Modeling the locomotion of the African trypanosome using multi-particle collision dynamics

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Abstract. The African trypanosome is a single flagellated micro-organism that causes the deadly sleeping sickness in humans and animals. We study the locomotion of a model trypanosome by modeling the spindle-shaped cell body using an elastic network of vertices with additional bending rigidity. The flagellum firmly attached to the model cell body is either straight or helical. A bending wave propagates along the flagellum and pushes the trypanosome forward in its viscous environment, which we simulate with the method of multi-particle collision dynamics. The relaxation dynamics of the model cell body due to a static bending wave reveals the sperm number from elastohydrodynamics as the relevant parameter. Characteristic cell body conformations for the helically attached flagellum resemble experimental observations. We show that the swimming velocity scales as the root of the angular frequency of the bending wave reminiscent of predictions for an actuated slender rod attached to a large viscous load. The swimming velocity for one geometry collapses on a single master curve when plotted versus the sperm number. The helically attached flagellum leads to a helical swimming path and a rotation of the model trypanosome about its long axis as observed in experiments. The simulated swimming velocity agrees with the experimental value.

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1. Introduction

Nature is very inventive in creating strategies for micro-organisms to move in their highly viscous fluid environment [1]. A prominent example is the *Escherichia coli* bacterium that swims with the help of a rotating bundle of helical filaments called flagella, each driven by rotary motor [2]. Sperm cells use a bending wave that propagates along the flagellum from the head to the tail and pushes the sperm cell forward [3]. The alga *Chlamydomonas reinhardtii* possesses two of these flagella and performs a breast stroke to propel itself [4]. Since micro-organisms move at low Reynolds number, they immediately come to a halt when they stop their swimming stroke [5]. Their inertia does not play any role. Instead, they have to go through periodic shape changes, like the bending wave passing through a sperm cell, and use anisotropic or time-varying friction with the viscous fluid to propel themselves [6]. Simple swimming strategies at low Reynolds number have been suggested, such as the two-hinged Purcell swimmer [5], the three-sphere swimmer [7] or the constant-torque swimmer [8]. More detailed fluid dynamics studies of theoretical models for micro-organisms started in the early 1950s with Taylor’s work on sperm cells [9]. The numerous investigations in the existing literature include work on the squirmer [10–14], the spiroplasma bacterium [15, 16] and an artificial microswimmer with a superparamagnetic flagellum [17, 18]. In this paper, we present a detailed modeling of the micro-organism African trypanosome using the simulation method of multi-particle collision dynamics (MPCD). Our goal is to contribute to the understanding of its locomotion strategy.

1.1. The African trypanosome

The African trypanosome causes a deadly disease called sleeping sickness in both humans and animals [19]. It mainly goes through two stages in its life cycle. During the first stage, it reproduces in the midgut of its carrier, the tsetse fly. After a bite from the tsetse fly, trypanosomes are transmitted into the bloodstream of the host. Once the micro-organisms cross the mammals’ blood–brain barrier, the disease shows its heavy symptoms.
The trypanosome has an elongated cell body to which a single flagellum is firmly attached. Therefore, the beating flagellum causes characteristic distortions of the cell body during locomotion [20]. Experiments have shown that the trypanosome evades attack from antibodies of the infected mammal using the flow fields it creates during swimming [21]. When cultivated on the surface of semisolid agarose, swimming trypanosomes form and move cooperatively within colonies [22]. Depending on their size and speed, they can also be separated from red blood cells using microfluidic devices [23]. All these examples show that motility is an important property of the African trypanosome. Since motility helps the micro-organism to survive in the mammalian host, it is crucial to understand all facets of the trypanosome’s motility, including the way the flagellum is attached to the cell body and the flagellar beating pattern.

In this work, we model the blood form of the African trypanosome in order to study its locomotion in an unbounded Newtonian fluid. The African trypanosome is about 25 µm long, has a relatively thick posterior end with a diameter of about 3 µm and a very thin anterior end so that its shape is similar to a spindle [19]. The flagellum emanates from the cell body close to the posterior end and runs along the long axis toward the anterior end. It has the classical 9 + 2 microtubule axoneme architecture [19, 20]. Historically, it was thought that the flagellum wraps around the cell body in a left-handed helical fashion and a wave propagating through the flagellum from the thin anterior to the thick posterior end pushes the cell body forward [19]. A recent work proposed that helical waves of alternating chiralities run along the flagellum producing kinks [24].

In this paper, we show that simple bending waves running along the flagellum are sufficient for understanding the locomotion of a trypanosome. In particular, by assuming a helical attachment of the flagellum, the cell body rotates about its long axis in agreement with most recent experiments [25]. We study in detail the cell body conformation during locomotion, the swimming velocity and the helical swimming trajectory of our model trypanosome. We also show that the sperm number, a characteristic dimensionless number used in elastohydrodynamics, determines the locomotion of the model trypanosome [6, 18, 26–29].

We concentrate here on the ballistic motion initiated by a few beat cycles. On long times, the trypanosome follows a random walk characterized by two relaxation times [30]. The short time belongs to a decorrelation of the periodic flagellar beating due to internal noise, which we do not include in our model. The second relaxation time is due to rotational diffusion of the whole cell body and beyond our simulation time.

1.2. Multi-particle collision dynamics (MPCD)

A variety of methods have been proposed to simulate flow fields in a Newtonian fluid created, for example, by moving bodies. The method of mobilities treats the fluid implicitly and describes hydrodynamic interactions between moving particles (see, for example, [31]). The method of MPCD solves the Navier–Stokes equations using fictitious or coarse-grained fluid particles that obey an artificial dynamics that locally conserves momentum [32–36]. Thermal fluctuations are inherent to this technique. We use here a version that employs an Anderson thermostat and where the angular momentum of the fluid particles is also conserved [32, 37–39]. The original variant of MPCD invented by Malevanets and Kapral is called stochastic rotation dynamics [33–36]. With both variants of MPCD, a variety of problems has been studied such as the dynamics of fluid vesicles under shear flow [40–42], the dynamics of squirmers [13, 43],
thermal diffusion of a semi-flexible sheet \cite{44} and swimming sperm cells both in two \cite{45} and
three \cite{46} dimensions, just to name a few. Finally, Reid \textit{et al} \cite{47} investigated the flow field
around two-dimensional (2D) fish-like shapes with the help of MPCD. The stiff shapes were
approximated by polygons with the aim to make them deformable in future work.

