Rowers coupled hydrodynamically. Modeling possible mechanisms for the cooperation of cilia

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Abstract. We introduce a model system of stochastic entities, called *rowers* which include some essentials of the behavior of real cilia. We introduce and discuss the problem of symmetry breaking for these objects and its connection with the onset of macroscopic, directed flow in the fluid. We perform a mean field-like calculation showing that hydrodynamic interaction may provide for the symmetry breaking mechanism and the onset of fluid flow. Finally, we discuss the problem of the metachronal wave in a stochastic context through an analytical calculation based on a path integral representation of our model equation.

PACS. 05.65.+b Self-organized systems – 64.60.Cn Order-disorder transformations; statistical mechanics of model systems – 87.16.Ka Filaments, microtubules, their networks, and supramolecular assemblies

1 Introduction and overview

We set up a model system of entities, called *rowers*, that may organize spontaneously breaking left-right symmetry of the motion and give rise to an ordered macroscopic flow and beating patterns. Rowers are active, stochastic elements that "live" in a fluid with low Reynolds number and are capable to exert influence on each other by means of hydrodynamic coupling.

The motivation for this analysis comes from the motion of cilia, long and thin extroflections of the eucaryotic cell membrane that are able to generate motion [1,2]. The cilia are used by the cell for self-propulsion or to stir the surrounding fluid. A cilium has an internal structure (the axoneme) containing an arrangement of microtubule doublets attached to a basal body anchored to the cell membrane. A complex, symmetric net of protein bridges and links among the doublets gives the whole structure elastic properties. Biochemical reactions at the level of such proteins represent the energy source for the ciliary motion, a cyclic beating composed of two phases: the *effective stroke* – which is active in propulsion or in fluid transport – and the *recovery stroke*, which is passive. A ciliated cell generally has a field of hundreds of cilia which beat in a coordinated manner, setting up wave-like time dependent patterns. This phenomenon is referred to as *metachronism*.

In the framework of a purely mechanical description, the physics of ciliary motion involves the balance of hydrodynamic and elasticity; the forced nature of the system is modeled through the elastic constitutive equations, which contain the *engine* supplying energy in a deterministic way.

In this paper we adopt a stochastic approach to ciliary motion and its associated macroscopic fluid flux. We analyze some physical assumptions which are required as necessary conditions for the existence of a macroscopic net flow in the surrounding fluid and for the onset of coordination, or metachronism.

Our spirit is to approach the system from the point of view of Statistical Mechanics, looking at macroscopic effects and keeping as few as possible the number of relevant variables. As our model is designed to be studied as much as possible with analytical tools, we do not model in detail the internal features of the single object- the rower – which inherits from the real cilium the only peculiarity of undergoing a two-phase motion. We consider hydrodynamic interaction and energy supply, which is switched on and off at times controlled by a stochastic process, and possibly correlated to the configuration of the object.

We think that some of the questions pointed out in this study, may be of general interest – independently of the problem of ciliary motion – for the Statistical Mechanics in far from equilibrium systems.

Looking at the literature about cilia and flagella in a viscous fluid one realizes that such studies are mainly mechanics–oriented, the stochastic aspects of the phenomena being, in general, disregarded.

Early works on these subjects date since 1955 with the early model by Gray and Hancock (one cilium in a fluid) [3] and with the study by Machin (1963 – locally

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contractile flagellum) [4]. Later, mathematical models for simulating the motion of cilium (and flagellum) have been developed, we refer to the works by Brokaw *et al.* [5–9], (curvature controlled models) and by Murase *et al.* [10–13] (excitable dynein models and directional mechano-sensitivity of cilium as a possible mechanism for the onset of metachronal waves *via* hydrodynamic interaction [12]).

The description of metachronism, was addressed to model multicilia dynamical configurations in a suitable way to generate Stokes flow in the surrounding fluid (Liron *et al.* [14–16]); the problem of fluid transport was investigated for different geometries of fluid confinement [17–21]. In 1984 Liron in his work [22], based on the discrete cilia approach [20], described fluid transport by cilia, assuming metachronal coordination between ciliary moves (propagating wave) and periodicity conditions.

More recently, Gueron *et al.* proposed a model which accounts for multicilia hydrodynamical interactions [23–26] and energetics [27]. The dependence of the metachronal wave on observable ciliary parameters [28] – and the effect of varying fluid viscosity [29] have been studied by Priel *et al.* They also proposed a model involving hydrodynamically coupled oscillators [30–32].

In building up the model, we represent the system in terms of two-phase hydrodynamically coupled oscillators. The nonequilibrium drive (active motion) is realized as stochastic transitions between two internal states, acting together with Gaussian thermal fluctuations.

In this paper we are interested in focusing two crucial problems. The first is symmetry breaking.

