BIOPHYSICS

Sander Tans

We aim to understand autonomous self-organization in biology focusing on the single protein and single cell level. Key techniques are optical tweezers and single-molecule fluorescence for the former, and 3D microscopy and deep learning driven cell tracking and analysis for the latter. These methods can uniquely reveal the conformational dynamics of amino-acid chains during protein biogenesis, and the growth, differentiation, and spatial organization of cells in developing organoid systems. The approaches we develop and the organizational principles we aim to elucidate are relevant to a wide range of questions regarding protein homeostasis and tissue maintenance.

Highlights

- We showed that cellular motility can explain the coexistence of different bacterial populations, which also opens up direct study of spatial ecology questions.
- We found that proteins are disaggregated by the processive translocation of amino acid chains.
- We developed novel approaches to quantify the dynamics of cells within organoids.
- We developed methods to reveal co-translational protein assembly at the single-molecule level.

Plans

In our single cell organoid research, we will extend to rare cell types in the intestine, as they are poorly understood yet key to several conditions, and will start exploring cancer models and immune cell interactions. To do so, we will continue to expand our collaborative network with various biology groups, also driven by our cell tracking methods. Technically, we will continue to expand deep-learning enabled methods. Our molecular research will be focused on co-translational assembly and ubiquitin mediated protein processing, which both are unaddressed at the single-molecule level. In the latter we will integrate with partner groups that focus on ribosome profiling, which provides genome-wide data, and cryo-EM, which provides insight at the atomic level.

Key research items

1. M.M. Naqvi, M.J. Avellaneda, A. Roth, E.J. Koers, A. Roland, V. Sunderlikova, G. Kramer, H.S. Rye, S.J. Tans, *Protein chain collapse modulation and folding stimulation by GroEL-ES*, Sci. Adv., 8 (9), eabl6293 (2022)

2. F. Büke, J. Grilli, M. Cosentino Lagomarsino, G. Bokinsky, S.J. Tans, *ppGpp is a bacterial cell size regulator*, Current Biol., 32 (4), 870 (2022)

3. S. Gude, E. Pince, K.M. Taute, A.B. Seinen, T.S. Shimizu , S.J. Tans: *Bacterial coexistence driven by motility and spatial competition*, Nature 578 (7796), 588 (2020)

4. M.J. Avellaneda, K.B. Franke, V. Sunderlikova, B. Bukau, A. Mogk, S.J. Tans: *Processive extrusion of polypeptide loops by a Hsp100 disaggregase*, Nature 74, 212 (2020)

5. G. Huelsz-Prince, R.N.U. Kok, Y. Goos, L. Bruens, X. Zheng, S.I. Ellenbroek, J. van Rheenen, S.J. Tans, J.S. van Zon, *Mother cells control daughter cell proliferation in intestinal organoids to minimize proliferation fluctuations*, Elife 11, e80682 (2022)

ClpB disaggregase protein (white) translocates an amino-acid loop, as we revealed for the first time using single-molecule methods.