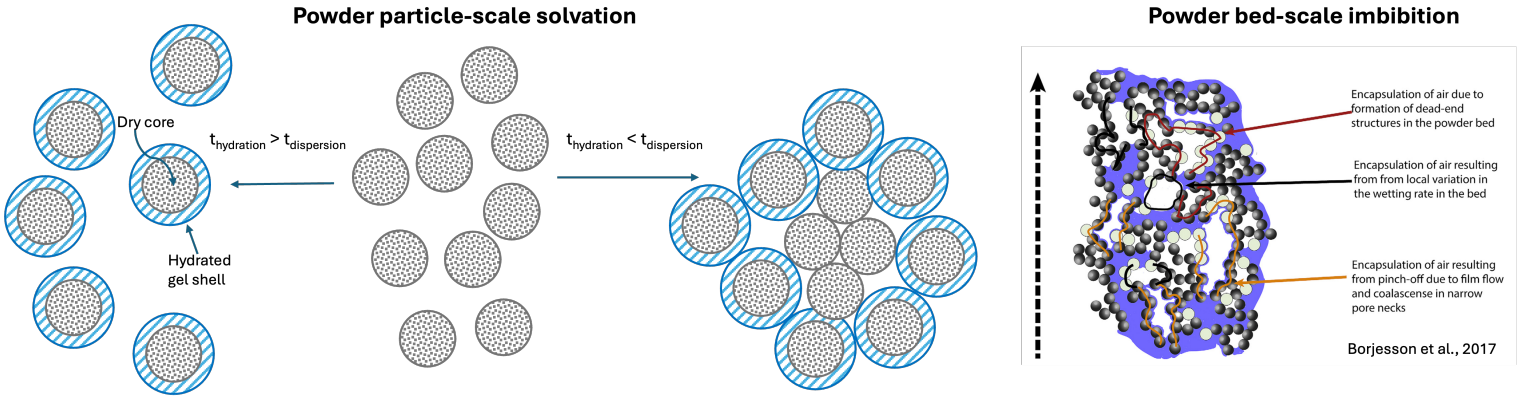

Figure 1: Schematic of fish-eye formation from dry powder particles that solvate faster than they can be dispersed into individual particles. Because their exterior is a sticky, attractive gel once solvation starts, they readily agglomerate into troublesome chunks known colloquially as fish-eyes. Also shown is a schematic from Borjesson et al.[1] showing the hypothesized structure of powder pores during imbibition of a liquid front and the resulting gas displacement and trapping. This work will quantify these dynamics but also provide quantitative structural and mechanistic explanations.

Fundamentally the formation of fish-eyes comes from a mismatch in the relative rates of solvation and dispersion. If powders are able to solvate more rapidly than they are dispersed, the outer solvated layer forms the dreaded fish-eye structure with dry, un-solvated particles inside, Figure 1. While more efficient dispersion can be a process aid, there are often more fundamental limitations to solvation that must be handled in different ways. Delayed and arrested solvation often occur as a result of the phase properties of the molecules in the granule, and these must be quantified and addressed to fix the issues. Such an approach requires quantifying the particle-scale dynamics as liquid moves into a powder, but the consequences of incomplete solvation can also impact larger-scale structures. In a powder bed there will be gas-containing pores that also contribute to structure and mechanical response of the solid. Here incomplete solvation will cause complex displacement and trapping of gas volumes when the structure has sufficient elasticity to resist the pressures, right-hand side Figure 1. Past work has used structural imaging tools and mapped some liquie flow, but has not linked well to particle-scale structural transitions[1–3] and effects. **We need an approach that can map structural variations at the powder bed scale but also supply mechanistic, compositional, and structural insights at the particle scale.**

In most mass-produced powder solvation steps, the biggest hindrance to completion is the spontaneous formation of discontinuities in concentration during diffusion of solvent into particle cores. Two mechanisms cause most of these discontinuities: amphiphile liquid crystalline phase formation and polymer structural relaxation and entanglement. When liquid crystals form during solvation of a powder, the effect on solvation is significant because of the dramatic physical properties of the more concentrated phases. Hexagonal and lamellar liquid crystalline phases have viscosities several orders of magnitude higher than more dilute, micellar solutions. As a result, the diffusion coefficient through these phases is much lower than might be expected. The high elasticity of these phases also makes their dispersion more demanding. Both effects dramatically slow solvation and greatly increase fish-eye formation. **However, the effect is not limited to polymeric or surfactant systems and can occur in other materials like proteins, flavors, and dietary fiber, for example.**

The formation of troublesome phases in powders can be studied by microscopic observations of the solvation process. Placing a powder particle in water or the chosen solvent allows visualization of the phases