If the internal (mechanical) engine which generates motion is removed the cilium is free of moving in a cone with cylindrical symmetry, O(2) in 3D with fixed basis. However, cilia and flagella are observed to perform planar motion. In the case of sea-urchin sperm cell flagella the plane of motion can be imposed by external perturbations [33].

The internal couple of microtubules in the axoneme may give an explanation to the breaking of the O(2) symmetry.

The problem whether, once moving in a plane, there is any preference for right or left-directed effective stroke is, to our knowledge, open. It is invaluable by purely anatomic reasons of the individual, that is, there is no *structural* symmetry breaking. Flagella, for example, are observed to beat symmetrically.

In *paramecia* this left right symmetry is broken in connection with an intrinsically oriented structure of the whole cell cortex (the so-called kineties), which is absent in ciliated epithelial cells [34].

Therefore real cilia need a symmetry-breaking mechanism to push the fluid in a directed way. This could be due to regulatory processes that establish a cortical anisotropy followed by the cilia. With our simplified model we show that hydrodynamic interactions in collective motions of rowers could be enough to realize this symmetry breaking. This situation is interesting from the point of view of statistical mechanics, because a local, a priori isotropic

release of energy is transformed in a self organized way in a macroscopically relevant collective state with a well-defined directionality (see also [35]).

The second problem is the physical source of metachronism. With our model we show that metachronism is not a wave phenomenon of the traditional kind, but, instead, a phenomenon of statistical nature. In fact, it can not be sustained by oscillations around the ground state of the system in thermodynamical equilibrium, but it is more understandable as a time-dependent pattern created by the counteracting active beating and dissipative processes.

In Section 2 we present the general features of the model. The elementary component is a rather abstract object (the rower). It includes a few observed features of real cilia, mainly the distinction between effective stroke and recovery stroke. Our rowers are one dimensional but not intrinsically oriented, that is, they have left-right symmetry. The observed two-phase beating is represented as the motion of a particle in two different potentials – active and passive – alternatively switched on and off by a two-state stochastic process. These potentials are analogues of states of a filament in which the collective action of the dyneins determines two different minimum energy curvatures.

In Section 3 we show how to compute averaged quantities for the single rower, of which the most interesting is the current that it generates as a function of the external velocity of the fluid.

We then use this result, together with known techniques of fluid mechanics, to compute the self-consistent velocity field in a low Reynolds number Stokes fluid with an array of rowers as velocity sources. This can be taken as a demonstration that cooperative effects arising from the hydrodynamic interaction may make our stochastic rowers spontaneously break symmetry and set up a macroscopic flux. This result is obtained in a mean-field like picture, and is independent of a more-refined investigation on the collective motion of rowers.

In the last section, we discuss the premises for the onset of metachronal waves, defined as spatio-temporal anisotropic ground states of the system. Pointed out the role of hydrodynamic interactions in models that include thermal noise, we proceed employing a path integral representation of our model equations to obtain information on the most probable history (path in the configurational space) and first excitations.

We analyze in more detail the case in which any feedback mechanism of position and internal state is avoided. The cyclic nature of ciliary motion (*i.e.* the fact that its intrinsic time scale is larger than relaxation times) is taken explicitly into account. We prove that the onset of metachronal waves is compatible with such a system, but it is frustrated by the presence of random solutions with the same statistical weight.

This means that, if there is no exchange of signals between cilia, (nether chemical nor mechanical) the onset of metachronism due to hydrodynamic interaction is not relevant. However, a nearest neighbor coupling between

the internal state of the rowers is enough to stabilize this wave-like solution.

We also argue that if the transition probabilities between states are coupled with the configuration of the rower – the coupling may be realized for example as a stochastic version of the "geometric switch" introduced by Gueron *et al.* [36] – the problem of metachronism becomes formally analogous to the problem of modulated phases in membranes with defects [37].

2 The rower

A rower is the elementary tile of our model, and is designed to contain some of the essentials of the cilium.

Our starting point is the observation that a single cilium beat pattern can be divided into two phases [2]. During the *effective stroke* it moves almost as a straight rod, transversally to the fluid, while during the *recovery stroke* it glides back softly, in a tangential motion. Thus the effective stroke is associated with high viscous load and actually propels the fluid, whereas the recovery stroke brings back the cilium to its equilibrium position minimizing the viscous resistance.

A rower is characterized by two degrees of freedom, a continuous one corresponding to its position (the cilium center of mass, for example), and a discrete one corresponding to its internal state. The rower is alternatively subject to two different potentials and viscous loads, with different hydrodynamical characterization. In state 1 (recovery stroke) the viscous coefficient is low and the particle "sees" a concave potential V_1, while in state 2 (effective stroke) the viscous coefficient is high and the potential V_2 looks like a mexican hat. The transitions between the two states are stochastic. The switching between two potentials makes our rower an active element, and is the analogue of the active component of the force in the mechanical models of the cilium. The two different viscous loads mimic the behavior of a slender body moving transversely or tangentially in the fluid.

