Bacterial confinement in hydrogels to develop living therapeutic materials

Shrikrishnan Sankaran,[1] Shardul Bhusari,[1] Priyanka Dhakane[1] & Aránzazu del Campo[1, 2]

[1]*INM – Leibniz Institute for New Materials, Campus D2 2, 66123 Saarbrücken, Germany*
[2]*Chemistry Department, Saarland University, 66123 Saarbrücken, Germany*

"Living therapeutics" refers to the use of engineered bacteria in the human body to produce drugs on-site. In spite of expected advantages for targeted delivery and cost savings in drug synthesis/isolation/encapsulation, clinical applicability of living therapeutics has not been realized yet. Many important issues are associated with the delivery of engineered bacteria into the body, which remain to be solved. "Living materials", where active bacteria are encapsulated in a synthetic matrix that sustains their activity, regulates proliferation and prevents bacterial escape, might overcome many problems associated with the use of bacteria in a biomedical context. Similar to natural biofilms, the mechanical properties and geometry of the synthetic matrix play crucial roles in modulating bacterial behavior. Likewise, depending on the bacterial strain, matrix modifications and drug production traits can vary. I will present my work in developing optogenetically-engineered bacterial hydrogels capable of producing and releasing proteins[1] or metabolically synthesized drugs[2] regulated by light. The effects of chemical and physical cross-linking of the synthetic matrix on bacterial growth, division and drug production will be discussed. The behavior of two very different bacterial strains, *Escherichia coli* and *Streptomyces albus* within these environments will also be described.

[1] Sankaran, S. & del Campo, A. Optoregulated Protein Release from an Engineered Living Material. *Advanced Biosystems* **3**, 1800312 (2019).

[2] Sankaran, S., Becker, J., Wittmann, C. & del Campo, A. Optoregulated Drug Release from an Engineered Living Material: Self-Replenishing Drug Depots for Long-Term, Light-Regulated Delivery. *Small* **15**, 1804717 (2019).