This paper is organized as follows. In section 2, we introduce our model trypanosome and
review how we simulate its locomotion using the method of MPCD. Section 3 presents our
results and we conclude in section 4.

2. Model

We first explain in section 2.1 how we model the spindle-shaped cell body of the African
trypanosome using an elastic network of vertices connected by springs and an additional
bending rigidity along the long axis of the cell body. We introduce two model trypanosomes
with either a straight or a helically attached flagellum along which an actuating bending
wave propagates. Section 2.2 explains the method of MPCD and how we couple the model
trypanosome to the MPCD fluid of coarse-grained fluid particles. Finally, in section 2.3 we map
the units of the MPCD method to physical units.

2.1. Modeling the African trypanosome

We explain with the help of figure 1 how the spindle-shaped cell body is made up of vertices.
We create 20 circles and place them along the long axis of the cell body. We index each circle
by \( i \) starting from the thicker posterior end (\( i = 0 \)) up to the thinner anterior end (\( i = 19 \)) and
choose the radius of circle \( i \) as

\[
S(i) = (i + 0.15)^4 \exp(-0.006(i + 0.15)^2), \quad 0 \leq i \leq 19,
\]

where \( S(i) \) is given in the unit length of our simulation method to be defined below. Through
this choice, the model cell body attains the characteristic shape of the trypanosome as illustrated
in figure 1 with an average radius \( r_c = 0.8 \). We define each circle by ten vertices with an angular
distance of \( \pi/5 \). We connect adjacent vertices on the circle (bond BC in the blow-up of figure 1)
and from neighboring circles (bond BC) by Hookean springs with the spring potential

\[
U_s = \frac{1}{2} \kappa_s (l - l_0)^2.
\]

Here \( \kappa_s \) is the spring constant, \( l \) the actual distance of two vertices and \( l_0 \) the equilibrium length
of the springs. For each pair of vertices it is chosen according to the equilibrium shape of the
cell body in figure 1. In particular, the lengths of all the bonds AB in figure 1 are chosen as
\( l_0 = 1 \). This procedure defines the cell body as an elastic network of vertices and ensures its
integrity during the simulations. Diagonal springs connecting two vertices across a circle (see,
for example, bond BD in the blow-up of figure 1) stabilize the cylindrical shape of the cell body
by preventing it from collapsing towards a completely flat shape. In order to keep the cell body
stable, relatively stiff springs are used with spring constant \( \kappa_s = 10^7 \) throughout our simulations,
meaning that the variation in length is less than 10%.

In reality, the cell body of an African trypanosome is defined by a cortex of microtubules,
stiff biopolymers, that run along the long axis of the cell body \cite{19}. They are connected to
each other by proteins and thereby give the cell body an overall bending rigidity. We model this
situation by applying a bending potential to each of the ten lines of vertices running from the posterior to the anterior end (see figure 1):

$$U_b = \frac{1}{2} \kappa_b (\cos \theta_0 - \cos \theta)^2. $$

Here $\theta$ is the angle between two tangent or bond vectors $t_i$ and $t_{i+1}$ as shown in figure 1, $\theta_0$ is its equilibrium value adjusted to the equilibrium shape in figure 1, and $\kappa_b$ is the bending stiffness. The bending energy prevents the 20 cross-sectional circles of the model trypanosome from sliding against each other and thereby prevents crumbling of the cell body. Not all microtubules of the real cell body reach the thin anterior end and the cell body becomes more flexible toward the thinner part. To mimic this property in our model, we progressively reduce the bending stiffness by a factor of 0.95 along the line of vertices starting from the center toward the anterior end. So the bending stiffness at the anterior end becomes $(0.95)^{10} \kappa_b = 0.6 \kappa_b$. Choosing a smaller factor destabilizes the model cell body. In the simulations, both the anterior and the posterior end are closed by hemispheres that are not visible in any of the figures in this paper.

The next question we have to address in modeling the trypanosome is how to attach a flagellum to the cell body that is heavily debated in the literature [24, 25]. We consider two cases. The first is a straight flagellum that starts from the posterior end and extends all the way to the anterior end along the long axis of the cell body. In figure 2(a), the blue line indicates

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**Figure 1.** A snapshot of the model African trypanosome at the start of the simulation. The blow-up of the initial two circles from the posterior end shows how springs connect different vertices of the cell body. For further explanations, see the main text. The black dots define a line of vertices along the long axis of the cell body to which we apply a bending potential. The blow-up shows the tangent or bond vectors $t_i$ and $t_{i+1}$ which connect neighboring vertices and enclose an angle $\theta$.
Figure 2. The model African trypanosome with (a) a straight flagellum and (b) a helical flagellum indicated by the blue line.

the straight flagellum. In the following, we call this case the straight flagellum model. The old literature always indicated a helical attachment of the flagellum [19]. A recent experimental investigation confirms such an attachment and provides evidence for the following realistic model [25] illustrated in figure 2(b). The flagellum runs straight from the posterior end to the center of the cell body and then winds around the cell body by an angle of $\pi$. We refer to this case as the helical flagellum model. Note that since the flagellum is defined by vertices from the model cell body, the flagellum is always firmly attached to the cell body. Through both the straight and helically attached flagellum, we let a planar bending wave pass from the thin anterior to the thick posterior end. Following [45], we use the bending potential

$$U_w = \frac{1}{2} \kappa_w [t_{i+1} - R(l_i \alpha) t_i]^2, \quad \text{with } \alpha = B \sin(k d_i + \omega t).$$

(4)

Here $\kappa_w$ is again some bending stiffness with respect to a bent reference state. To introduce this state, we rotate one tangent or bond vector of the flagellum, $t_i$, against the neighboring bond vector $t_{i+1}$ using the rotation matrix $R(l_i \alpha)$, where $l_i = |t_i|$ is the bond length. The matrix $R(l_i \alpha)$ rotates $t_i$ by an angle $l_i \alpha$ about the local normal of the cell body. The rotation angle $\alpha$ varies like a propagating sine wave along the flagellum, where $d_i$ is the distance from the posterior end of the flagellum to its vertex $i$. The amplitude $B$ is always kept as 1 in all the simulations reported in this paper. Further characteristics of the wave are the wave number $k = \frac{2\pi}{\lambda}$, where $\lambda$ is the wavelength for which we always choose $2L/3$ in relation to the length $L$ of the cell body. We also have the angular frequency $\omega$ and time $t$ is measured in the time unit of the MPCD method as defined in section 2.2. For both the straight and the helically attached flagellum, $\kappa_w = 10^4$ in all the simulation results reported in this paper.

