

Modulating Aggregation in Microemulsions: The Dispersion by Competitive Interaction Model

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Abstract

A phenomenological model has been developed for the mechanism of action of phase modifiers as additives that control aggregation phenomena within water-in-oil emulsions. Unlike the qualitative “cosolvent” and “cosurfactant” paradigms previously discussed in the literature, the new “Dispersion by Competitive Interaction” model (DCI) explicitly considers the strength and prevalence of different intermolecular interactions that may compete (or act cooperatively) to influence aggregate dispersion and influence phase phenomena within microemulsions. The prior cosolvent and cosurfactant models are considered distinct “regimes” within DCI where either self- or cross-interactions dominate within the landscape of intermolecular interactions. The specific system under consideration, the N,N,N',N'-tetraoctyl diglycolamide amphiphile extractants with tributyl phosphate or dihexyl octanamide phase modifier additives, represents a new regime – labelled the polar disruption regime – where the phase modifier interactions with the polar micellar core (cross-interactions between different components) are strong enough to disrupt the self-interactions of polar-solute molecules amongst themselves.

Microemulsions are essential to many industrial processes including but not limited to pharmaceutical,^{1,2} food,³ and petroleum industries,⁴ cosmetics⁵ and in chemical separations.⁶ Phase transitions (including phase separation or “third phase” formation) complicate industrial processes that use microemulsions, as in liquid-liquid extraction (LLE), one of the most widely employed industrial purification technologies.^{7–10} Phase modifiers are amphiphile additives employed to influence the solution structure and subsequent phase behavior of microemulsions.^{11,12} These additives may stabilize the microemulsion by modifying the solubility of analytes in a particular phase^{11,13} or be used to avoid undesirable phase separation.¹² A molecular level understanding of microemulsion behavior in LLE is a rapidly developing area.^{14,15} Generally these are considered water-in-oil systems with reverse-micelle-like aggregates that consist of a small polar core of water and acid along with the analyte of interest (generally a metal ion) that is surrounded (or ligated) by an amphiphilic extracting molecule.^{7,16–19} Mechanistic paradigms that describe how phase modifiers influence microemulsion are in their nascent stages, with two models generally considered.

In the *cosolvent* model the phase modifier solvates the aggregates within the microemulsion, providing a cushion between the aggregates to minimize merging events and improve the dispersion of aggregates within the diluent-phase.^{20–23} On the other hand, the *cosurfactant* model has the phase modifier molecules distributed within the surfactant layer of the aggregates along with the primary extractant to interact with the polar core of aggregates.^{23,24} Importantly, in both the cosolvent and cosurfactant models the interactions of the polar core are presumed to be stronger than all other interactions such that the micellar core itself is not perturbed by the presence of the phase modifier. Although the cosolvent and cosurfactant models are often used to rationalize microemulsion behavior in the presence of a phase modifier, their mechanism of action in the context of intermolecular interactions within the solution are an unexplored paradigm for their delineation.

Experimentally it is difficult to discern between the proposed cosolvent and cosurfactant models, as the composition of the aggregate’s surface and its impact on polar core

characteristics²⁵ cannot be uniquely characterized. Among a handful of studies, investigations led by Palazzo et al.²⁶ on the interfacial surface of CTAB/water/n-pentanol/n-hexane microemulsions using pulsed gradient spin-echo NMR, suggested that addition of cosurfactants modulate the interfacial surface area.²⁶ A more recent study focusing upon 1-octanol as a phase modifier in amine extraction²² using small-angle scattering coupled with surface-tension measurements inferred that 1-octanol primarily acts as cosolvent and minimizes aggregate merging. Empirical relationships between the size of aggregates at the critical aggregation concentration (CAC) and phase modifier concentration using dynamic light scattering (DLS) and small angle neutron scattering (SANS) further indicate that a phase modifier may influence aggregate size in addition to their dispersion.^{12,27} A paucity of molecular level insight has inspired this work to employ molecular dynamics simulations and detailed network analysis algorithms to elucidate the molecular driving forces that underpin phase modifier behavior. Based upon our analyses we place the prior cosurfactant and cosolvent paradigms as being “regimes” within a more comprehensive *Dispersion by Competitive Interaction* (DCI) model developed within this work. This model explicitly considers the relative strengths and predominance of different intermolecular interactions that compete or reinforce one another to yield the observed microemulsion structure. The current study employs two phase modifiers, where perturbation of the intermolecular interactions within the polar core additionally create a new regime with the DCI model - labelled the polar disruption regime.

