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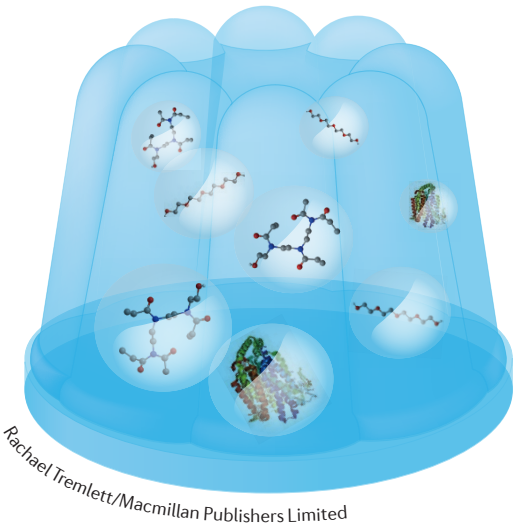
MULTI-PHASE SYSTEMS

# Hydrogel-driven compartmentalization

These multi-compartment materials may be used for controlled release systems, such as artificial cellular matrices for tissue engineering or for responsive soft materials

Separating entities and preventing them from mixing, also known as compartmentalization, has a key role in certain biological and industrial processes. Compartmentalization is fundamental to life because it enables functions such as metabolism, transport, communication and motion. Additionally, compartmentalization is important in encapsulation, structuring materials and controlling delivery of drugs, fragrances, pesticides and flavours. In synthetic systems, compartmentalization generally occurs through one of two processes: emulsification of immiscible phases or vesicle encapsulation. However, most synthetic compartmentalized systems have two main limitations. Aqueous compartments are usually separated by hydrophobic barriers, which hamper the exchange of polar constituents. Furthermore, most systems can have only one or two different types of compartment.

Although emulsions are readily produced and stabilized on a large scale, generating loaded vesicles is more complicated and not easily scalable. We need a more facile route to forming microcompartments that can contain polar constituents without using hydrophobic barriers. Inspired by early work of Keating, who investigated aqueous two-phase systems by using lipid vesicles, Jan van Esch and colleagues have found a generic method of compartmentalizing aqueous media. In their study, published in *Angewandte Chemie International Edition*, a microcompartmentalized material is prepared from a polymer emulsion, which is trapped in a supramolecular hydrogel so that it does not phase separate.



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The van Esch group made use of two aqueous non-mixing polymer solutions — one containing poly(2-ethyl-2-oxazoline) and the other dextran — to create microemulsions. This mixed state was preserved by introducing a poly(ethylene glycol)-functionalized tris(hydrazone), a gelator previously used by the group. The resulting supramolecular gel formed around the micelles, 'freezing' the microstructures into a compartmentalized hydrogel. The rate of gel formation had to be substantially faster than the rate of phase separation of the two polymer solutions. Thus, the gel kinetically traps the phase-separating solutions within a fibrous network at intermediate stages of demulsification.

The volume fraction of the polymer phases affects the size and composition of the microscopic spherical domains. The resulting compartmentalized microstructures are stable for at least a week, which highlights that coalescence of the microdroplets is retarded by entrapment within the static fibre network of the supramolecular gel.

It turns out that the process is generalizable; the team led by van Esch were also able to apply this protocol to several other aqueous two- and three-phase systems. The new materials not only permitted diffusion of several polar molecules, but also allowed large biomolecules to pass through the system. The latter process is very unusual in conventional synthetic compartmentalized systems.

Although the work here is very demonstrative, "a vast amount of research is needed," lament van Esch and co-workers. In particular, molecular-level understanding and further control of the reaction kinetics and interactions between system components is required. With that said, compared to classic water–oil emulsions or surfactant systems, the materials described in this elegant study have several unique features: the systems are completely water-based, can be prepared from biomolecules, allow free solutes to move from one compartment to another and can contain different compartments. "These multi-compartment materials may be used for controlled release systems, such as artificial cellular matrices for tissue engineering or for responsive soft materials," predicts van Esch.

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**ORIGINAL ARTICLE** Mytnyk, S. *et al.* Compartmentalizing supramolecular hydrogels using aqueous multiphase systems. *Angew. Chem. Int. Ed.* http://dx.doi.org/10.1002/anie.201706272 (2017)

**FURTHER READING** Aumiller, W. M. Jr *et al.* Coupled enzyme reactions performed in heterogeneous reaction media: experiments and modeling for glucose oxidase and horseradish peroxidase in a PEG/citrate aqueous two-phase system. *J. Phys. Chem. B*, **118**, 2506–2517 (2014) | Boekhoven J. *et al.* Catalytic control over supramolecular gel formation. *Nat. Chem*, **5**, 433–437 (2013)