Modelling and visualisation of nascent biofilms

and the action of anti-biofilm treatments

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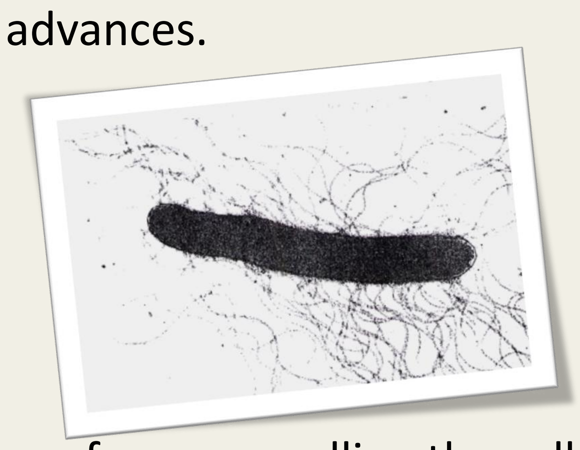
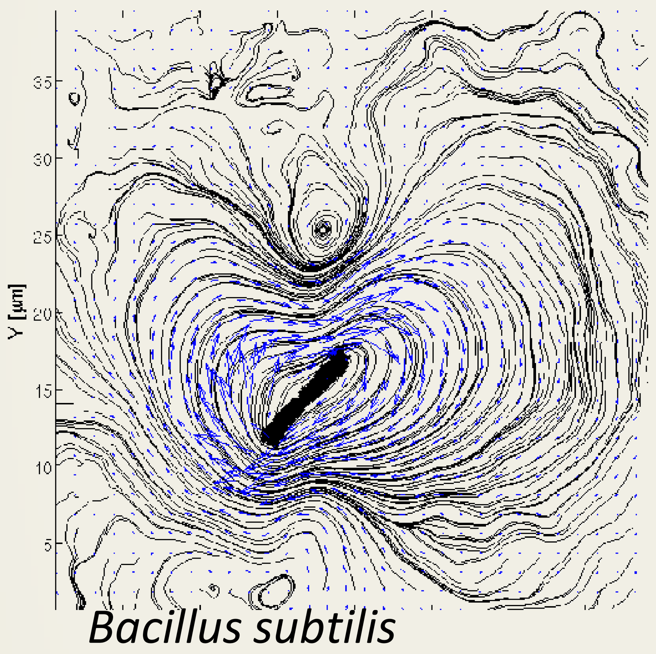
1. ABSTRACT

- Lactam analogues (developed by Unilever) disrupt biofilm formation and may feature in a range of products (e.g. domestic cleaning).
- The active components can jam quorum sensing, acting as antagonists of signal molecule receptors on Gram negative bacteria.
- Action of the lactam analogues is not completely understood. Unilever requires a physical understanding of the biofilm inhibitors for regulatory purposes.
- Using mechanistic modelling (analytical and numerical) and visualisation techniques (particularly high-speed holographic microscopy), we investigate the three-dimensional fluid dynamics of nascent biofilms and the action of anti-biofilm treatments.
- These approaches aim to identify how lactam analogues limit biofilm growth, and inform the design of next generation anti-biofilm technologies.
- Here, we present some of the methodological advances.

2. CONSTRAINED FLOWS

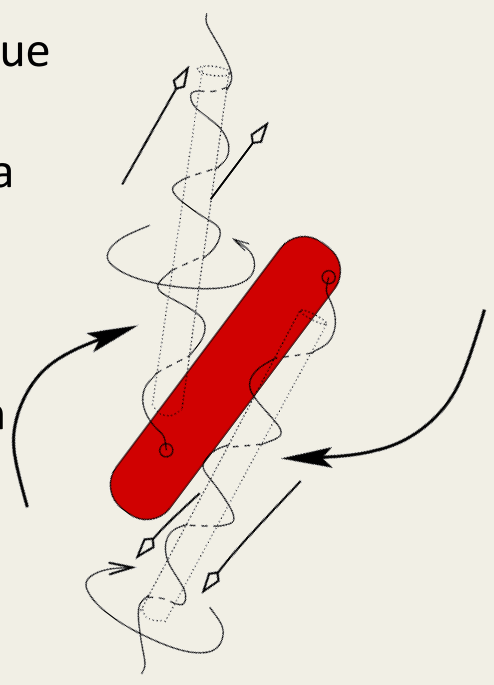


When bacterial flagella corotate, flagella bundles can form, propelling the cell forwards. **However, constrained cells produce larger, complex flows.**