The extractant N,N,N',N'-tetraoctyl diglycolamide (TODGA), a potent actinide extractant of actinide lanthanide separation process (ALSEP) is employed considering its phase-splitting behavior under moderate acid concentration as reported from SANS and vapor-pressure osmometry.^{7,18,19,28} Addition of tri-n-butyl phosphate (TBP)²⁹ and dihexyl octanamide (DHOA)²⁹⁻³¹ amphiphiles inhibit phase-splitting by increasing the CAC and are chosen as phase modifiers for our investigation. Classical molecular dynamics simulations with benchmarked force fields (see Supplementary Information) were performed at 0.1 M

TODGA, 0.2 M H₂O and 0.15 M HNO₃ in dodecane (Table S1). Under this condition, mixed-aggregates of the form (TODGA)_m(H₂O)_n(HNO₃)_o are observed (Figures 1) as dominant species where the polar core is relatively medium in size - comprising maximum of 60 H₂O and/or HNO₃ (Figure S1 with mean size of 9 b) surrounded by generally less than 5 TODGA (though up to 10 TODGA may be observed on the reverse-micelle surface, Figure S1 c). To this solution was added 0.5 M DHOA *or* 0.5 M TBP (Supporting Information, Table S1) as the phase modifier. These concentrations have been reported to optimize extraction performance for actinide-partitioning with 0.1 M TODGA.^{29,32}

Introduction of the phase modifier causes several notable perturbations across length-scale. As presented in Figures 1b-c and Figure S1, the phase modifier severely affects the size distribution of (TODGA)_m(H₂O)_n(HNO₃)_o mixed-aggregates. This perturbation largely derives from a decrease of the polar core size that necessarily reduces the overall number of TODGA that may be accommodated on the periphery of the reverse-micelle like structure (Figure S1). The letter-value plots of the size distribution of the polar cores confirm this striking reduction in the presence of phase modifier, more so for TBP (Figure 2). These changes are coupled to massive perturbations in the intermolecular interactions that derive from both competitive interactions amongst the phase modifier molecules and TODGA, as well as changes to TODGA's own intermolecular interactions that are modulated by its conformationally dependent dipole moment. Prior work has noted the importance of the conformationally dependent dipole moment of amphiphiles upon their self-association.³³ A maximum value of 4.82 D is observed for the *cis*-conformation of TODGA in which both carbonyl groups are aligned parallel (Figure S2 and S3). In the absence of phase modifier, the ensemble of solution conformations leads to a TODGA dipole moment distribution that is left-skewed with a mean of 4.22 D ($\sigma = \pm 0.23$) (Figure S3). This changes upon addition of TBP or DHOA to a more normal dipole moment distribution with higher prevalence of the *trans*-conformation (Figure S2 and S3) with a range of 3.75 - 4.25 D and a mean of 4.13 D and 4.09 D in the presence of DHOA and TBP, respectively.