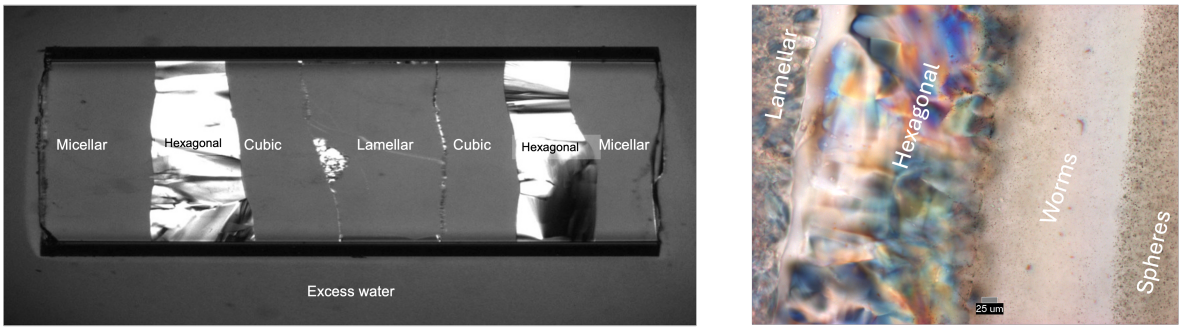

Figure 2: On the left, visualization of liquid crystalline phases in a $C_{12}E_6$ surfactant powder being solvated. As water diffuses in, the concentration varies but sharp phase boundaries form at high surfactant levels. Polarized light enables identification of these boundaries for anisotropic phases like hexagonal and lamellar phases. On the right, an image of surfactant in water that has colloidal tracer particles added to map rheological as well as phase transitions. In addition to the liquid crystalline structures mapped like those on the left, the colloidal particles are stopped at a similarly sharp boundary on the right of the image as a result of wormlike micelle formation (Worms) that has a mesh size small enough to allow water transport but block colloidal movement outside of the spherical micellar region (Spheres).

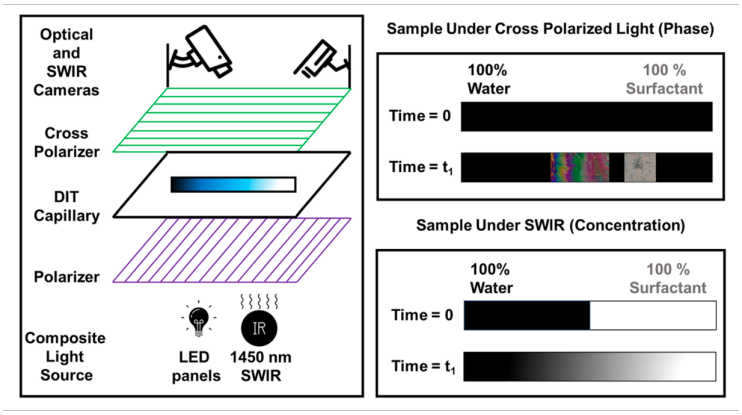

Figure 3: Schematic of combined imaging of hydrating samples using short-wave IR (SWIR) to quantify water concentrations and polarized light to identify liquid crystalline structures. In our laboratory we also incorporate fluorescence imaging to quantify local rheology and structural transformations. Image reproduced from Kelkar et al.[5]

because of their unique optical and rheological properties[4], Figure 2. Phases that are known troublemakers can be assigned blame for process problems, but without compositional information there is limited ability to troubleshoot a process or formulation. Fortunately advanced imaging techniques make quantification of water levels possible in an image like Figure 2. Short-wave infrared imaging is a technique used in computer vision applications to identify the presence and concentration of water, enabling spatial and temporal tracking of water transport in powders and other solids[5]. Determination of the composition of phases and structures that hinder solvation allow two benefits for process and product design: The first is prediction of kinetic limitations in processes and applications with local diffusion coefficients in each of the phases present. Time-dependent microscopy allows measurement of interface velocities to quantify diffusion rates and their sudden slowing as viscous phases form[6]. Secondly, knowledge of the kinetics of solvation allow design of processes to avoid or mitigate fish-eye formation by adjusting driving force through changes to ingredient order of addition, for example.

