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Engineering synthetic cells with RNA origami

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Today's living cells emerge from the complex interplay of thousands of molecular constituents. Our vision is to create a simpler model of a cell that consists of a lipid vesicle and operates based on our own custom-engineered molecular hardware made from highly functional and folded RNA realized using the co-transcriptional folding of RNA origami. Building on previous work with DNA nanotechnology, where we demonstrated DNA-based mimics of cytoskeletons, capable of cargo transport, force generation and signal transduction [1], we now demonstrated that similar functions can be genetically encoded with RNA origami and expressed inside of vesicles. We developed a high-throughput image-based screening technology based on photopolymerization, to select for highly functional variants of the initially rationally engineered synthetic cells. Ultimately, by coupling vesicle division [2] to their informational content and their function, we aim for a prototype of a synthetic cell capable of evolution. In the context of Physics and Medicine, I will highlight the relevance of both, DNA/RNA origami and image-based selection, for applications in organoid research [3] and immunology [4].

[1] Zhan, P., Jahnke, K., Liu, N., & Göpfrich, K. (2022). Functional DNA-based cytoskeletons for synthetic cells. *Nature Chemistry*, 14(8), 958-963.

[2] Dreher, Y., Jahnke, K., Bobkova, E., Spatz, J. P., & Göpfrich, K. (2021). Division and regrowth of phase-separated giant unilamellar vesicles. *Angewandte Chemie International Edition*, 60(19), 10661-10669.

[3] Afting, C., Walther, T., Drozdowski, O.M., Schlagheck, C., Schwarz, U.S., Wittbrodt, J., & Göpfrich, K. DNA microbeads for spatio-temporally controlled morphogen release within organoids. Under review in *Nature Nanotechnology*.

[4] Göpfrich, K., Platten, M., Frischknecht, F. & Fackler, F. Bottom-up synthetic immunology. *Nature Nanotechnology*, accepted.

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