We consider a one-dimensional rower, that is, the rower breaks rotational but not left-right symmetry. This is different from most models of ciliary activity found in the literature, which treat cilia as structurally asymmetric objects. In both states one has to take into account the external drive due to the velocity of the fluid. At one-body level, the velocity of the external fluid enters as a linear bias the active and passive potentials; with such a bias the left-right symmetry will be broken.

Making the additional hypothesis that we are in the overdamped regime (low Reynolds number) [38], we can use the following Langevin equation to describe the dynamics of each rower (see [39] for a similar equation in a different context)

$$\dot{x} = v - \frac{1}{\gamma_\sigma} \frac{\partial V_\sigma(x)}{\partial x} + \xi_\sigma \qquad (1)$$

where $\sigma(t)$ may take values in $\{-1, 1\}$ and is the stochastic process describing the switching between phases.

The simplest choice for this noise is a random telegraph process, with Poisson distributed jumps. Alternatively, one could allow the transitions between the two states to depend on the configuration of the rower. For example one could require the transition probability to increase at the two ends of the rowing oscillations, with a mechanism which is the analogue for our rower of the "geometric switch" introduced in [36].

We will stick for simplicity of exposition to the first case throughout this section and the next, as the results do not change in substance from the point of view of a "mean field"-like description. In Section 4 we will distinguish between the two mechanisms.

In equation (1) ξ_σ is a Gaussian white noise with zero average and correlation

$$\langle \xi_\sigma(t) \xi_\sigma(t') \rangle = \frac{2T}{\gamma_\sigma} \delta(t - t').$$

In the same equation v is the component of the surrounding fluid velocity along the direction of our one-dimensional rower.

In the dynamics described by equation (1) we have eliminated two "fast" modes with characteristic times $\tau_{+,\sigma} = \frac{m}{\gamma_\sigma}$, where m is the mass of the particle. Thus, we are left with the "slow" modes with relaxation times $\tau_{-,\sigma} \simeq \frac{\gamma_\sigma}{\kappa_\sigma}$, where κ_σ is the curvature of potential V_σ at its minimum(s). In order for the model to represent effectively the movement of a rower, the average time between two stochastic transitions must be greater than the characteristic times $\tau_{-,\sigma}$. This implies in the first place that the system has to be far from criticality (see [40]).

Of course our rowers overlook many details of the mechanism of contraction of real cilia. In the first place they are not filaments but "points". On the other hand we do not want to focus on the detailed modeling of real cilia but instead on the organization through hydrodynamic coupling, and they are designed to this aim. In fact, the statistical mechanics of an internally driven filament is quite a difficult subject (one object has infinitely many degrees of freedom), while our rowers turn out to be much milder.

## 3 Symmetry breaking and onset of macroscopic flux

3.1 Single rower

It is convenient to pass from equation 1 to the Fokker-Planck description, that deals with the distribution functions $P_\sigma(x, t)$ for the probability to find the rower with position x at time t in state σ. These distributions obey the equations

$$\begin{cases} \partial_t P_1(x,t) = -\partial_x J_1(x,t) - \omega_1 P_1(x,t) + \omega_2 P_2(x,t) \\ \partial_t P_2(x,t) = -\partial_x J_2(x,t) + \omega_1 P_1(x,t) - \omega_2 P_2(x,t) \end{cases}$$

$$(2)$$

with probability currents

$$J_\sigma = v P_\sigma - \frac{1}{\gamma_\sigma} \frac{\partial V_\sigma}{\partial x} P_\sigma - \frac{T}{\gamma_\sigma} \frac{\partial P_\sigma}{\partial x}$$
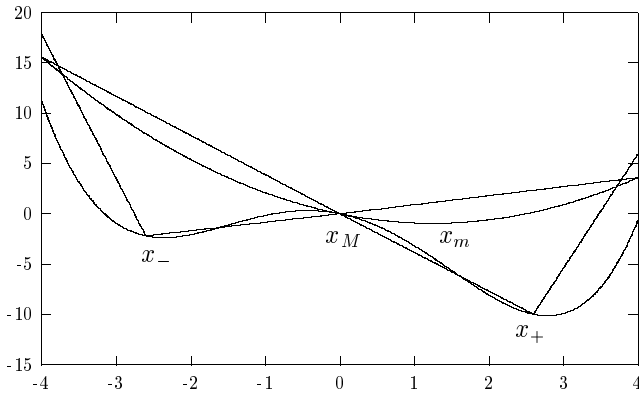
Fig. 1. Model potentials with incorporated external fluid velocity. For the passive phase $V_1(x) = \frac{a}{2}x^2 - vx$; for the active phase $V_2(x) = \frac{b}{4}x^2(x^2 - x_0^2) - vx$. Here rescaled parameters are plotted $a = 1.2; b = 0.8; x_0 = 3.7; v = 1.5; \gamma_1 = 1.0; \gamma_2 = 1.5$. Piece-wise linear potentials are also drawn. Realistic parameters are: $x_0 \sim 5\mu$m; $v \sim 10^{-5}$ to $10^{-4}\mu$m/s ; $\gamma_2 \simeq 1.5\gamma_1, \gamma_1 \sim 10^{-3}$N s/m; $a \sim 10^{-6}$ N/m.

where ω_σ is the probability of transition from the state labeled by σ to the other (these quantities would depend on x if one chooses a configuration-dependent case). Typical values for these quantities are around 60 s^{-1}.

