Self-organized beat of cilia through the non-equilibrium dynamics of ratchets

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I. INTRODUCTION

Cilia are elongated cillyndrical structures present in many eukariotic cells, such as mammalian Sperm cells, human lung cells, or the unicellular algae Chlamydomonas (Fig. 1, left). Their fundamental role is motility, achieved by a periodic beat pattern. The internal structure of a cillia is composed of 9 microtubule dublets (MT's), which can bend; Dynein motors connecting the MT's, which consume ATP to shear them; and nexin connecting adjacent MT's, which constrain the shearing forces producing bending (Fig. 1, right).

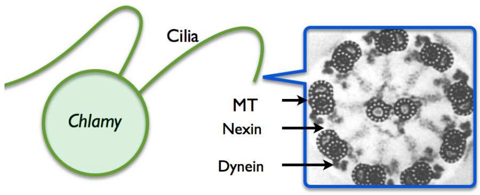

FIG. 1. **Left.** Schematic view of Chlamydomonas with two cilia. **Right.** Cross section of cilia with its main components.

The two main open questions which we address are: Can a minimal model based on these ingredients explain the beat pattern and swimming behaviour of cilia? And what is the mecano-chemical feedback to the motors which gives raise to the periodic beat? Ultimately, we would like to infer properties of the motors by comparing our theory to different experimental conditions.

II. MECHANICS AND HYDRODYNAMICS

Our cilia model is characterized by the free energy G, which accounts for elastic and active forces; and a simple fluid model, resistive force theory:

$$G=\int_0^L [\frac{\kappa_b}{2}C^2+f\Delta+\Lambda \mathbf{t}^2]\mathrm{ds} \;\Rightarrow\; [\mathbf{nn}\xi_\mathrm{n}+\mathbf{tt}\xi_\mathrm{t}]\cdot\partial_\mathrm{t}\mathbf{r}=\frac{\delta \mathrm{G}}{\delta \mathbf{r}}$$

In the free energy there is an elastic term characterized by κ_b and the curvature C, a tensile term with the Lagrange multiplier Λ, and a term with work performed by an internal force f in creating shear Δ (Fig. 2, left). This force itself has three components $f=f_m-\kappa_s\Delta-\xi_s\partial_t\Delta$. The first is the motor force, the second is the shearing elasticity κ_s, and the third the shear friction ξ_s (Fig. 2, right). These elastic forces are balanced by fluid friction forces proportional to the velocity $\partial_t\mathbf{r}$ through two friction coefficients: ξ_n in the normal direction $\mathbf{n}$, and ξ_t in the tangential direction $\mathbf{t}$.

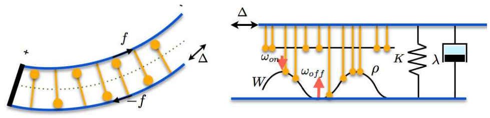

FIG. 2. .
Left. Schematic representation of a cilia, with opposing motors creatin a pair force f which generates a shear Δ. **Right.** Ratchet model of the molecular motors.

This model is compared with experiments performed by our group with Chlamydomonas. We describe the motor force as a plane wave, of which we take all parameters from experiments besides the amplitude, which we fit. With this description we are able to obtain the right swimming of the cilia: translational and rotational velocity, as well as path curvature.

III. SELF ORGANIZED CILIARY BEAT

In the previous model the oscillating motor force was provided ad-hoc, however it should emerge as a collective property of the interaction between motors and cilia. Several motor models are possible: motors could respond to normal forces, to stretching of their arms, to curvature, or to shear displacements. Here we use a ratchet model (Fig. 2, right), in which the localized detachment and attachment of motors in certain points of the cilia drives motor oscillations. The probability of bound motors evolves as:

$$\partial_t P(x)=-\partial_t\Delta\partial_x P+\omega_{on}(x)(1-P(x))-\omega_{off}(x)P(x)$$

As mentioned above, detailed balance violation $\omega_{off}(x)\neq\omega_{on}(x)e^{\Delta W(x)}$ (and thus ATP consumption) is necessary to drive the motors into an oscillatory regime. The elastic coupling of the motors through the ciliary structure coordinates the local motor oscillations, finally giving raise to a beat pattern.

Changing the parameters of the motors affects the beat pattern. Future work involves decoding properties of the dynein arms in cilia by comparing the beat patterns of several mutants to the beat patterns of the theoretical model when altering motor properties.

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