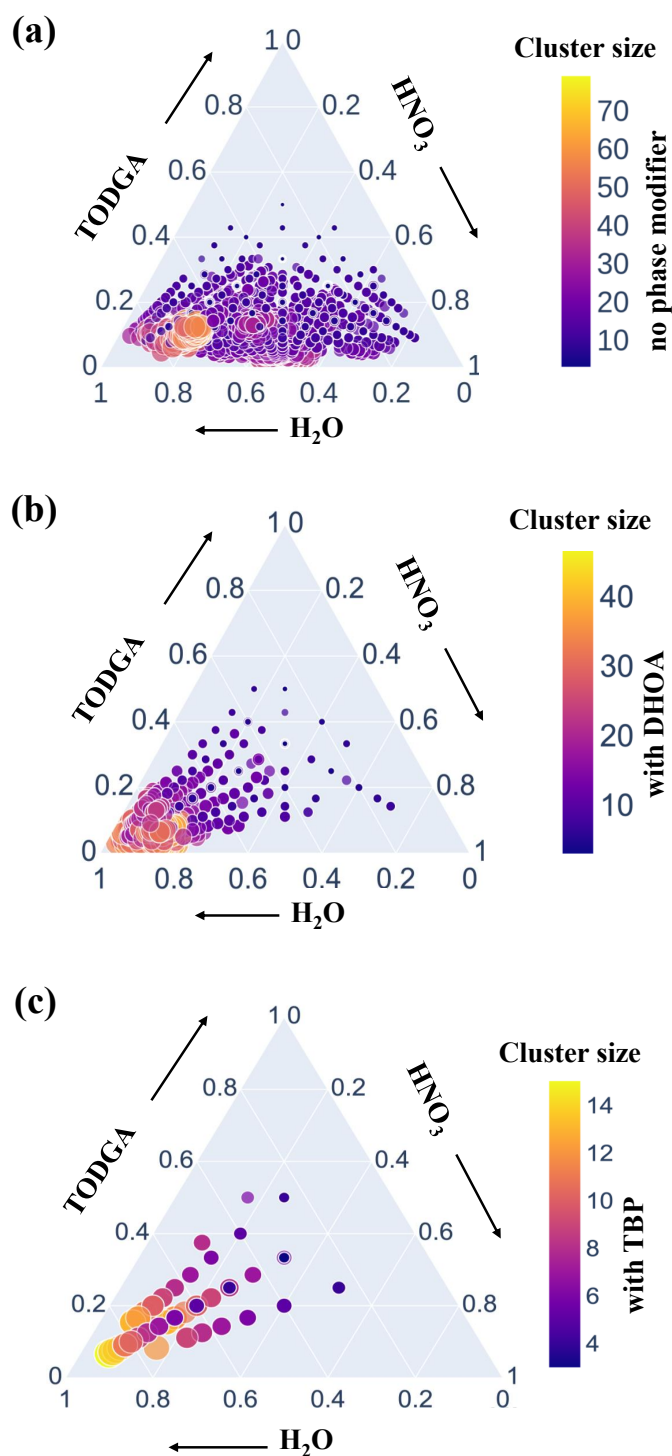


Figure 1: The fractional composition and size of $(\text{TODGA})_m(\text{H}_2\text{O})_n(\text{HNO}_3)_o$ reverse-micelle-like aggregates in 0.1 M TODGA, 0.2 M H_2O , and 0.15 M HNO_3 in dodecane: (a) without phase modifier (b) with 0.5 M DHOA as phase modifier (c) with 0.5 M TBP as phase modifier. The color bar indicates the aggregate size, whereas the diameter of scattered points indicates the size of its polar core. The number distribution of the different species within $(\text{TODGA})_m(\text{H}_2\text{O})_n(\text{HNO}_3)_o$ are presented in Figure S1.