The motion of the rower looks like an oscillation between the bottoms of the two potentials, and each phase of the cycle has a mean duration of $\tau_i = \omega_i^{-1}$.

Equations (1, 2) resemble formally those of a two-state thermal ratchet model (*e.g.* [39]). Actually, in our model the physical situation is quite different. In fact, if we consider the stationary Fokker-Planck equation for the sum of probability currents $J_{tot} = J_1 + J_2$, because of the absence of periodic boundary condition, $\partial_x J_{tot} = 0$ implies that J_{tot} is zero. That is, a global flow of probability is not possible: the rower can't just run away.

One should not worry about the fact that the overall net current is zero, because the two strokes of the rower produce much different perturbations in the surrounding fluid, thanks to the differences in viscosity. The problem becomes then if the two probability currents $J_i(x)$, which have opposite sign, are nonzero.

Let us compute the mean stationary value of the velocity during the effective stroke. We can write the average active current as

$$I \equiv I_2 = -I_1 \tag{3}$$

with

$$I_i = \int J_i(x)\mathrm{d}x.$$

With a little manipulation of equation (2) it is easy to obtain a third order differential equation for P_1 (or P_2) that, once solved, allows to compute explicitly the above averages. We have been able to solve analytically this equation by transfer matrix method in the case of piece-wise linear potentials (Fig. 1). For more general cases, typically that of a quadric V_1 and a quartic V_2 (Fig. 1), we have resorted
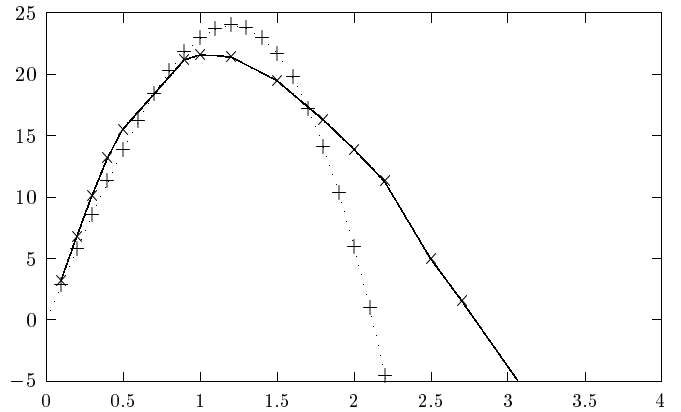
Fig. 2. Active current $I(v)$ as a function of the surrounding fluid velocity from calculation with the potentials of Figure 1 (points with dotted line for piece-wise linear potential).

to solve numerically equation (2) and look at its long-time behavior.

From simulations and calculations it's clear that, when $v = 0$, $I_1 = I_2 = 0$ and there is no biased pumping. For $v \neq 0$ instead the average currents are finite and sustain fluid flow. In Figure 2 we show the computed average active current $I(v)$ as a function of the surrounding fluid velocity; and it is nonzero for $v \neq 0$ – negative values for $I(v)$ are just an artifact, because by increasing v the minimum of V_1 passes the right minimum of V_2.

We now give a heuristic argument that, for low temperature and driving velocity, justifies this behavior. In these conditions, the process is well approximated by a sequence of jumps between the minimums of the two potentials. These jumps are unbiased as long as there is no driving velocity, since the left-right symmetry is not broken. The presence of the linear term induces a bias in the jump probability, so that from the minimum $x_m(v)$ of V_1 (Fig. 1) the rower has a probability of $1/2 + \pi(v)$ to fall into x_+ and $1/2 - \pi(v)$ to fall into x_-. Thus we can estimate the average current as $\frac{2\pi(v)}{p}$, where p is the period of the rowing cycle.

If we make the further assumption that in the recovery phase the probability distribution for the position of the rower relaxes to a Gaussian centered in $x_m(v)$, with width $\frac{T}{a}$, it is easy to see that

$$\frac{1}{2} + \pi(v) = \sqrt{\frac{T}{a}}\mathrm{erf}(x_m(v) - x_M(v))$$

which, substituting, gives the same qualitative behavior for the average current as that shown in Figure 2.