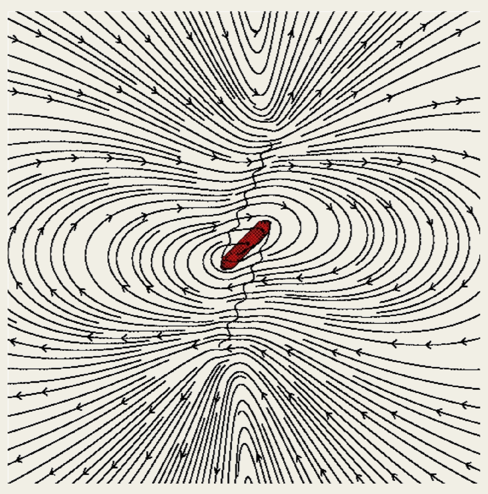


Bacillus subtilis

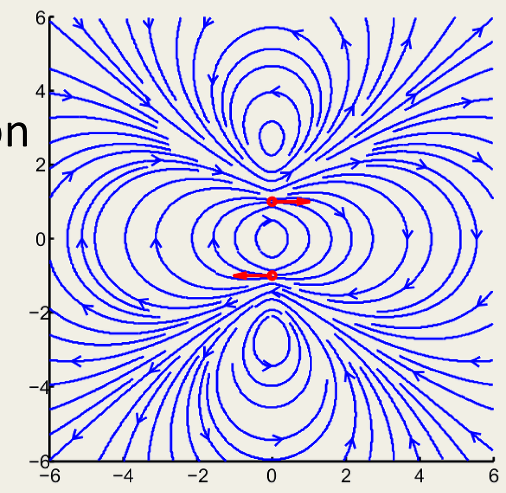
Rotating flow due to a cell constrained in a thin film (PIV); flagellar arrangement associated with asymmetric surface interaction [1]



Simulation in semi-infinite region: method of regularised Stokeslets [1]

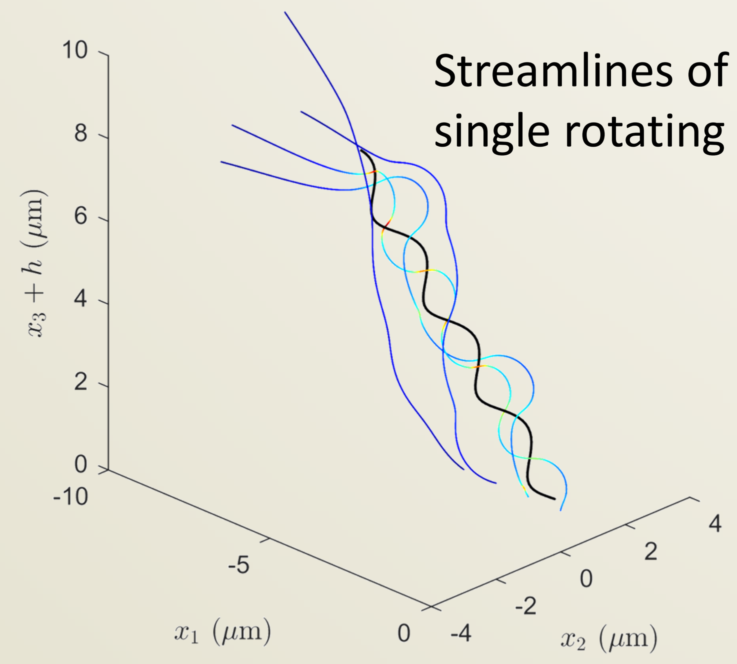


Force couple: Green's function (singular solution) for a thin-film approximation [2]