A typical experiment of this type forms the core of the proposed research and is shown in a schematic in Figure 3. An immobilized powder particle, or powder bed of particles has some proportion of excess water or solvent added to it. As diffusion proceeds, the sample spans the entire concentration range of solvent, from 0-100%, so that even small variations in structure can be detected by microscopic study. The combined imaging techniques allow mapping of local phase and composition as a function of time, enabling kinetic characterization. This does not address local mechanical properties or rheology that can also dramatically hinder solvation kinetics. Addressing this requires addition of fluorescence imaging to the techniques in Figure 3. Fluorescent colloidal tracers with diameter around 0.5 μm added to the swelling solvent can be used to map formation of molecularly permeable but colloidally impermeable[7] structures. The right-hand side of Figure 2 shows an image of $C_{12}E_6$ surfactant being solvated. As in the left-hand side of Figure 2, liquid crystalline phases are visible but so is a sharp boundary on the right of the image where all colloidal tracer particles have stopped. This is where spherical surfactant micelles transition to elongated, wormlike

micelles that create a mesh impermeable to particles but permeable to water. Because wormlike micelles are also difficult to mix and disperse, an image like Figure 2 can be used with SWIR imaging to determine the water concentration where the worms form and cause fish-eyes due to transport limitations.

Similar to the wormlike micelles, polymers delivered as a powder are known to exhibit unusually slow solvation rates. Unlike surfactants, however, concentrated glassy polymers are impermeable to water, meaning a map of the water concentration across a polymer powder particle might have a dramatic transition from a continuous diffusion profile to a fixed or zero water concentration region. This effect is known to be the result of a polymer's glassy to rubbery transition, where the glassy state admits little to no solvent until the local molecules relax sufficiently. The effect is so distinct it is termed anomalous or non-Fickian diffusion because the system has abrupt changes rather than continuous progression of solvent into the solid matrix[8]. The imaging techniques described above can also map these sorts of structural transitions. Unlike non-glassy powders, where transport is governed by diffusion rate and Fick's transport equations that predict a moving diffusion front that scales with the square root of time, t:

$$c = kt^{\frac{1}{2}} \tag{1}$$

where k is a rate constant. Non-Fickian systems, on the other hand, can exhibit non-diffusive behavior where the solvent front moves at a faster rate than diffusion dependent only on polymer relaxation times:

$$c = kt^{n} \tag{2}$$

where n can vary from 0.6-1, as opposed to 0.5.

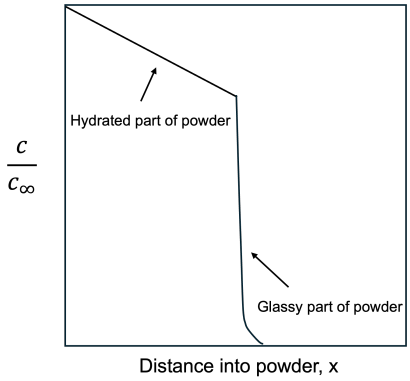

Figure 4: Schematic of the unusual concentration progression of solvent into a dry polymer powder when normal, Fickian diffusion does not control the overall behavior as it would produce a more traditional exponential decay in concentration with distance. Schematic modified from de Kee et al.[8].

Figure 4 shows a schematic of water concentration profile in a glassy powder during solvation. At short times the concentration follows a linear profile rather than the exponential decay predicted by Fickian diffusion. While it is hard to compare such different phenomena, the assumption of an incorrect model would be grossly inaccurate to describe the rate of transport into such a powder, leading to inaccurate predictions of fish-eye formation. There is a very specific need for kinetic mapping of transport in these systems in order to allow development of predictive models of solvation and its effects on process and product dynamics. While computational fluid dynamic simulations provide enormous insight into process and mixing process design, the success criteria needed for powder handling and incorporation are still missing. We will provide quantitative measurements of powder solvation kinetics for incorporation into process simulations and correlations.

The methods that will be used here combine multiple imaging techniques that will be applied to determine the kinetics of solvent transport into individual micron-scale powder particles as a function of key microstructures using advanced imaging with varied illumination sources. The same techniques will then be applied at millimeter scales to powder bed systems during liquid imbibition. Combining length scales will provide new insights into structural evolution at colloidal and granular length scales and provide a quantitative explanation of bulk measurements from past studies using powder bed wetting and Washburn-type testing.

Detailed description of the proposed program

Year 1 - Individual powder particle studies of water transport and fish-eye formation

A wide range of powdered materials can exhibit fish-eye formation, including polymers like starch in foods, drug delivery vehicles and pharmaceuticals, and polyethylene oxide in consumer products and cosmetics. Polymers can be inherently delayed in their solvation as a result of glassy or non-Fickian diffusion of solvent into the polymer[8,9]. Surfactants and emulsifiers that self-assemble into liquid crystalline layers can also vary greatly in their solvation rates as the rheological and transport properties of the resulting phases can vary by several orders of magnitude. More conventional powders like soluble proteins, flavors, or fiber can also be hindered in solvation and their kinetics and structure can be mapped just as easily.