Thus, for nonzero external velocity field v, $I(v) \neq 0$, and the rower breaks left-right symmetry. In this situation, the average *excess* Stokes force exerted by the rower on the surrounding fluid, is

$$F_S = (\gamma_2 - \gamma_1)I(v)$$

and there is biased pumping of the fluid as long as the two viscosities are different. In the above expression, the

information on the transition times is contained in I. The dependence of the force on the fluid velocity is reminiscent of the *mechano-sensitivity* found by Murase in [12].

3.2 Array of rowers

In the case of a planar array of N interacting rowers beating in the same direction and arranged on a lattice (which can also be random), we have N equations that look like equation (1), but the surrounding fluid velocity term v has to be substituted by the contribution of all the other rowers through hydrodynamic interactions. That is, we have a sum of all the other particles velocities to which we apply the mobility matrix, which we take as $\bar{H}_{II} = \mathbf{1}$, $\bar{H}_{IJ} = \mathbf{H}(\mathbf{r}_{IJ})$, where $\mathbf{H}(\mathbf{r}) = \frac{1}{8\pi\eta r}(\mathbf{1} + \hat{\mathbf{r}}\hat{\mathbf{r}})$ is the Oseen tensor, which has a dependence on the inverse distance (see [41] p.68). Then we write (I and J label lattice sites and $\hat{\mathbf{d}}$ is the unit vector directed along the rower's motion):

$$\mathbf{v}_I = \sum_{J \neq I} \bar{H}_{IJ} \left[\left(-\frac{\partial V(\sigma_J, x_J)}{\partial x_J} + \xi_{\sigma_J} \right) \hat{\mathbf{d}} \right]$$

and the analogous of equation (1) is:

$$\dot{x}_I = \mathbf{v}_I \cdot \hat{\mathbf{d}} - \frac{1}{\gamma_{\sigma_I}} \left[\frac{\partial V(\sigma_I, x_I)}{\partial x_I} + \xi_{\sigma_I} \right]. \qquad (4)$$

The problem is hard to tackle analytically as is, because it is a selfconsistency problem in which the instantaneous configuration of the rowers affects the Stokes field, which in turn enters the equation of a single rower as the (local) velocity of the surrounding fluid. Nevertheless, a mean field calculation is fairly easy. That is, we examine if a macroscopically steady constant flow can be sustained by the beating rowers.

We can write (see [41]) the average velocity field in one point $\mathbf{R}$ of the surrounding fluid as

$$\mathbf{v}(\mathbf{R}) = \sum_J \bar{H}(\mathbf{R} - \mathbf{r}_J)\gamma(\sigma_J)(\mathbf{I}_{\sigma_J} - \mathbf{v}).$$

Which, averaged and projected along the direction of beating, taking into account the average force exerted by the single rower, gives the self-consistency relation for the constant fluid velocity

$$v_{\text{fluid}} = \frac{H^{\text{int}}(\gamma_2 - \gamma_1)}{1 + H^{\text{int}}(\gamma_2 + \gamma_1)} I(v_{\text{fluid}}).$$

The quantity H^{int} is a number that derives from the sum over the (finite) lattice sites of the Oseen propagators, and I is the average active current, as defined in equation (3). If H^{int} is big the equation becomes $v_{\text{fluid}} = \frac{\gamma_2 - \gamma_1}{\gamma_2 + \gamma_1} I(v_{\text{fluid}})$, whereas in the limit of small H^{int} we get $v_{\text{fluid}} = H^{\text{int}}(\gamma_2 - \gamma_1) I(v_{\text{fluid}})$. The value of H^{int} depends of course on the arrangement of the rowers on the lattice, and can be easily calculated. When the number of rowers is not finite problems may arise because of the $\frac{1}{r}$
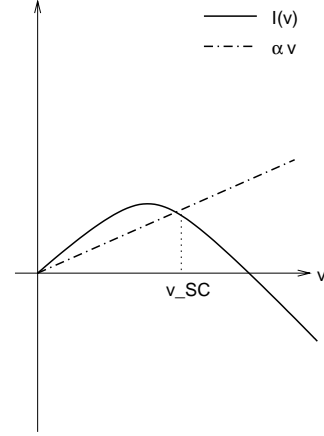
Fig. 3. Sketch of the selfconsistent velocity calculation $\alpha = \frac{1 + H^{\text{int}}(\gamma_2 + \gamma_1)}{H^{\text{int}}(\gamma_2 - \gamma_1)}$.

dependence of the Oseen tensor, but this situation is not realistic for systems of cilia. Following Landau [42], one could extend the sum over the penetration length of the hydrodynamic interaction, so that the constant will be a function of the surface density of rowers.

Then, the velocity field can be either zero, or take the (positive or negative) selfconsistent value $v_{SC} \neq 0$ (Fig. 3).