For the helical flagellum model, we choose the bending rigidity for the vertex lines in equation (3) as $\kappa_b = 1.8 \times 10^5$ in most of the simulation runs unless otherwise stated. For the straight flagellum model, $\kappa_b = 3 \times 10^4$ for all the results reported in this paper. We had to increase the bending stiffness of the helical flagellum model; otherwise the cell body became unstable. Experiments measured the average end-to-end distance of an active trypanosome during directed motion, which amounts to 60% of the contour length of the cell body (varying between 40 and 80%), while during tumbling motion the average end-to-end distance is 40% (varying between 20 and 60%) [48]. In this study, we adjusted the bending stiffness of the model cell body to come as close as possible to the experimental value and obtained an average distance of 77% during swimming (varying between 69 and 85%) as discussed in section 3.2.2. When the bending stiffness was further reduced, the model trypanosome became unstable. The real length to thickness ratio of the African trypanosome is about 25 $\mu$m/3 $\mu$m $\sim 8$ [19, 21, 23, 24], while in our modeling we always keep this value at approximately 7.4 in all our simulations, thus trying to mimic the geometry of the African trypanosome as close as possible. High-resolution electron microscopy reveals a short protrusion of the flagellum beyond the anterior end of the
cell body [19, 24]. In our model trypanosome, we do not incorporate this part of the cell body since it is extremely difficult to keep it stable during the simulations.

Forces from the spring and bending potentials acting on the vertices determine the dynamics of the cell body. For each vertex with mass \( m = 1 \) (in MPCD units introduced below) we perform a molecular dynamics (MD) step. We update its position and velocity using the velocity Verlet algorithm [49] where \( \delta t_{\text{MD}} \) is the integration time step:

\[
\mathbf{r}_i(t + \delta t_{\text{MD}}) = \mathbf{r}_i(t) + \delta t_{\text{MD}} \mathbf{v}_i(t) + \frac{1}{2} \delta t_{\text{MD}}^2 \frac{\mathbf{F}_i(t)}{m},
\]

\[
\mathbf{v}_i(t + \delta t_{\text{MD}}) = \mathbf{v}_i(t) + \frac{1}{2} \delta t_{\text{MD}} \left( \frac{\mathbf{F}_i(t) + \mathbf{F}_i(t + \delta t_{\text{MD}})}{m} \right).
\]

Here, \( \mathbf{r}_i \) and \( \mathbf{v}_i \) are the respective position and velocity of the \( i \)th vertex of the cell body and the force \( \mathbf{F}_i = -\nabla_i (U_s + U_b + U_w) \) acts on this vertex. To perform the gradient \( \nabla_i \) of the sum of the spring, bending and bending wave energies, \( U_s + U_b + U_w \), with respect to \( \mathbf{r}_i \), the energies are discretized in the position variables \( \mathbf{r}_i \). In all our simulations, we had to choose the integration time step very small, \( \delta t_{\text{MD}} = 10^{-4} \), to keep the model cell body stable. To test the model, we performed MD simulations without coupling the cell body to a viscous fluid. As expected, the total energy was conserved and the total force and torque on the cell body was zero. The latter condition should, of course, be satisfied by any low-Reynolds-number swimmer.

2.2. The method of MPCD

The swimming trypanosome induces flow fields in its viscous fluid environment and thereby experiences frictional forces. We determine these flow fields using the method of MPCD. It introduces coarse-grained or fictitious fluid particles that obey an artificial dynamics through a succession of streaming and collision steps. Since during the collision step momentum is conserved, the MPCD method is equivalent to solving the Navier–Stokes equations [33, 34]. At low Reynolds number, where one has to solve Stokes equations, MPCD is a quick simulation technique and relatively easy to implement, which also includes thermal fluctuations [32–34].

The simulation starts with point particles distributed randomly in a 3D simulation box of linear dimension \( L_{\text{box}} \) using periodic boundary conditions. To reduce the time for equilibrating the MPCD fluid, we already assign to each of the fluid particles a velocity from a 3D Gaussian distribution with variance \( 3k_B T/m \), where \( k_B \) is the Boltzmann constant, \( T \) is the temperature and \( m \) is the mass of the fluid particle. In MPCD units, we set thermal energy \( k_B T = 1 \) and \( m = 1 \).

We now explain how streaming and collision steps are performed in the MPCD method. In the streaming step, the fluid particles move ballistically during a small time interval \( \delta t \):

\[
\mathbf{r}_i(t + \delta t) = \mathbf{r}_i(t) + \delta t \mathbf{v}_i(t).
\]

Here \( \mathbf{r}_i(t) \) and \( \mathbf{r}_i(t + \delta t) \) are the respective positions of the particle \( i \) before and after the streaming step and \( \mathbf{v}_i(t) \) is its velocity. Before we perform the streaming step, we go through a number of MD steps of the cell body, where this number is given by \( \delta t / \delta t_{\text{MD}} \). During one MD step or one streaming step, some fluid particles might enter the cell body. In both cases, we shift these particles to the surface of the cell body, give them the velocity of the nearest vertex of the cell body and move them with half the respective time steps \( \delta t_{\text{MD}} \) or \( \delta t \). The works in [50–52] showed that this procedure gives the same result as if one would identify the exact time of

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collision between the fluid particles and the cell body. We repeat the procedure until all the fluid particles are placed outside the cell body. To conserve momentum, we add up all the momentum changes of the displaced fluid particles and equally distribute the resulting momentum on all vertices of the cell body. This procedure together with the collision step described in the next paragraph implements the no-slip boundary condition with an accuracy of about 5%. Finally, we mention that in the simulations we always chose $\delta t \leq 0.01$ in MPCD units.