The changes to intermolecular interactions are reflected within the radial distribution functions between the ethereal oxygen atoms of TODGA molecules (O_{TODGA}), and between the O_{TODGA} and O-atom of H_2O (O_W). The presence of DHOA and TBP is correlated with a decrease in the number of interactions TODGA has with the micellar polar-solutes, as indicated by the $O_{TODGA}\dots O_W$ RDF in Figure S4 and the decreased number of TODGA on the periphery illustrated in Figure S1. Further decreases to the nearest neighbor correlations between $O_{TODGA}\dots O_{TODGA}$ at c.a. 4.5 Å and long-range correlations at 7 and 9 Å are both observed (Figure S4). The average number of TODGA...TODGA interactions between 3 - 5 Å decreases from ~ 6 to ~ 4 upon introduction of DHOA and down to ~ 2 upon addition of TBP. The greater interaction strength of TBP relative to DHOA³⁴ (which contains one phenolic oxygen) for both sets of pair-wise interactions causes the impact of TBP to be substantially more pronounced than for DHOA (Figure S5 in Supporting Information).

These data demonstrate that one way in which DHOA and TBP increase aggregate dispersion is by decreasing the size of the reverse-micelle like structures which is dominated by the number of solvent molecules in the polar core that provide the surface area needed for the surface amphiphile adsorption. Importantly, this indicates that the phase modifier influences the interactions within the polar core itself - a feature not previously considered within the cosolvent and cosurfactant descriptions. However other characteristics of cosolvent or cosurfactant behavior may be observed within this system. Cosolvent behavior requires close proximity of the phase modifier with the outer TODGA layer of $(TODGA)_m(H_2O)_n(HNO_3)_o$,^{22,23} whereas the polar core will share interactions with the phase modifier and TODGA in the cosurfactant model.^{23,24} To further delineate between these scenarios we analyzed the prevalence of two types of phase modifier interactions within the simulation data:

- **Cosolvent character:** defined by instances where the phase modifier molecules interact with the surface of the $(TODGA)_m(H_2O)_n(HNO_3)_o$ reverse-micelle like structure but do *not* interact with the polar core. Distance cutoffs of 10 Å between the DHOA carbonyl O-atom (O_{DHOA}) and O_{TODGA} , and 11.5 Å between the phosphoryl O-atom

of TBP (O_{TBP}) and O_{TODGA} were used to define the surface interactions and are based upon the corresponding RDF profiles (see Supporting Information, Figure S6).

- **Cosurfactant character:** defined when the phase modifier clusters interact with the polar core of $(TODGA)_m(H_2O)_n(HNO_3)_o$ through hydrogen bonding interactions (as defined in the Supporting Information).

Importantly, each phase modifier possesses characteristics of both the cosolvent and cosurfactant without preference for one type of interaction over another. Statistically 57.5 % of all DHOA and 52.2 % of TBP interact with the $TODGA_m(H_2O)_n(HNO_3)_o$ mixed-aggregates as a cosolvent. The remaining 42.5 % of DHOA (47.8 % of TBP) participate as cosurfactant in the outer periphery of the polar core. The predominant interactions are through hydrogen bonding interactions with H_2O of the polar core rather than the interior HNO_3 .

Whether the phase modifier acts a separating unit between the $TODGA_m(H_2O)_n(HNO_3)_o$ aggregates was also investigated, as this has been suggested as a mechanism of action in prior work.^{22,23} Here, we counted the instances in which a group of phase modifier molecules (irrespective of their attachment with the polar core) bridge distance-separated $TODGA_m(H_2O)_n(HNO_3)_o$. As observed in Figure S7, small clusters of pure phase modifier molecules are observed, though they constitute a relatively small concentration of the environments that the phase modifier participates in. To be considered a bridging constituent, the phase modifier cluster must act as a cosolvent within the first coordination shell of bridged $TODGA_m(H_2O)_n(HNO_3)_o$ (within 10 or 11.5 Å as described above). Every instance of bridging behavior was tracked, alongside the size of the $(TODGA)_m(H_2O)_n(HNO_3)_o$ involved. These data (Figure S8) indicate a relatively low likelihood of occurrence. Complementing this, we investigated the instances of the $(TODGA)_m(H_2O)_n(HNO_3)_o$ bridging small clusters of phase modifier molecules. Interestingly, there is a much larger prevalence of this extended interaction. In the absence of preferential interactions of the phase modifier with the polar core vs. surface of the reverse-micelle structure, it is logical that any bridging interactions would largely depend upon surface area of the aggregates that are present. The

larger surface area of $(\text{TODGA})_m(\text{H}_2\text{O})_n(\text{HNO}_3)_o$ presents more opportunity for interactions with the phase modifier cluster and as such may be more statistically likely to act as bridging constituents when they are encountered in solution.