This means that the system of rowers is able to set up a macroscopic (and macroscopically steady) flow in the fluid. As this flow is selfconsistently maintained by the array of rowers, we can see this process as a spontaneous, dynamic symmetry breaking.

The question whether this symmetry breaking process could be relevant for real cilia is beyond the descriptive capabilities of the model. Nevertheless, we have established that ideal, minimal, cilia-like object as the rowers that are not intrinsically oriented, may achieve a directionality collectively.

4 Metachronal coordination

The mean field approach of the above paragraph prevents by construction the analysis of wave-like patterns in the beating of the rowers. It tells us that the fluid is pumped by the rowers but not if they pump it *coordinately*.

In this section we want to analyze the possible active role of hydrodynamic interaction not only in breaking left-right symmetry but also in creating patterns. Given that this interaction (alone) is able to generate directed fluid flux, we are now looking for the premises for spatial coordination. To escape from the mean field description we turn to a path integral representation of equation (4).

The entity of interest is the effective action for the configuration variables. It is from the minima and from the curvature of this action that we expect to get evidence about the existence of waves (patterns).

In our description we are considering the "ground" state of the system to undergo continuous changes driven

by the dynamics of the discrete field σ. Thus, in our model the metachronal wave cannot have the nature of a small oscillation around an equilibrium state but rather it is a far-from-equilibrium oscillatory pattern. This implies that standard techniques relying on conservation laws or symmetry breaking (see for example [44]) cannot be employed to find waves in the form of propagating modes. In this view, the assumption that the time scales of thermalization are fast compared to σ is very important in order to see any kind of oscillation.

In what follows we outline the calculation.

The reduced partition function to the configurational variables is

$$
Z(J_I(t)) = \left\langle \exp\left[\sum_I \int \mathrm{dt} J_I(t) x_I(t) \right] \right\rangle_{\xi,\sigma}.
$$

The two averaging steps involved are integration on thermal noise ξ and on the noise σ. Integration on thermal noise is straightforward (see [43]).

The second integration is a much more delicate step. First, σ is not only an additive noise, but it has a multiplicative role too, second σ has to be described on greater time scales than the thermalization times.

It is convenient to rewrite the mobility matrix as

$$
L_{IJ} = H_{IJ} + \eta \sigma_I \delta_{IJ}
$$

– where the dependence on σ has been isolated and H_{IJ} has the same off-diagonal terms as the Oseen tensor – and to approximate the inversion of L up to first order in η. We choose for simplicity to have the potentials $V_{\sigma,I} = \frac{1}{2}a(x_I - \sigma_I)^2$, so that the symmetry breaking is assumed and the two wells are quadratic with the same stiffness a. This choice allows us to analyze the existence problem of the metachronal wave using straightforward algebra. (Keeping into account more general potentials involves non-linearities which, however, do not affect space-time derivatives and consequently do not change our analysis about the metachronal wave.)

Integration on thermal noise is carried on with

$$
\langle \xi_I(t) \rangle = 0 \quad ; \quad \langle \xi_I(t)\xi_J(t') \rangle = L_{IJ}^{-1}\delta(t - t')
$$

and gives an effective dynamical action depending on the fields x and σ:

$$
S = \int \mathrm{dt}(\mathcal{L}_x + \mathcal{L}_{x,\sigma} + \mathcal{L}_\sigma)
$$

where $\mathcal{L}_x$ depends only on the configurations, $\mathcal{L}_\sigma$ involves the field σ, and $\mathcal{L}_{x,\sigma}$ is an interaction term.

We find

$$
\mathcal{L}_x = \sum_{I,J} x_I \left[H^{-1}\left(-\partial_t^2 + a^2 H^2\right)\right]_{IJ} x_J + 2a^2\eta \sum_I x_I
$$

$$
\mathcal{L}_\sigma = a^2 \sum_{I,J} \sigma_I H_{IJ}\sigma_J + \eta a^2 \sum_I \sigma_I
$$

$$
\mathcal{L}_{x,\sigma} = 2a \sum_I \sigma_I \left(\dot{x}_I + a\sum_J H_{IJ}x_J \right)
$$
$$
+ \eta \sum_I \sigma_I \left[a^2 x_I^2 - \sum_{PQ} H_{IP}^{-1}\dot{x}_P H_{PQ}^{-1}\dot{x}_Q \right].
$$

Let us now consider the integration in σ.

We proceed with M.S. technique and consider the functional measure for the integration in σ. The fact that such a noise has a cyclic nature cannot be ignored, so we write the measure in the form:

$$
\mathrm{d}\Sigma(\sigma) = [\mathrm{d}\sigma] \exp\left\{ -\frac{1}{2} \sum_{I,J}\int \mathrm{dt}\, \sigma_I(t)\, \Sigma(\partial_t)_{IJ}\sigma_J(t) \right\} \cdot \quad (5)
$$

We can observe that, in view of this expression and the above ones, the complete effective kernel for σ is

$$
a^2 H + \Sigma. \qquad (6)
$$

This quadratic form determines, through its lowest eigenvalue, the most probable configuration around which one can study the fluctuations. Assuming space-time translational invariance, the spectrum will depend on a wave-vector k and a frequency ω.