In the collision step, which here includes also the vertices of the cell body, we divide the simulation box into cells of edge length $a = 1$, so $a$ defines the MPCD unit length. We follow a procedure known from the Anderson thermostat of a conventional MD simulation to assign each fluid particle in the cell a new velocity after the collision, which becomes the particle velocity at time $t + \delta t$ [32]. We calculate the center-of-mass velocity of each cell, $\mathbf{V}(t)$, and then give each particle in the cell a random relative velocity $\mathbf{v}_{i,\text{ran}}$ from a Gaussian distribution with variance $3k_B T / m$:

$$
\mathbf{v}_i(t + \delta t) = \mathbf{V}(t) + \mathbf{v}_{i,\text{ran}} - \sum_{\text{cell}} \mathbf{v}_{i,\text{ran}} / N_c + \left\{ m \mathbf{\Pi}^{-1} \sum_{j \in \text{cell}} \left[ \mathbf{r}_{j,c} \times (\mathbf{v}_j - \mathbf{v}_{j,\text{ran}}) \right] \times \mathbf{r}_{i,c} \right\}. 
$$

(7)

$\mathbf{\Pi}$ is the moment of inertia tensor of the particles in the cell and $\mathbf{r}_{i,c} = \mathbf{r}_i - \mathbf{R}_c$ is the relative position of particle $i$ with respect to $\mathbf{R}_c$, which is the center-of-mass position of all particles in the cell. The third term on the right-hand side of equation (7) is added to conserve the center of mass velocity or momentum during collision in the cell. The last term in equation (8) implements angular momentum conservation. Since the trypanosome also rotates in space, this term is important to avoid unphysical behavior. We add a few remarks. Firstly, using the Anderson thermostat is also convenient since it keeps the temperature constant by definition. Secondly, during one streaming step fluid particles stay mostly within the cell as our $\delta t \ll 1$. Therefore, artificial correlations develop between the particles within one cell, which we avoid by a random shift of the cells before each collision step as was proposed in [53, 54]. Thirdly, in our simulations we measure time in units of $a \sqrt{m / k_B T}$, the characteristic MPCD time.

In our simulations, we always chose $\rho_0 = 10$ particles per cell. For a simulation box size of $L_{\text{box}} = 60$ this means that we simulate 2.2 million fluid particles per simulation. The MPCD method provides analytic expressions for the viscosity which are reproduced in the simulations when the number of particles in a cell is above five [32, 40]. The kinematic viscosity has contributions from the streaming ($\eta_s = 0.64 \delta t$) and collision ($\eta_c = 0.036 / \delta t$) steps. The total viscosity in MPCD units then amounts to $\eta = \eta_s + \eta_c$. Reducing $\delta t$ increases the viscosity of the solvent but also increases the total simulation time as more MPCD time steps have to be performed. We chose $\delta t$ as small as possible keeping the simulation time at a reasonable value between 2 and 6 weeks.

2.3. Comparison with physical units

We now connect our simulations in MPCD units to the real trypanosome system. The length $L$ of the African trypanosome in our simulations in units of the cell size $a$ is 18.9. Compared to the typical length of an African trypanosome, which is about 25 $\mu$m, the cell size in real units is $a \approx 1.32$ $\mu$m. The density of the MPCD fluid should be the density of water, meaning $\rho_w = \rho_0 m / a^3 = 1000$ kg m$^{-3}$, where $\rho_0 = 10$ in our simulations [50]. This gives the mass of the fictitious fluid particles in physical units as $m = 3 \times 10^{-16}$ kg. As the trypanosomes are studied at room temperature $T \sim 300$ K, we can calculate the MPCD unit for time in physical
units as $t_\varepsilon = a \sqrt{m/k_B T} = 3 \times 10^{-4}$ s. Using the expressions for the streaming and collision contributions to the kinematic viscosity in MPCD units from the previous paragraph, we can calculate the kinematic viscosity in real units as

$$\eta = \left[ 0.64\delta t + 0.036 \frac{1}{\delta t} \right] a^2 t_\varepsilon.$$

For $\delta t = 0.01$ used in most of our approximations, the collision contribution determines the viscosity and we obtain $\eta \approx 6 \times 10^{-3} \text{ m}^2 \text{s}^{-1}$, which is about a factor of 16 smaller than the kinematic viscosity of water. When we use typical swimming velocities from our simulations and the length of the trypanosome, we arrive at $Re \approx 10^{-2}$, which is still in the regime of low Reynolds numbers.

3. Results and discussion

In section 3.1, we apply a static bending wave to the flagellum and study the relaxation of the model trypanosome towards its equilibrium configuration. This helps us to identify the so-called sperm number as the relevant dimensionless parameter. In section 3.2, we investigate in detail the locomotion of the model trypanosome including the mean-square displacement (MSD), cell body conformations during swimming, swimming velocities and swimming trajectories. Finally, section 3.3 compares some of our findings with experimental results on real trypanosomes.

3.1. Relaxation dynamics of the model trypanosome

Before we let a bending wave propagate through the flagellum of the model trypanosome, we first apply a static bending wave meaning $\omega = 0$ in equation (4). This helps us to tune our parameters so that the properties of the model trypanosome are close to experimental observations. Secondly, we also obtain a characteristic time scale as discussed in the following. We start with the straight model trypanosome of length $L$ and the helically attached flagellum. We investigate how the cell body relaxes to a bent equilibrium configuration under the static bending wave by monitoring its end-to-end distance $\ell$ with time. In the inset of figure 2, we plot the relative end-to-end distance $\epsilon = \ell / L$ versus time for several bending stiffnesses $A = 10\kappa_b$ of the cell body. The factor 10 comes from the ten lines of vertices along the body axis for which we defined the bending potential in equation (3). Clearly, the equilibrium end-to-end distance increases with $A$ since the cell body resists more and more the static bending wave applied through the bending potential $U_w$ of equation (4) with constant $\kappa_w$. A closer inspection of $\epsilon(t)$ reveals a fast relaxation that is identical for all values of $A$. We can attribute it to the relaxation of the elastic springs (connecting the vertices) to some quasi-equilibrium value. A second, slower relaxation describes the bend deformation of the whole cell body. We observe that both relaxation processes are exponential in time. For the slow bend relaxation we plot the relaxation time $t_0$ versus the cell body stiffness $A$. Interestingly, $t_0$ is proportional to $A^{-1}$ as the fitted solid line shows. In the following, we briefly explain this behavior. During time $t_0$, the cell body relaxes toward the static bending wave. Now, if the frequency $\omega$ of the propagating bending wave is much smaller than $1/t_0$, the cell body always has time to relax toward the momentary bending wave and the cell body goes through a sequence of quasi-equilibrium conformations.