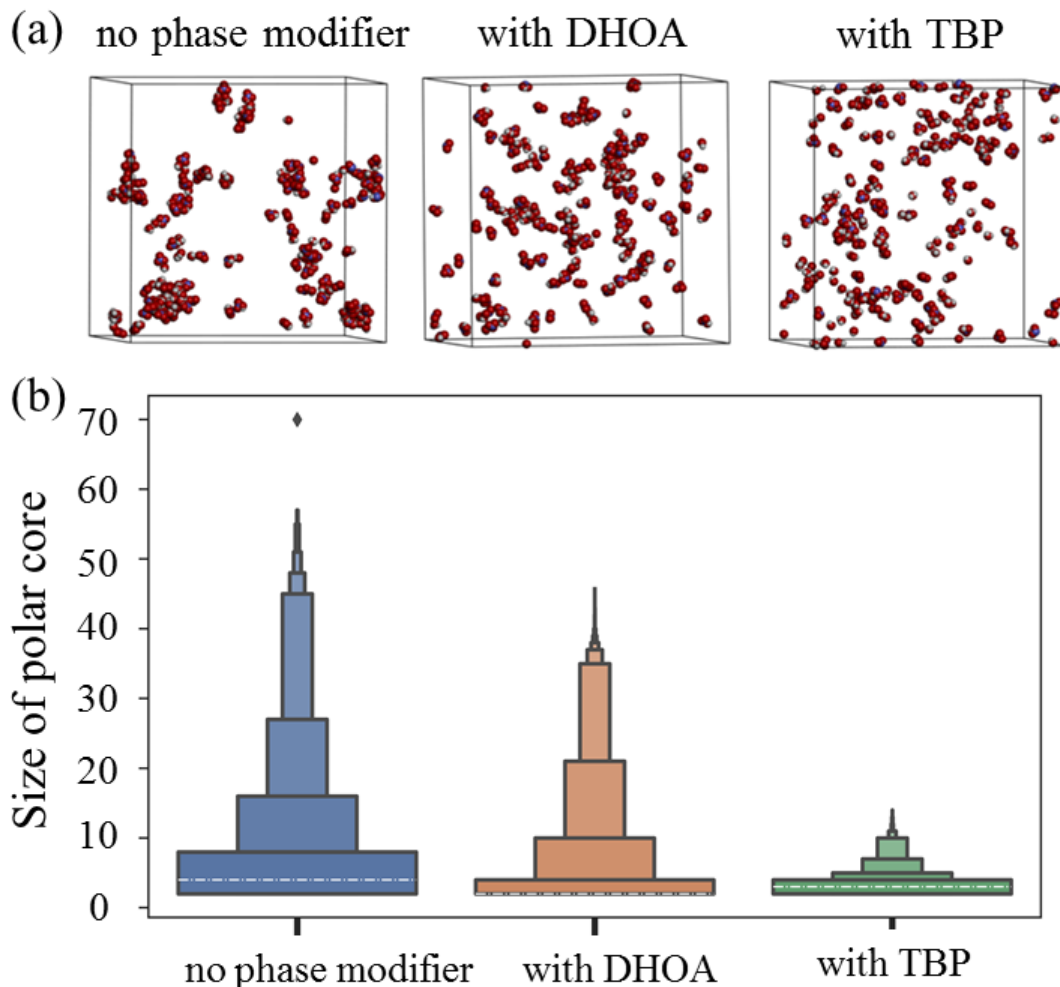


Figure 2: (a) Representative distributions of polar solutes (H_2O and HNO_3) within the simulation box at the end of the simulation trajectory. The corresponding 2D-number density maps from the last 10 ns production run are provided in Figure S9. (b) Letter-value plots depicting the size distribution of polar core in the absence and presence of phase modifier. The white dashed horizontal line of the individual plots corresponds to the median of the distribution. The range of the widest box corresponds to 25 to 75 percentile, whereas further plot of quantiles indicates the span of the distribution.

These data support the premise that TBP and DHOA perturb the interactions within the polar core of $(\text{TODGA})_m(\text{H}_2\text{O})_n(\text{HNO}_3)_o$ reverse-micelle like aggregates. As discussed in prior work,³⁵ the polar core contains a balance of interactions, where water prefers self-

solvation but competition of HB acceptor sites with HNO_3 limits the growth of $(\text{H}_2\text{O})_n$ clusters. TBP and DHOA further introduce competition for hydrogen bonding sites both within the polar core itself and between TODGA and H_2O and HNO_3 . TBP, in particular, has a significant affect upon the $\text{H}_2\text{O}\dots\text{H}_2\text{O}$ interaction energy as a result of a greater number of HB acceptor sites (one phosphoryl and three ester O-atoms) and the stronger hydrogen-bond accepting ability of phosphoryl³⁴ compared to carbonyl, which favors TBP... H_2O and TBP... HNO_3 interactions. The distributions of all HB interactions are presented in Table S4, where 40 % of all H_2O are observed to be hydrogen bonded to the DHOA and 93.6 % to the TBP (Table S2). Addition of the phase modifier decreases the average number of HBs between TODGA and polar-solutes as well as reduces HBs