The question whether the hydrodynamic interaction can give rise to metachronism is then equivalent in this formalism to asking whether adding H to Σ can change the minimum eigenvalue of the quadratic form for the field σ, determining a ground state configuration corresponding to well defined wave-vector k^* and frequency ω^*, both different from zero, that will generate the metachronal wave.

As we do not have a microscopic theory for the internal engines of the rowers, we have some freedom to choose the probability measure in formula 5 Σ. The case we would like to investigate first is the one in which $\sigma_I(t)$ are spatially independent random variables. We will find that even in this case there are wave like solutions, but they are canceled out by the noise when averaging.

We take a Σ which is diagonal in space and has kernel which is *not* monotonically increasing in time. This last requirement is crucial. In fact, with a noise with a monotonically increasing kernel the system should be purely dissipative. It is easy to prove that the equation for the classical (most probable) field admits the null-path as unique solution, with fluctuations exponentially decreasing both in space and time. In the large time limit the probability distribution becomes

$$
P_{\mathrm{stat,hydr}} \sim \mathrm{e}^{-\frac{1}{2}\sum_J x_J^2}
$$

so that H_{IJ} does not intervene in any way in the stationary probability measure, but it may just modify the thermalization times. This means that if one models the energy release with a stochastic "white-like" process, the hydrodynamic interaction cannot have influence on the stationary configuration of the system, and cannot set up any spatial coordination.

Thus, we assume that Σ is *not* monotonically increasing and analyze this case.

Notice that what follows is independent of the specific choice of the operator Σ, for example one can write – as in the Brazovskii model [45] – $\Sigma = (C^2\,\partial_t^4 + D^2\,\partial_t^2 + B^2)$. With this kernel the most favored modulation in time is $\omega^* = |\frac{D}{\sqrt{2}C}|$ and it can be identified with the transition

frequency. The fact that this modulation may correspond to a zero–mode is not a problem with a bounded field.

We proceed summing over σ. Since in our case the zero–mode can not be resolved by exploiting symmetry, we must assume that the field $x_I(t)$ is limited in width. The results that we can easily obtain with this assumption are equivalent to the results of a different, more heavy but mathematically more careful analysis.

Thus, we look for the classical solution with field $x_I(t)$ – the most probable path and first excitation – of the form $\underline{x} = \underline{x}^0 + \eta \underline{x}^1 + \cdots$.

It is easy to verify that $\underline{x}^0$ e $\underline{x}^1$ are solutions of the equations (from hereafter we will take $a = 1$):

$$\sum_J \left[\left(-\partial_t^2 + H^2 \right) \frac{\Sigma}{H(H + \Sigma)} \right]_{IJ} x_J^0 = 0 \qquad (7)$$

and

$$\sum_K \left[\left(-\partial_t^2 + H^2 \right) \Sigma \right]_{IK} x_K^1 = \sum_J H_{IJ}$$
$$- \frac{1}{2} \sum_J (-\partial_t + H)_{IJ} \left[\left(x^0 \right)^2 + \left(H^{-1} \dot{x}^0 \right)^2 \right]_J - \cdots \quad (8)$$

Considering $\underline{x}^0$ first, the positivity of $(-\partial_t^2 + H^2)$ and the existence of H^{-1} imply (Eq. (7)) that $\underline{x}^0$ is a solution if $\Sigma \underline{x}^0 = 0$. This means that the properties of the internal state field σ are transferred to x trough functional integration, so that the classical path is random in space. Moreover, it describes a null velocity for the fluid environment (from the symmetry of H).

Consider now the first correction in η. As one can see by equation (8), $\underline{x}^1$ has a space-time source. Nevertheless, like for $\underline{x}^0$, there is no explicit dependence on spatial variables. It is relevant that, instead, $\underline{x}^1$ gives a non zero fluid velocity, that is: the rowers are idoneous to pump fluid, but again without coordination.

We shall now consider the fluctuations and limit our study to the quadratic part of the effective action. Our task is to analyze the paths which correspond to non-zero eigenvalues λ of the operator in equation (7) (which gives the solution $\underline{x}^0$).

The paths are $x_I(t) = \mathrm{e}^{\mathrm{i}\,(\omega t + kI)}$ with dispersion relation

$$\lambda = (\omega^2 + H(k)^2) \frac{\Sigma(\omega)}{H(k)[H(k) + \Sigma(\omega)]}. \qquad (9)$$

For each λ this relation gives a "band" of solutions with the same statistical weight. Together with the true waves – the *metachronal waves* – there is a solution of the same kind of $\underline{x}^0$, namely with spatial *randomness*. These solutions are obtained, for each λ, by considering the limit $k \to 0$ and recalling that H is essentially the inverse of the Laplacian – in fact, for $k \to 0$ the operator that we are considering reduces to $\Sigma(\omega)$.