To understand the relation $t_0 \propto A^{-1}$, let us approximate the cell body by a rigid rod of length $L$, average cell body radius $r_c$ and bending stiffness $A$. When such a cylinder moves in a
Figure 3. Relaxation of the model trypanosome with the helically attached flagellum from the straight shape to a conformation with a static bending wave. The graph shows the relaxation time $t_0$ versus the inverse of the bending stiffness $A = 10k_b$ of the cell body. Symbols are simulation results with a viscosity $3.6$ in MPCD units. The solid line is a fit to $0.85 \times \xi_\bot L^4/A$. The inset shows the relaxation of the reduced end-to-end distance $\epsilon$ as a function of time for different bending stiffnesses $A$. The solid lines are exponential fits to the slower relaxation.

Newtonian viscous fluid at low Reynolds number, a small displacement $h$ perpendicular to the rod axis obeys the hyperdiffusion equation [6, 26, 27]

$$\xi_\bot \frac{\partial h}{\partial t} = -A \frac{\partial^4 h}{\partial x^4},$$

where according to resistive-force theory $\xi_\bot = \frac{4\pi \eta L}{\ln(L/(2r_c))}$ is the perpendicular friction coefficient per unit length [6]. From equation (9), one can calculate the relaxation of a bent rod towards its straight configuration or of the straight rod toward a configuration with, for example, a static bending wave. In both cases the characteristic relaxation time has to scale as $t_0 \sim \xi_\bot L^4/A$ [6, 28], which confirms the observed behavior of $t_0$ in figure 3.

Now, rescaling time with the actuating frequency $\omega$ of the rod and length by $L$, the hyperdiffusion equation (9) contains only one parameter called the sperm number, which determines the dynamics of our model cell body [6, 18, 27–29],

$$S_p = \frac{L}{l_h} = \left(\frac{\xi_\bot \omega L^4}{A}\right)^{1/4},$$

where $l_h = (A/\xi_\bot \omega)^{1/4}$ is the hydrodynamic penetration length of elastohydrodynamics. The sperm number compares frictional forces to the bending strength of the cell body. In addition,
in our case, the behavior of the cell body is strongly determined by the actuating bending wave. If we use the fit to the relaxation time $t_0$ versus $A^{-1}$ in figure 3, $t_0 \approx 0.85 \times \xi_{\perp} L^4 / A$, we can rewrite the sperm number as

$$S_p = (\omega t_0 / 0.85)^{1/4} = 1.04(\omega t_0)^{1/4}.$$  \hspace{1cm} (11)

So $S_p$ directly compares the actuation frequency $\omega$ to the relaxation time $t_0$ and $S_p < 1$ means that the cell body goes through a sequence of quasi-equilibrium conformations.

3.2. Locomotion of the model trypanosome

We now let a bending wave with nonzero angular frequency propagate along the flagellum from the thin anterior to the thick posterior end using the bending wave potential of equation (4). Since the flagellum is attached to the cell body, the whole cell undulates, which ultimately pushes the model trypanosome forward against the direction of the propagating wave, similar to a sperm cell. The model trypanosome moves ballistically through the fluid; however, rotational diffusion will randomly change its direction of motion. The supplementary data includes movies of the swimming model trypanosome for both the cases, the helically attached and the straight flagellum. For clarity, we have removed all the fluid particles. One clearly recognizes the sinusoidal bending wave passing through the flagellum (blue line) from the anterior to the posterior end. The cell body has to react to the beating flagellum and goes through a sequence of complex swimming conformations of the cell body. In both cases, the model trypanosome swims with the anterior end in the front. In the helical flagellum model, we observe a corkscrew-like motion along a left-handed helical trajectory. We now discuss the locomotion of the model trypanosome in detail.

3.2.1. Mean-square displacement. In figure 4, we plot the MSD of the center of mass position for the helical flagellum model

$$\langle R^2 \rangle = (\mathbf{r}_{cm}(t) - \mathbf{r}_{cm}(0))^2$$  \hspace{1cm} (12)

as a function of time for both a passive cell body ($\kappa_w = 0$) and the actively swimming model trypanosome ($\kappa_w > 0$). The passive cell body (squares) performs a nearly ballistic motion due to the ballistic MD steps and then at $t \approx 1$ passes over to a purely diffusive motion with $\langle R^2 \rangle \propto t$ as expected. The swimming model trypanosome does hardly move until $t \approx 10$ when the bending wave has propagated just one wavelength along the cell body. Then the ballistic swimming begins, indicated by $\langle R^2 \rangle \propto t^2$ in figure 4. Note that rotational diffusion of the whole cell body occurs on the characteristic time scale $\tau = D_r^{-1} = 10^4$, where $D_r$ is the rotational diffusion coefficient of the cell body to be given below. Since $\tau$ is larger than the simulation time it does not influence the ballistic motion in figure 4.

From the diffusion of the passive cell body in figure 4, we extract a diffusion coefficient according to $D = \langle R^2 \rangle / (6t)$. We now approximate the cell body as a cylinder of length $L$ and radius $r_c$, which has an average translational diffusion coefficient of $D = k_B T \ln(L / (2r_c)) / (3\pi \eta L)$ \cite{55}. Together with $L = 18.9$ and viscosity $\eta = 3.6$, we obtain $r_c \sim 0.8\alpha$, which is in excellent agreement with the average radius of the cell body in our simulations.

1 See supplementary movie 1 (available from stacks.iop.org/NJP/14/085012/mmedia).
2 See supplementary movie 2 (available from stacks.iop.org/NJP/14/085012/mmedia).
3.2.2. Conformations during swimming. In figure 5, we plot the end-to-end distance for the helical flagellum model when the flagellum performs one complete beating cycle. We note that the attachment of the flagellum is straight from the thick posterior end to the middle of the cell body and then makes a half turn to the left going toward the thin anterior end. The bending wave along the flagellum has a wavelength of $2L/3$. At $t = 21$ it tries to rotate the center of the cell body to the left and both ends to the right; in particular at the anterior end the rotation is against the sense of winding of the flagellum. This straightens the cell body as much as possible and $\epsilon(t)$ assumes its maximum value. At $t = 58$, after two-fifth of the cycle, the flagellum-induced rotation of the cell body at the anterior end goes with the left-handed turn of the flagellum, while the center rotates in the opposite direction. This twisting causes the cell body to buckle in the center and very strongly at the tip, which reduces the end-to-end distance to its minimum value. At $t = 78$ or after three-fifth of the cycle a local maximum of $\epsilon(t)$ occurs, followed by a local minimum at $t = 88$. The local minimum appears since the flagellum, tries to twist the cell body against the winding direction of the helically attached flagellum. Finally, at $t = 121$ the flagellum assumes its initial conformation. We note that some of the conformations illustrated in figure 5 show a striking resemblance to some of the micrographs of the African trypanosome in [24, 25].