A key need is to map the kinetics of transport by following the local concentration of solvent as it moves into the powder particle using microscopy techniques like fluorescent imaging, hyperspectral mapping, and particle tracking[10]. The combination provides a way to see signatures of physical behavior, like discontinuities at phase boundaries, local variations in microrheology, and structural changes like polymer glass relaxation. If these measures are superimposed onto other measurements, like local birefringence, additional structural information can be obtained and used to explain and help predict kinetics.

Year 1 we will map these kinetics and structural dynamics for individual powder particles of model systems in water and in solutions of the powders with various concentrations. The experiments will allow us to map the effect of solvation resistance while the varied solution concentration allows mapping the effect of solution driving force on the time scales of solvation. These time scales then provide the basis for the following year that will study transport for larger beds of the same powders to probe gas phase effects on resistance to transport. These experiments will be performed with all samples in liquid so that wetting of container walls is not an influence on the measured kinetics.

Year 2 - Powder bed-scale imbibition and transport studies

While some diffusion-limited transport measurements have been made for surfactant pastes[6], coupled particles in powder beds with embedded pore structures and gases, have not been studied at this resolution during imbibition. Transport models have been proposed for glassy polymer interfaces[8,11], but we know of no studies linking these to agglomerated powder bed transport length scales. **Year 2 of this work will study transport and structure evolution in powder beds with varying porosity and compression. The combined imaging techniques are able to quantify transport in the larger bed length scales to compare to the single particle studies. The information determined in Year 1 for individual particles will be used to explain larger-scale effects based on the particle-scale kinetics.**

A key output here needs to be a quantitative measure to allow objective comparison of materials and processes. Although fish-eye formation is a common issue and can be identified readily, obtaining a relative quantitative measure of the underlying properties that lead to such issues is needed to allow efficient selection of materials and processes rather than using more qualitative observations and comparisons. The work in Year 2 will define a quantitative criterion, based on kinetic measurements of solvation rates, to establish whether a material will form fish-eyes under defined mixing conditions.

Year 3 - Fish-eye prediction linked to kinetic parameters and mitigation strategies

This program's targeted contribution is the combination of microscopic probes of rheology, structure, and composition with time to resolve and link critical kinetics in the fish-eye transformation that plagues numerous industries. Microrheology, infrared imaging, and three-dimensional light sheet fluorescence imaging will map and enable fundamental criteria for fish-eye formation in formulation and process contexts. But once this information is known, the development of avoidance and mitigation strategies must follow. **Year 3 will examine how to convert fundamental measures of solvation kinetics into strategies to avoid fish-eye formation or, more realistically, strategies to mitigate the occurrence in existing processes.**

For example, driving force for diffusion is a key determinant of the rate of powder solvation. Common approaches to fish-eye avoidance include increasing the solubility of the powder or solvated phase so that a fish-eye agglomerate is not stable for significant times. Determining the efficacy of these approaches can be done using the imaging techniques described above. Measurement of transport rates for powder solvation as the solubility of the powder is systematically increased, for example by addition of small amounts of solvents to the water phase, will enable determination of the threshold for fish-eye formation.

Other approaches to fish-eye avoidance include the use of so-called disintegrants that swell and aid in dispersion of powder components rather than binding them together to form fish-eyes. Year 3 will include

work to measure the solvation kinetics of the systems studied in Year 1 and Year 2 with small amounts of disintegrant polymers mixed in at different proportions. In addition to the measurement of solvation kinetics, the kinetics of swelling driven by disintegrants can also be measured so that any effects on solvation and dispersion can be distinguished and used as a basis to determine their efficacy.

Outline of what will be accomplished each year

Fish-eye formation affects almost all formulated material industries, causing problems in manufacturing and product uses alike. Because the phenomenon occurs in widely-used materials like starch, polyethylene oxide polymers, and surfactants/emulsifiers, the study will prioritize fundamental descriptions that allow determination of kinetic parameters for a wide range of pure as well as impure, applied materials during solvation and fish-eye formation.