among polar-solutes (Supporting Information, Table S5). The underlying dynamics of HB pairs are also perturbed. When compared with TODGA... H_2O , considerably higher average lifetime of hydrogen bonds (τ_{av}) are observed for phase modifier HBs with H_2O , particularly for TBP (Table S6). The phase modifier further increases the $\text{H}_2\text{O}\dots\text{H}_2\text{O}$ τ_{av} , with a larger impact observed for TBP as compared to DHOA (Table S7) and such observation extends also to other hydrogen bonded pairs (*i.e.* $\text{HNO}_3\dots\text{H}_2\text{O}$, TODGA... H_2O) (Table S6 and S8). These results can be rationalized in terms of the scarcity of H_2O at the immediate vicinity of TODGA bound water (or HNO_3 hydrogen bonded H_2O) to compel H_2O to maintain the existing hydrogen bonds for longer duration (Table S2). This behavior is well-known in interfacial environments where there is a scarcity of hydrogen bonds, as in interfaces such as in the hydrogen bond lifetime of interfacial waters of proteins and water/vapor and water/organic interfaces.^{36,37}

The net result of the increased hydrogen bonding, and strong hydrogen bond strength, of the phase modifier with the polar-solutes, is a decrease in the the average potential energy observed between TODGA... H_2O and TODGA...TODGA (Figure S5). Analysis of the percent of H_2O (out of the total present) that resides within 0 – 3.8 Å of TODGA, DHOA, TBP and HNO_3 reveals a drop of H_2O content around TODGA (by 28.1 % and 61.9 % for DHOA and TBP, respectively) and nitric acid (by 23.5 % and 64.8 % for DHOA and TBP,

respectively) (Table S2 and S3). The presence of TBP reduces the size of water clusters within the polar core to < 10 . Whereas, in the case DHOA, the size of water cluster gets restricted to 32 and the size distribution of water cluster varies between 10–32.