In section 3.1, we argued that the sperm number defined in equations (10) or (11) indicates a quasi-static dynamics of the model trypanosome when $S_p < 1$. We have tested this statement with different parameter sets. In figure 6(a), we plot the end-to-end distance of the cell
Figure 5. The relative end-to-end distance $\epsilon$ versus time for one beating cycle of the flagellum with $\omega = 2\pi/100$. The helical flagellum model is considered with $\eta = 3.6$. Characteristic conformations of the cell body at the extrema of $\epsilon(t)$ are shown.

Figure 6. The relative end-to-end distance plotted against normalized time $\omega t$. (a) For $\eta = 3.6$ and different sperm numbers $S_p$; (b) at $\omega = 2\pi/10$ for $\eta = 3.6$ (solid line) where $S_p \approx 0.9$ and $\eta = 9$ (dashed line), where $S_p \approx 1.1$. Inset: the same viscosities but $\omega = 2\pi/100$ meaning $S_p = 0.5$ and $S_p = 0.6$, respectively.

body during swimming as a function of time for different $S_p$, which we changed by varying $\omega$. When normalizing time by the actuation frequency $\omega$, all curves have the same period. For $S_p = 0.5$ and 0.9, both curves $\epsilon(t)$ are indistinguishable from each other, indicating the
Figure 7. Velocity of the swimming model trypanosome versus frequency $\omega$ of the actuating bending wave for two different viscosities. The solid line has a slope of 1/2.

quasi-static regime. Already at $S_p = 0.9$, the amplitude of $\epsilon(t)$ decreases, which becomes even more pronounced for $S_p > 1$. So, the cell body can no longer relax to its equilibrium conformations. In figure 6(b), we keep $\omega = 2\pi/10$ constant but vary viscosity from $\eta = 3.6$ (solid line, $S_p \approx 0.9$) to $\eta = 9$ (dashed line, $S_p \approx 1.1$). Again, we see the transition from the quasi-static to the dynamic regime. In the inset of figure 6(b) we decrease frequency to $\omega = 2\pi/100$. Now, for both frequencies clearly $S_p < 1$ and the quasi-static regime is again realized.

3.2.3. Swimming velocity. From our studies on the MSD of the model trypanosome with the helical flagellum, we extract the swimming velocity as $v_{cell} = \sqrt{\langle R^2 \rangle} / t$. To clarify the importance of diffusion relative to ballistic motion, we introduce the Peclet number $Pe = v_{cell} a / D$, where $D$ is the diffusion coefficient of the passive cell body [51]. All our studies were conducted at $Pe = 4 – 65$. So thermal fluctuations at times smaller than the rotational correlation time $\tau$ (introduced earlier) are not important as is the case for most microorganisms.

In figure 7, we plot the swimming velocity versus frequency $\omega$ for two different viscosities $\eta$. We observe that the velocity increases approximately as $\omega^{1/2}$. Interestingly, this coincides with a result of Lauga, who studied locomotion in the regime around $S_p = 1$ using an undulating elastic filament [28]. When the cell body attached to the filament dominates hydrodynamic friction, he determined the swimming velocity $v_{cell}$ by simple scaling arguments, rescaling all lengths by the hydrodynamic penetration length $l_h$ introduced in equation (10) [28]. We give $v_{cell}$ here in terms of our relevant parameters,

$$v_{cell} \sim \frac{A}{\eta} \oint_0^L \frac{\partial h}{\partial x} \frac{\partial^4 h}{\partial x^4} dx \sim (A \omega \eta^{-1})^{1/2} \sim \omega S_p^{-2}. \quad (13)$$

In our case, the whole cell body of the trypanosome resists motion with a large friction coefficient which agrees with Lauga’s assumptions. Generally, the swimming velocity increases with $\omega$ since the bending wave traveling against the swimming direction generates a larger thrust.
force through friction with the surrounding fluid. As expected, the swimming velocity in figure 7 goes down with increasing viscosity since viscous drag forces on the cell body act against its propulsion.

In figure 8, we plot the swimming velocity of the model trypanosome versus sperm number \( S_p \) for both the helical and straight flagellum models. Two values for the viscosities are used. To vary the sperm number \( S_p \), we varied frequency \( \omega \). From equation (13) and \( S_p \propto \omega^{1/4} \), we then expect \( v_{\text{cell}} \propto S_p^2 \) which is roughly confirmed by the figure. Equation (13) suggests to plot the reduced velocity \( v_{\text{cell}}/(L\omega) \) versus \( S_p \). As expected the data set for the two different viscosities collapse onto one master curve that behaves like \( S_p^{-2} \). Only beyond the quasi-static regime at \( S_p > 1 \), deviations occur. Of course, the data set for the straight and the helical flagellum model collapse on different master curves since they describe different realizations of the model trypanosomes. In particular, they differ in the mean end-to-end distance of the cell body, which is 0.71 for the the straight flagellum and 0.76 for the helical flagellum.

### 3.2.4. Swimming trajectories

In figure 9, we plot the trajectories of the posterior end of the cell body with a straight (a) or a helical (b) flagellum. In the first case, the trajectory is more or less straight. In addition, we recognize a back and forth movement due to the bending wave propagating along the flagellum. In the second case, for the helically attached flagellum, the back and forth movement is also visible but now the trajectory has a helical shape. Due to the helical attachment of the flagellum, the whole cell body rotates about its long axis and, in addition, moves on a helical path. This has recently been observed in experiments [25]. In figure 9(b) we also observe that the direction of the helical axis changes
with time. We attribute this rather small but visible effect to the rotational diffusion of the whole cell body. If we approximate again the cell body by a cylinder of length \( L \) and radius \( r_c \), its rotational diffusion coefficient becomes \( D_r = \frac{3k_B T \ln[L/(2r_c)]}{\pi \eta L^3} \) \([55]\). In MPCD units we obtain \( D_r = 10^{-4} \). For the total simulation time \( 10^3 \), we calculate the mean-square angular displacement \( \langle \theta^2 \rangle = 4D_r t = 0.4 \) or a variation of the helix direction by about 34\(^\circ\), which qualitatively fits to figure 9(b).