This further level of analysis which includes fluctuations confirms the mean field result on the presence of an effective macroscopic pumping of the fluid by the rowers, as an effect which is first order in η. However, the hydrodynamic interaction is frustrated in sustaining the metachronal waves because for every metachronal mode there is a path, with the same probability, and the same random nature of the classical solution. Furthermore the metachronal waves are always depressed with respect to the classical solution.

In conclusion, without exchange of chemical information between rowers, the sole hydrodynamic interaction does not generate coordination. This is mainly due to the fact that, going back to equation (6), if Σ is diagonal in space, adding the term $H \sim 1/k^2$ does not determine a modification in the minimum eigenvalue of the spectrum giving rise to a well-defined mode.

The situation is different if the functional measure for the field σ contains a spatial interaction, which can be short ranged, between the internal states σ_I. For example, one could consider a nearest neighbor interaction with coupling constant α, giving rise to a Laplacian on the lattice. This does not affect the minimum around the homogeneous configuration in absence of hydrodynamic interaction.

However, in presence of H, the spectrum becomes

$$H + \Sigma \sim \frac{1}{k^2} + \alpha k^2 + \Sigma(\omega)$$

and there is a minimum for the particular value $|k^*|^4 = \frac{1}{\alpha}$ of the wave vector, together with the usual value ω^* for the frequency. Integrating on σ and looking for the eigenvalues of the effective quadratic form for x one is forced to keep this minimum energy "spatio-temporal mode" into account and obtains wave-like solutions with frequency ω^* and wave-vector k^*.

This solution can be called metachronal wave according to our definition. It is sustained by hydrodynamic interaction, but it needs a preexisting short ranged interaction between the internal states of the rowers to be formed. This preexisting interaction is unable by itself to set up a mode.

The physical interpretation for this short ranged coupling could be that one cilium can feel the depletion in ATP concentration due to the activity of nearby cilia of the same cell.

In order to obtain metachronism one can also consider an alternative scenario in which the σ is dynamically related to the configuration. This scenario includes as a special case the stochastic analogous of the "geometric switch" mechanism found in [36] and [27], in which the transitions between the active and passive phases of the cilium are determined by its reaching some limit configurations.

If we include a dependence on the configuration in the dynamical equation for the field σ, so that the quantities ω_i in equation (2) become necessarily functions of the space coordinate of the rower. The results of Sections 2 and 3 do not change. On the contrary, the functional integral study undergoes a dramatic change. Time modulation of σ noise need not be required *ab initio*. In this case there are two interacting fields, $x_I(t)$ and $\sigma_I(t)$, the functional integral is well defined and a correct perturbative analysis can be carried on. The scenario is formally

equivalent to the one for modulated phases in membranes with defects [37]. Dealing with quadratic potentials, for example, it is possible to integrate out the continuous configurational degrees of freedom – as in [46] – obtaining an effective model for the field σ.

5 Conclusions

We introduced a model system, the rower, which contains some essentials of the cilium and, being economic in degrees of freedom, enables to deal with stochastic features of this system.

We computed the probability current of one rower interacting with a surrounding fluid in a steady state, and we used the result to deal with the problem of left-right symmetry breaking of this entity.

The same expression of the current was then used in a self-consistent mean field-like calculation for a planar array of rowers coupled hydrodynamically. The result was that rowers can cooperate to set up a macroscopic flow in the fluid.

Finally, we presented the problem of metachronal coordination in terms of correlation between rowers, and discussed a path-integral calculation that enables to point out some features that are sufficient for the model to exhibit this behavior.

This kind of calculation can be a useful tool in general for systems driven far from equilibrium by a stochastic process that switches the Hamiltonian locally.

The indications that come from the last two calculations are that

- 1) For our rowers the metachronal wave is not necessary to set up a macroscopic flow in the surrounding fluid. This is supported by a mean field like analysis and confirmed when we include fluctuation.
- 2) Without any direct interaction between rowers the hydrodynamic interaction generates metachronal waves which are frustrated by the presence of random fluctuations of the same statistical weight, together with the random dominant solution.
- 3) A short ranged coupling of internal states (that could have for example chemical origin), unable by itself to set up a mode, can stabilize the wave and make the pattern formation statistically relevant.
- 4) Alternatively, provided that the only interaction between rowers is hydrodynamic, a sufficient condition for the onset of a metachronal wave is the presence of a coupling between position and transition frequency of the single rower.

These results are qualitative theoretical predictions. They have a definite interest from the point of view of the model, but they need to be examined in greater detail to fully understand their implications for the real system.

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