The ability of the phase modifier to enhance dispersion of smaller-sized polar core reverse-micelle like aggregates can be further studied through examination of the structural entropy of the solution as a whole. The structural entropy (SE), as defined in the Supplementary Information, is a measure of the likelihood of choosing a molecular node within the network of all intermolecular interactions that is participating within an individual reverse-micelle like aggregate. If all molecule participate in a single aggregate the value of SE is zero, while the maximum value is reached if all molecules act as individual clusters (or monomers). As observed in Figure S13, the structural entropy of polar network increases in the presence of phase modifier, where TBP induces the largest SE followed by DHOA - in agreement with the growth of smaller reverse-micelle like aggregates in solution under those conditions. Monitoring the SE over time also provides interesting insight into the dynamics among polar solutes. For example, the largest fluctuations in the SE are observed in the absence of phase modifier - indicating that the more dynamic hydrogen bond network in the absence of the phase modifier may also support more facile interconversion between different size and composition of aggregates. As the hydrogen bond strength of the phase modifier is increased, disrupting the polar core interactions and causing stronger phase-modifier interactions with the polar core, the fluctuations between the number and size of aggregates decreases - causing narrower distributions of the SE over the production run of the trajectory. These data, in combination with the hydrogen bond dynamics analysis, indicate that the phase modifier stabilizes the dynamics of the reverse-micelle like aggregates concurrent to the enhanced dispersion.

The analyses presented thus far clearly indicate that there is no energetic preferences that support the cosolvent and cosurfactant models for the dispersion of aggregates within the TODGA, TBP and DHOA system under study. Instead, a new perspective is needed for

understanding the mode of action of phase modifiers upon microemulsion solution structure. Using the intermolecular interactions between all components as a starting point, we can first consider that in order for a phase modifier to act as a cosolvent, the amphiphile interactions with the polar core must be reasonably strong, and the phase modifier interactions amongst themselves and the non-polar surface of the aggregates are stabilizing. As such, the phase modifier solvates the aggregates and buffers their aggregate...aggregate interactions to improve dispersion.²⁰⁻²³ In contrast, the cosurfactant model implies that the phase modifier and amphiphile ligand have comparable interactions with the polar core and that these interactions are stronger than those of the amphiphile or phase modifier molecules amongst themselves. Thus, the phase modifier molecules become distributed within the surfactant layer of the aggregates along with the primary extractant to interact with the polar core of aggregates. Yet the results of the phase modifiers TBP and DHOA with TODGA as an amphiphile extractant clearly point to the fact that the phase modifier may have very strong interactions with the polar core that disrupt interactions between the polar-solutes. Building upon this understanding, we present a more comprehensive model, the *Dispersion by Competitive Interaction model (DCI)* that encompasses different “regimes” within a solution where the self-interaction between the same components (amphiphile...amphiphile, phase modifier...phase modifier, polar-solute...polar-solute) or cross-interactions between different components (amphiphile...phase modifier, polar-solute...amphiphile, or polar-solute...phase modifier) influence the mode of action of the phase modifier in aggregate dispersion. As illustrated in Figure 3, when cross-interactions between different components are the most prevalent in the solution the cosurfactant regime is approached. When the self-interactions between the same components in the solution the cosolvent regime is reached. In-between these two extremes lies the ability of the phase modifier to disrupt the polar-solute core interactions and a new regime is introduced - the “polar disruption” regime.

The DCI model provides a basis for creating testable hypotheses and refinements to predictions of aggregate size, dispersion, and fundamental properties like the CAC or CMC.