Superimposed on the helical trajectory in figure 9(b) are small undulations due to the bending wave passing through the flagellum. When we average them out, we obtain the helix shown by the thick blue line. Also the center of mass exhibits helical motion, which we now want to study further. For two positions of the center of mass, \( \mathbf{r}_i \) and \( \mathbf{r}_{i+1} \), we can define unit tangent vectors to the helical path, \( \hat{\mathbf{t}}_i = (\mathbf{r}_{i+1} - \mathbf{r}_i)/|\mathbf{r}_{i+1} - \mathbf{r}_i| \). In addition, we also calculate the unit normal vector \( \hat{\mathbf{n}}_i = (\hat{\mathbf{t}}_{i+1} - \hat{\mathbf{t}}_i)/|\hat{\mathbf{t}}_{i+1} - \hat{\mathbf{t}}_i| \). For an ideal helix one can derive the following relations:

\[
\hat{\mathbf{n}}_{i+1} \cdot \hat{\mathbf{n}}_i = \cos(\Delta \theta_h) \quad \text{with} \quad \Delta \theta_h = k_h \Delta s,
\]

(14)

\[
\hat{\mathbf{n}}_{i+1} \cdot \hat{\mathbf{t}}_i = -k_h R \sin(\Delta \theta_h),
\]

(15)

where \( k_h = 2\pi/\ell \), \( \ell \) is the arc length of one full helical turn, and \( R \) is the helix radius. We also introduce the angular displacement \( \Delta \theta \) along the helical path which we sum over time. An average gives the mean angular coordinate \( \langle \theta_h(t) \rangle \). We plot it as a function of time in the inset of figure 10(a). As expected it grows linearly in time due to the ballistic motion of the cell body. We extract the angular velocity \( \Omega_h = \langle \theta_h(t) \rangle / t \), with which the center of mass circles about the helix axis, and we plot \( \Omega_h \) in figure 10(a) against the sperm number \( S_p \). Both, the swimming velocity \( v_{cell} \) and the angular velocity \( \Omega_h \), are generated by the traveling bending wave, where the nonzero \( \Omega_h \) is due to the helical attachment of the flagellum. We expect the angular velocity to scale as the swimming velocity like \( \omega^{1/2} \). This scaling is not really obvious in figure 10(a) due to statistical errors in determining small rotational frequencies. However, when we plot \( v_{cell} \) against \( \Omega_h \) in figure 10(b), the linear relationship becomes visible.

In figure 11, we plot \( \omega/\Omega_h \) against the sperm number \( S_p \). The ratio \( \omega/\Omega_h \) gives the number of beat cycles of the flagellum necessary for the cell body to perform a complete rotation by 360\(^\circ\). This ratio was observed in experiments as we discuss below. Since \( \Omega_h \) should scale as \( \omega^{1/2} \), we expect \( \omega/\Omega_h \) also to scale as \( \omega^{1/2} \) or as \( S_p^2 \), which is approximately confirmed by the solid line in figure 11.
Figure 10. (a) Angular velocity $\Omega_h$ versus the sperm number $S_p$ for two viscosities $\eta = 3.6$ (●) and $\eta = 9$ (■). The inset shows the mean angular displacement $\langle \theta_h(t) \rangle$ versus time. The slope gives $\Omega_h$. (b) Velocity of the cell body $v_{\text{cell}}$ plotted against $\Omega_h$ for the same viscosities as in (a). The straight line indicates the expected linear relationship between $v_{\text{cell}}$ and $\Omega_h$.

Figure 11. The number of beat cycles of the flagellum in a $2\pi$ rotation of the cell body is plotted as function of the sperm number for two different viscosities given in MPCD units 3.6 (●) and 9 (■).

Finally, we add a comment about the radius and pitch of the helical trajectory in figure 9(b). We did not investigate these parameters in detail. Certainly, the radius of the helical path depends on the ‘degree of chirality’ of the model trypanosome which can be tuned by the helical attachment of the flagellum. As a result, the beat pattern of the whole trypanosome is three-dimensional compared to the straight flagellum model where it is strictly in a plane. We expect the radius to be influenced by how strongly the cell body is deformed during one beat.
cycle. In the quasi-stationary state at $S_p < 1$, the radius does not depend on $S_p$ as the cell body deformations go through the same sequence independent of $S_p$. When $S_p$ is larger than one, the cell body cannot fully relax towards the equilibrium shape and variations in the cell body deformation decrease as indicated by the end-to-end distance in figure 5. Therefore, the radius of the helical path should also decrease with growing $S_p$. On the other hand, the pitch is directly proportional to the swimming speed of the trypanosome along the axis of the helical trajectory. The dependence of $v_{\text{cell}}$ on $S_p$ is illustrated in figure 8.

3.3. Comparison with experimental results

We now compare our findings to measurements on real trypanosomes to see if our modeling can reproduce them. A real trypanosome swims in water with a velocity of $v_{\text{cell}} \approx 5 \pm 2 \, \mu m$ [24]. In figure 7, we find swimming velocities of $v_{\text{cell}} \approx 0.01$ for the viscosity $\eta = 3.6$. Using the velocity unit $a/t_s = 4.4 \times 10^{-3} \, m \, s^{-1}$ following section 2.3, this gives a real velocity of $44 \, \mu m \, s^{-1}$. Since $\eta = 3.6$ corresponds to a viscosity a factor of 16 smaller than the viscosity of water (see section 2.3), we have to scale down our simulated velocity by this factor and thereby obtain excellent agreement with the experimental value.

Recent experiments measured the helical trajectory of the trypanosome [25], which we can compare to our simulation results. For example, we can determine the diameter of the simulated helical trajectory using equations (14) and (15). For $S_p < 1$ and in physical units, we obtain for the anterior and posterior ends diameters of about 8 and 4 $\mu m$, respectively. This again fits nicely to the experimental diameter of 6.6 $\mu m$ for the flagellar tip [25]. However, the number of flagellar beat cycles for a full rotation of the cell body is with the smallest simulated value of 20 still a factor of 2.5 above the measured ratio of 8 [25]. This difference is not relevant for swimming in an unbounded fluid. However, it might play a role when the trypanosome swims in a crowded environment such as blood. Experiments have already demonstrated that an African trypanosome swimming through an array of pillars has a propulsion speed enhanced by at least a factor of four [23, 25]. As already mentioned in the introduction, trypanosomes evade attack from the antibodies of the host organism using flow fields they create during swimming [21]. The flow field obtained from our modeling and reported in [8] qualitatively agrees with these experiments.