1. Year 1 - Map individual particle solvent transport kinetics for commercial and ideal powders using combined imaging techniques to link to phase trajectories. Also tune driving force by external concentration of the following powders:
   (a) surfactant like sodium dodecyl benzene sulfonate
   (b) polymer like polyethyelene oxide or starch
   (c) soluble powders like proteins and flavors
   (d) Screening of commercial mixtures to detect fish-eye transitions as a result of a small amount of impurity or other raw material variation.
2. Year 2 - Map solvation, with varying driving force as above, of powder beds of:
   (a) surfactant like sodium dodecyl benzene sulfonate
   (b) polymer like polyethyelene oxide or starch
   (c) soluble powders like proteins and flavors
3. Year 3 - Determine fish-eye predictive criterion based on driving force and length scales of powder:
   (a) Testing of specific fish-eye mitigation strategies of above samples using predictions of order-of-addition changes and different solvent driving forces.
   (b) Testing of model distintegrant aid, e.g., guar gum,[12] to link to transport kinetic effects
   (c) Suggest different trajectories of dilution or order of addition of currently-used solvents, for example, to avoid troublesome phase or structure transitions.[13]

Goals of the work

We propose to use advanced imaging techniques to study microstructural evolution in a solvating powder system. The imaging allows us to track multiple species, quantify evolution of powder bed structures, and how the structure responds to those microstructural changes. The imaging approach allows tracking of compositional variations, structural variations, packing density, and behavior adsorbed or free gases as they respond to the imbibition of liquid.

The approach can explain behavior observed previously only in the bulk while linking to particle-scale mechanisms of slow solvation, increasing accuracy of microstructural descriptions, informing modeling, processing, and formulation approaches by industrial partners. Because the technique is flexible across material and solvent types and can track solid, liquid, and gas in three dimensions, the method is broadly flexible for materials across diverse partner company needs. We will:

- Quantify the range of kinetic parameters possible in key powder formulation ingredients and link them to physical models of diffusion[6] and structural relaxation[11]. Develop a criterion for fish-eye formation that be be applied to the majority of powders and solvents based on the physical measurements.
- Study powder bed-scale dynamics and use the particle-scale insights from above to explain bulk pore and structure formation and evolution.
- Develop an open-source measurement approach for industrial partners to screen materials and formulations to optimize process specifications. Integrate and validate disparate theoretical approaches to powder solvation to enhance industrial simulation and design processes with relevant physical parameters.
- Test specific industrial systems for solvation kinetics and link to fish-eye formation by building on the idealized experiments listed above. Once known, use the imaging measurements to test possible mitigation strategies for fish-eye formation in the industrial systems, like changing solvent quality and order of addition of ingredients.

Critical unknowns that may influence the project direction/outcome

One key unknown is how complex mixtures and formulations respond when multiple behaviors and driving force responses are present. We may encounter systems with blends of phase and glassy behavior that aren't described by either model. We will use hybrid descriptions that assume additivity of the two behaviors. Because our approach utilizes imaging of the entire structure, and can map liquid, solid structure, and gas volume distributuion and shape, we can determine the relative importance of all components and gain mechanistic insight. If time permits, interactions that can arrest solvation kinetics, like starch-lipid complexation[14] or interfacial arrest[15] can be studied as well.

Another unknown is the effect of convection on deformation and local concentration in fish-eyes. Most powders are mixed and solvated under flowing conditions but the study of static powder samples is still needed. Convective mixing is still diffusion-limited at key length scales, so the work will provide a relative basis for determination of fish-eye formation during convection that can be validated in microfluidic channels.

How this project leverages existing research in our group

Our group has an extensive program on the study of three-dimensional soft materials and structures using light sheet fluorescence microscopy, LSFM, as a way to track labeled molecules or particles as well as solvents during process-critical changes like solvation. Although we initially target two-dimensional imaging in this work, we will probe the utility of three-dimensional LSFM study of solvation in Year 2 so that powder-bed scale agglomerate structures can be understood and linked to the particle-scale insights from Year 1. Other imaging techniques, like short-wave infrared (SWIR) microscopy and particle tracking microrheology, are heavily used in our research so that we can immediately quantify rates and fit to available theories of transport. Applying combinations of these techniques to the study of fish-eye formation and mitigation kinetics will provide the first holistic link between past work on liquid transport and the mechanistic behavior driving these processes at the particle and pore scales in diverse fish-eye forming systems.

Our recent work on nanofbril disintegrants[16] to create a sparse scaffold and aid in spray-dried particle design[17] provides a way to test the benefits of stored elastic energy to aid in powder solvation. We can use the protocols developed above to test these new scaffolds for disintegrant behavior and performance, if useful to industrial members.

Where IFPRI members could support the program

- The program is generalizable, so suggestion and supply of powder samples by industry members is part of the project plan. Once methods are established, they can easily test the models on complex mixtures. We solicit supply of specific solvents and materials like commercial emulsifiers, polymers, proteins, and mixed powders from the pharmaceutical, biomedical, food, cosmetic, and specialty chemical sectors.
- Member requests to assess relative benefit of solvent or order-of-addition changes can be directly tested, providing mechanistic insights into solvation kinetic optimization.

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