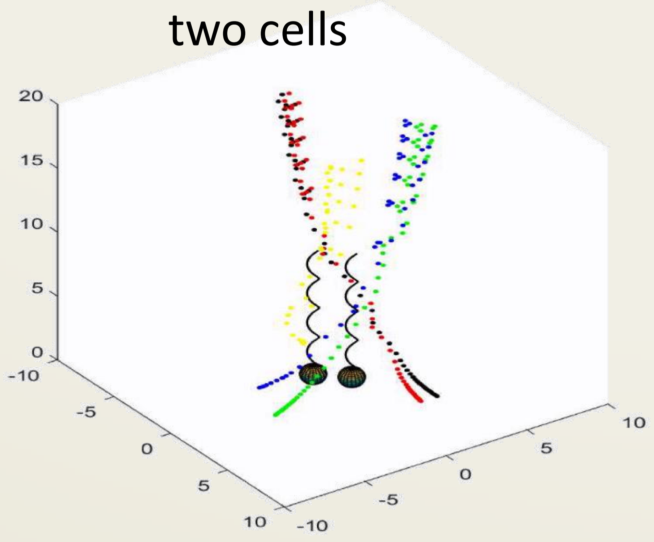
3. DYNAMICS OF HELICAL FLAGELLA NEAR BOUNDARIES

We use slender body theory to model the flow past nascent biofilms, consisting of cells stuck to a plane boundary. (Each flagellum is replaced by an arrangement of singular solutions together with their images to enforce no-slip boundary conditions.)

