

characterize the interplay between tumor cells and angiogenesis, as well as their proliferation, phenotypic transitions, and death. We use this model to predict early in course of neoadjuvant therapy—the eventual response of the individual patient. Success in this endeavor would enable replacing an ineffective treatment with an alternative regimen, thereby potentially improving outcomes and curtailing unnecessary toxicities. Furthermore, our approach can be applied to any disease site for which neoadjuvant therapy is indicated and the requisite data is accessible.

Platform: Bacterial Mechanics, Cytoskeleton, and Motility

1596-Plat

***Wolbachia pipientis* Colonizes *S. cerevisiae* with High Yields. Effects on the Host**

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Wolbachia pipientis is an obligate-endosymbiotic gram-negative bacterium, that naturally colonizes 40-60% of all insect species. It may be transmitted vertically transmitted via germinal cells or horizontally. Each *Wolbachia* strain is quite different to the rest, as *Wolbachia* coevolves with the host, where it manipulates protein expression, fertility and metabolism. *Wolbachia* may protect its host against infection by other organisms such as pathogenic viruses or bacteria. A major problem to study *Wolbachia* has been its inability to grow *ex-vivo* and the low yields obtained from insect cell cultures. The unicellular yeast *Saccharomyces cerevisiae* was infected with *Wolbachia pipientis*, obtaining large biomass yields. *Wolbachia* did not contribute to oxidative phosphorylation, but instead it seemed to rely on external supply of ATP, possibly precipitating premature death of the host. In contrast, *Wolbachia* does seem to contribute some coenzymes to the host. It also modifies the actin cytoskeleton. Premature death has been reported also in the artificially infected mosquito *A. aegypti* probably accounting for the decrease in vector disease activity of this host.

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Time-Lapse Atomic Force Microscopy Reveals New End Take Off (Neto) Dynamics in Mycobacteria

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Tuberculosis is a lung infection caused by *Mycobacterium tuberculosis*. One third of the world population is thought to be infected. Antibiotic treatment with antibiotics lasts 6 months, which is difficult to achieve in low-income countries. The uncommon ability of tuberculosis bacteria to persist during long periods is linked to various factors, one of which potentially being cell growth asymmetry. However, growth symmetry or asymmetry of mycobacteria remains a controversial topic as opposing descriptions have been reported in the literature.

Observing bacterial growth at the single cell level is inherently challenging due to the diffraction limit of optical microscopes and the small size of the cells. We built a new dedicated platform for long-term, correlated Atomic Force Microscopy (AFM) and fluorescence microscopy and obtained time-lapses of bacterial growth at an unprecedented resolution.

Surprisingly, the AFM high-resolution time-lapses did not match any of the two previously reported models of pure symmetry and pure asymmetry. Mycobacterial pole growth dynamics was rather an intermediate between the two, reminiscent of the well-known “new end take off” mechanism for fission yeast. Using AFM nanomanipulation we show that growth asymmetry is not a physical occlusion phenomenon, but is inherent to mycobacterial growth. Finally, using fluorescent photoconversion microscopy we identify biomolecular mechanisms linked to growth asymmetry, which in the future could be used to develop novel treatments for tuberculosis infection.

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Molecular Motors Govern Liquid-Like Ordering and Fusion Dynamics of Bacterial Colonies

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Institute for Biological Physics, University of Cologne, Cologne, Germany. Many bacteria are able to form communities called biofilms. Within these structured communities, they benefit from various advantages including facilitated gene transfer and increased antibiotic resistance. Bacteria can adjust the structure of colonies and biofilms to enhance their survival rate under external stress. The human pathogen *Neisseria gonorrhoeae* is able to aggregate into spherical colonies due to active retraction of its type 4 pili. Here, we explore the link between bacterial interaction forces and colony structure and dynamics. First, we show that the simultaneous expression of a functional and a nonfunctional variant of the motor protein PilT affects motor activity, namely the retraction velocity and the probability to be in the retracting, elongating or pausing state, respectively. Second, we demonstrate that motor activity enhances local ordering and accelerates fusion dynamics of bacterial colonies. Motor activity strongly affects the probability of two cells to be bound to each other. The radial distribution function of mature colonies shows local fluid-like order. The degree and dynamics of ordering are dependent on motor activity. At a larger scale, the fusion dynamics of two colonies shows liquid-like behavior whereby motor activity strongly affects the ratio between surface tension and viscosity. An estimate of colony surface tension using molecular interaction characteristics shows that surface tension is hardly affected by motor activity, indicating a strong effect on colony viscosity.

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DNA Origami as a Tool in the Targeted Destruction of Bacteria

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Antibiotic resistance is a growing worldwide human health issue. It is now threatening to render us vulnerable once again to infections that have been treatable for decades. Various approaches have been proposed in the effort to overcome this threat and effectively treat bacterial infections. We explore the possibility of creating and using DNA origami nanostructures as a vehicle for delivering functional molecules in a specific and efficient manner, in order to destroy bacterial targets. In the past few years, DNA origami has been used to successfully target eukaryotic cancer cells, with impressive results. However, there are no reports of the use of DNA origami to specifically target bacterial cells. We have created a DNA origami tile with five “wells” that can carry up to 10 molecules of antibacterial lysozyme. The origami tile has been modified to carry four aptamers that are specific to *Escherichia coli* bacteria and enable anchoring of tiles onto a bacterium. Each origami tile measures approximately 100 x 100 nm, allowing for multiple tiles to attach to any bacterium. We use direct stochastic optical reconstruction microscopy (dSTORM) to assess the efficiency of targeting the tile to the bacteria and we show that treatment with lysozyme-functionalised tiles slows bacterial growth more effectively than treatment with free lysozyme. We also assess the mechanical properties of the origami-treated bacteria with atomic force microscopy. Our study introduces DNA origami as a tool in the fight against antibiotic resistance, and our results demonstrate the specificity and efficiency of the nanostructure as a drug delivery vehicle.

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3D Fluorescence Microscopy Reveals Geometric Localization of Bacterial Cell Shape Proteins in Straight, Curved and Helical Rods

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The bacterial kingdom is full of complex cell shapes including straight, curved and helical rods. Using a computational fluorescent imaging approach to reconstruct experimentally obtained 3D shapes of individual cells with 50 nm precision, we have been exploring the geometric localization of the proteins associated with cell shape homeostasis in various species. In straight-rod shaped *E. coli*, for example, the actin-like protein