Dispersion by Competitive Interaction Model

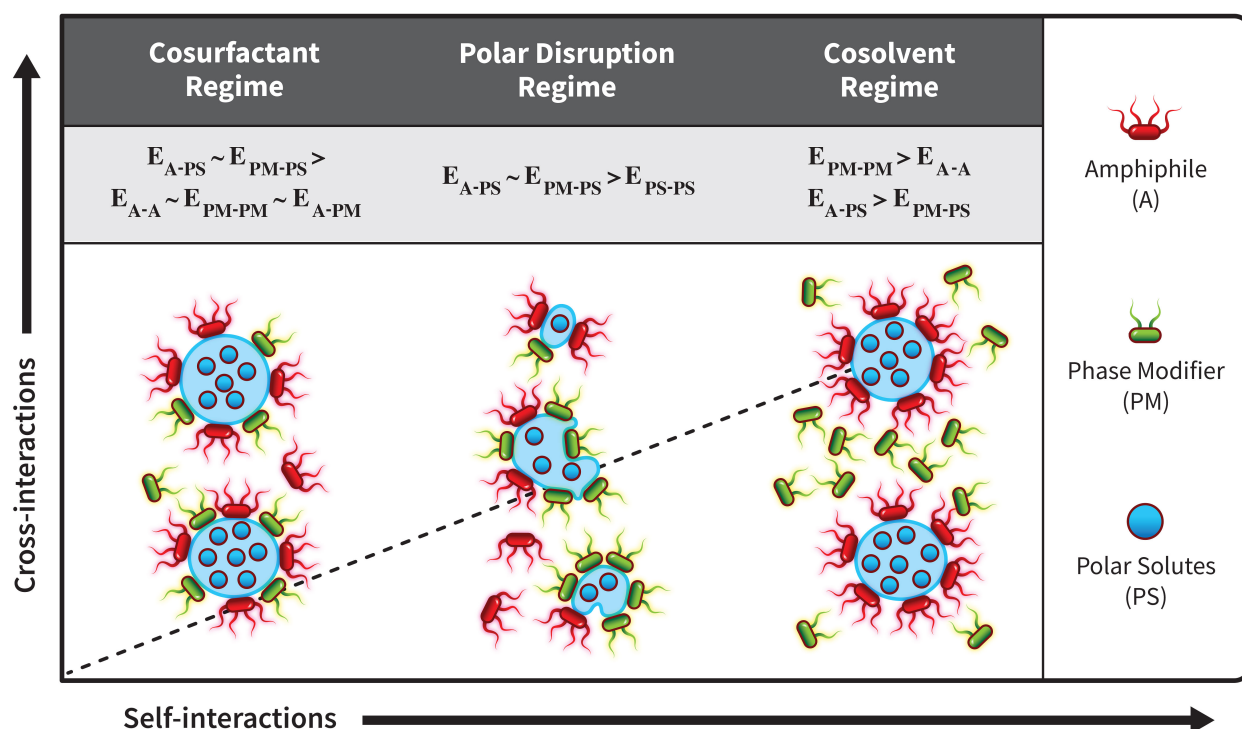


Figure 3: The proposed Dispersion by Competitive Interaction model (DCI) considers the strength and prevalence of “self-interactions” between components of the same type (e.g., polar-polar), “cross-interactions” between different molecular type components (e.g., phase modifier...polar-solute). Different mechanisms of action (cosolvent, cosurfactant, polar disruption) are proposed based upon which type of intermolecular interaction dominates the microemulsion system in the presence of the phase modifier.

With the growth of available data of solution conditions and experimentally determined size distributions, as well as those from simulation, we anticipate that the DCI can evolve from a phenomenological or observational model, to one with a distinct analytical expression derived from learning approaches that extend beyond this study but are part of ongoing work. Such a chemistry-informed approach toward prediction of microemulsion structure will dramatically improve existing approaches toward controlling phase phenomena and provide rational design strategies for solution characteristics.

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Supporting Information Available

Variation of structural entropy of network comprising water and nitric acid, relative change in water cluster distribution with phase modifier, plot of intermittent hydrogen bond lifetime correlation functions, RDF plots for TODGA-DHOA and TODGA-TBP interaction, Tables with calculated relaxation times obtained from the intermittent hydrogen bond lifetime correlation functions for TODGA-water, nitric acid-water and phase modifier-water.

Graphical TOC Entry