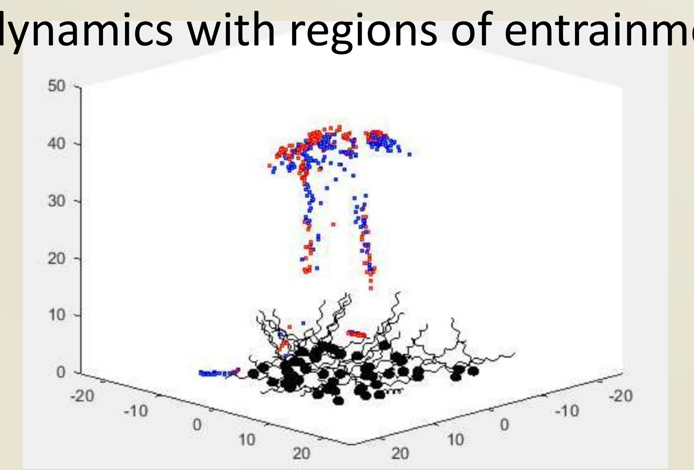


Streamlines of flow past a single rotating flagellum

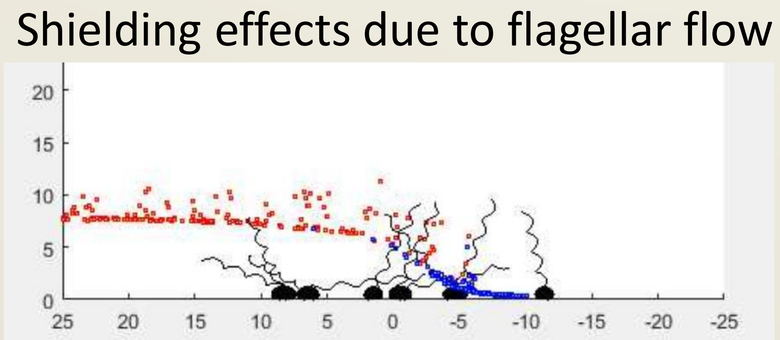
Particle paths near two cells



Multiple cells yield complex tracer dynamics with regions of entrainment

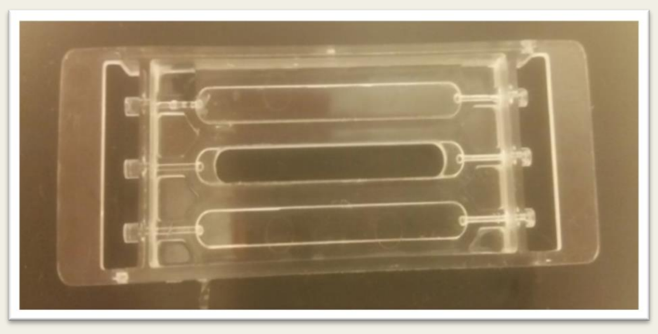


Shielding effects due to flagellar flow

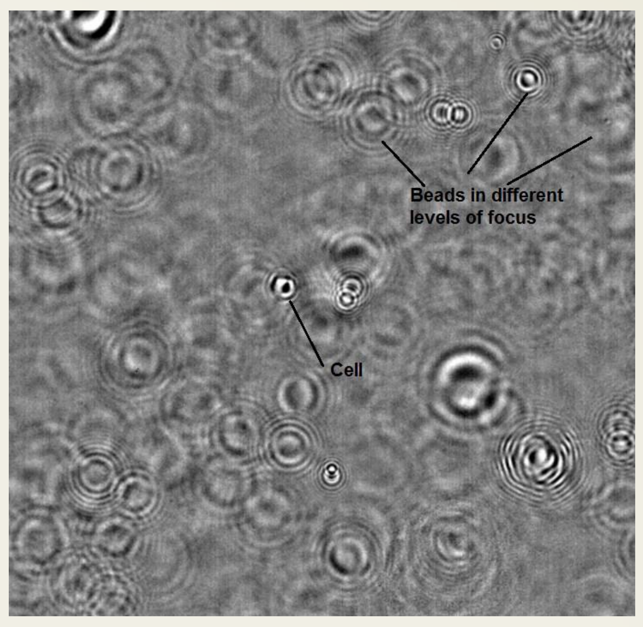


Dynamics of interacting flagella reveal bifurcation structure

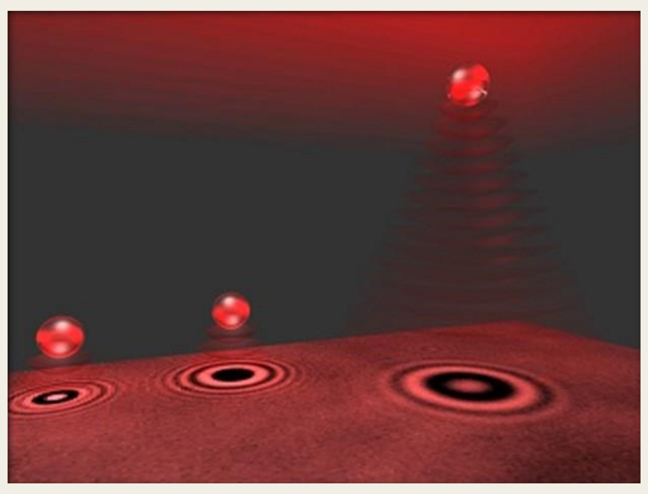
4. HIGH SPEED HOLOGRAPHIC MICROSCOPY - 3D FLOWS AROUND SURFACE-ATTACHED CELLS



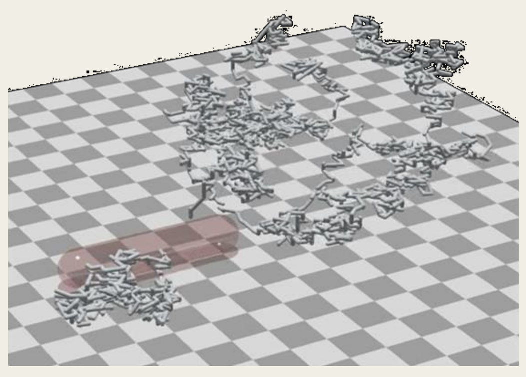
Flow cells



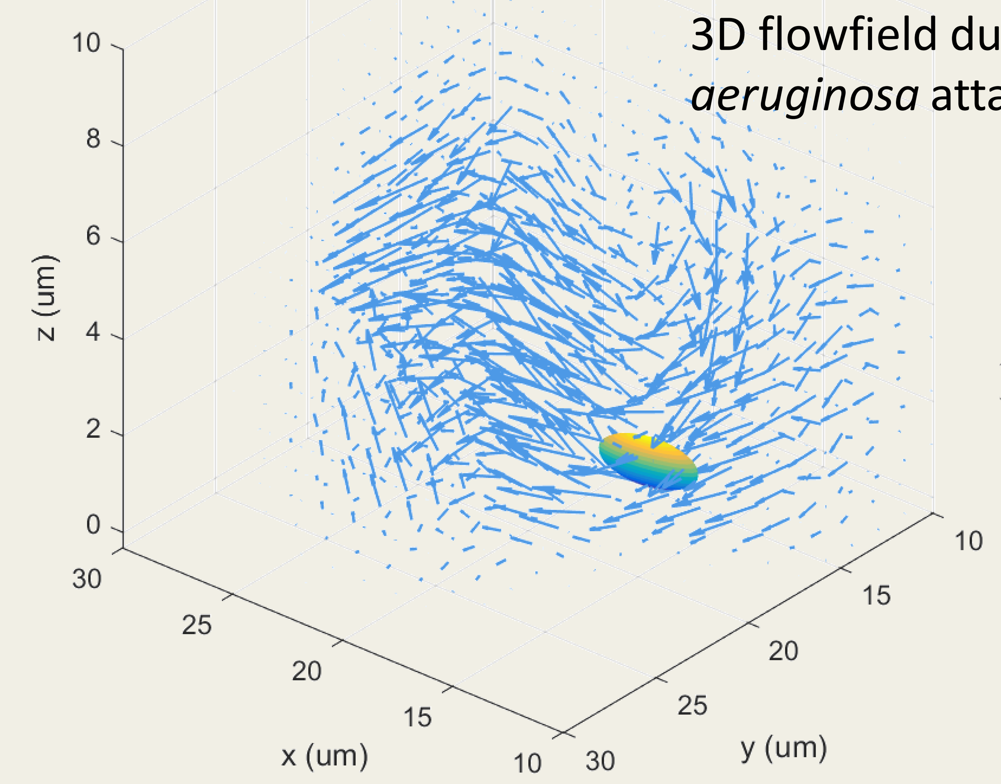
Interference pattern from coherent light illumination of tracer beads around surface-attached *Pseudomonas aeruginosa*



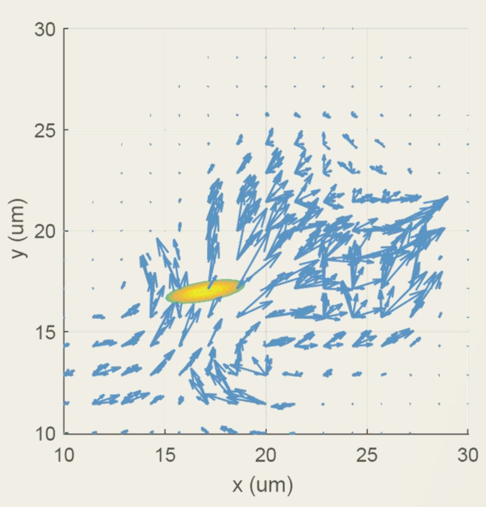
Interference patterns provide 3D locations of beads via Rayleigh-Sommerfeld back-propagation and gradient processing [3]



3D bead tracks



3D flowfield due to *Pseudomonas aeruginosa* attached to a surface



5. SUMMARY

- We can image the flow in three-dimensions due to cells attached to surfaces subject to shear using high speed holographic microscopy.
- These observations allow us to probe the physical action of Unilever's lactam analogues.

- Modelling using slender body theory and analytical techniques (not shown) provides a theoretical framework to test our mechanistic understanding of the system.
- The models reveal complex tracer dynamics in early-stage biofilms consisting of tens of cells, with regions of entrainment and shielding effects in shear flow. Our results suggest that flagellar flows play an important role in signal dispersal and recirculation among early-stage biofilm formers.
- Interacting flagella display a range of dynamical behaviour. Simplified descriptions provide a useful tool for scaling up.

- The lactam analogues have an effect on nascent biofilms beyond that of quorum sensing.

[1] Cisneros, Kessler Ortiz, Cortez & Bees. PRL 101 168102 (2008)
[2] Pushkin & Bees. Adv. Exp. Med. Biol., Biophysics of Infection 915 193 (2016)
[3] Wilson, Carter & Reece. PNAS 110 47 (2013)

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