4. Conclusions

In this paper, we have successfully modeled the African trypanosome as an elastic network of vertices connected by springs with additional bending rigidity along the long axis. Propagating a bending wave along the helically attached or straight flagellum, the spindle-shaped model micro-organism moves through a viscous fluid which we simulated using the method of MPCD. The relaxation dynamics under the influence of a static bending wave reveals the sperm number $S_p$ as an essential parameter for characterizing the dynamics of the model trypanosome. The sperm number is familiar from the elastohydrodynamics of a long slender rod and compares frictional to bending forces. Also the diffusion of the passive cell body can be modeled by a cylinder with a radius that agrees with the average radius of our model cell body.

Our results suggest that the locomotion of the African trypanosome occurs in a regime around $S_p = 1$ or even in the quasi-static regime ($S_p < 1$), where it moves through a sequence of equilibrium configurations. During swimming our model trypanosome with the
helically attached flagellum assumes characteristic, partially twisted and buckled conformations reminiscent of observations of real trypanosomes [24, 25]. The swimming velocity scales as the square root of the angular frequency of the flagellar bending wave, again similar to what one expects for an actuated elastic filament attached to a load with a large friction coefficient [28]. Plotting the reduced swimming velocity for different solvent viscosities against $S_p$, they all fall on the same master curve and confirm the importance of the sperm number. The swimming trajectories of the helical flagellum model reveal, as expected, helical trajectories. Their radii are in agreement with recent experiments [25]. Whereas the rotational velocity about the cell body’s long axis is too small by a factor of 2.5., the swimming velocities in physical units agree with the velocities of real trypanosomes in a pure viscous fluid.

Altogether, we have constructed a model trypanosome which provides a very good understanding of the locomotion of the real African trypanosome. We are now able to study the behavior of the trypanosome in more realistic situations: in a microchannel mimicking a blood vessel, in a fluid with obstacles mimicking viscoelastic blood and ultimately under pressure-driven blood flow. Recent experiments on African trypanosomes swimming through regular arrays of obstacles show a pronounced increase in swimming velocity when the distance of the obstacles is appropriately tuned [23, 25]. The trypanosomes use the obstacles to push themselves forward. This works well only when the swimming distance of one beat cycle is adjusted to the distance of the obstacles. We can implement this situation in our model and check the observations. Hence, our model is able to suggest an appropriate design for experiments and thereby contributes to an understanding of the locomotion of the African trypanosome in realistic environments.

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References

[1] Bray D 2001 Cell Movements: From Molecules to Motility (New York: Garland)
[2] Berg H C 2004 E. coli in Motion (New York: Springer)
[3] Camalet S and Julicher F 2000 Generic aspects of axonemal beating New J. Phys. 2 24
[4] Drescher K, Goldstein R E, Michel N, Polin M and Tuval I 2010 Direct measurement of the flow field around swimming microorganisms Phys. Rev. Lett. 105 168101
[5] Purcell E M 1977 Life at low Reynolds number Am. J. Phys. 45 3
[6] Lauga E and Powers T R 2009 The hydrodynamics of swimming microorganisms Rep. Prog. Phys. 72 096601
[7] Najafi A and Golestanian R 2004 Simple swimmer at low Reynolds number: three linked spheres Phys. Rev. E 69 062901
[8] Babu S B, Schmeltzer C and Stark H 2012 Swimming at low Reynolds number: from sheets to African trypanosome Nature-Inspired Fluid Mechanics, NNFM 119 25
[9] Taylor G 1951 Analysis of the swimming of microscopic organisms Proc. R. Soc. A 209 447
[10] Lighthill M J 1952 On the squirming motion of nearly spherical deformable bodies through liquids at very small Reynolds numbers Commun. Pure Appl. Math. 5 109
[11] Blake J R 1971 A spherical envelope approach to ciliary propulsion J. Fluid Mech. 46 199

New Journal of Physics 14 (2012) 085012 (http://www.njp.org/)
[12] Ishikawa T 2009 Suspension biomechanics of swimming microbes J. R. Soc. Interface 6 815
[13] Downton M T and Stark H 2009 Simulation of a model microswimmer J. Phys.: Condens. Matter 21 204101
[14] Thutupalli S, Seemann R and Herminghaus S 2011 New J. Phys. 13 073021
[15] Wada H and Netz R R 2009 Hydrodynamics of helical-shaped bacterial motility Phys. Rev. E 80 021921
[16] Wada H and Netz R R 2007 Model for self-propulsive helical filaments: kink-pair propagation Phys. Rev. Lett. 99 108102
[17] Dreyfus R, Baudry J, Roper M L, Fermigier M, Stone H A and Bibette J 2005 Microscopic artificial swimmers Nature 437 862
[18] Gauger E M and Stark H 2006 Numerical study of a microscopic artificial swimmer Phys. Rev. E 74 021907
[19] Ralston K S, Kabututu Z P, Melehani J H, Oberholzer M and Hill K L 2009 The Trypanosoma brucei flagellum: moving parasites in new directions Annu. Rev. Microbiol. 63 335
[20] Broadhead R et al 2006 Flagellar motility is required for the viability of the bloodstream trypanosome Nature 440 224
[21] Engstler M, Pfohl T, Herminghaus S, Boshart M, Wiegertjes G, Heddergott N and Overath P 2007 Hydrodynamic flow-mediated protein sorting on the cell surface of trypanosomes Cell 131 505
[22] Oberholzer M, Lopez M A, McLelland B T and Hill K L 2010 Social motility in African trypanosomes PLoS Pathog. 6 e1000739
[23] Holm S H, Beech J P, Barrett M P and Tegenfeldt J O 2011 Separation of parasites from human blood using deterministic lateral displacement Lab Chip 11 1326
[24] Rodriguez J A et al 2009 Propulsion of African trypanosomes is driven by bibehiral waves with alternating chirality separated by kinks Proc. Natl Acad. Sci. USA 106 19322
[25] Heddergott N, Krüger T, Babu S B, Wei A, Stellamans E, Uppaluri S, Pfohl T, Stark H and Engstler M 2012 Trypanosome motion represents an adaptation to the crowded environment of the vertebrate bloodstream PLoS Pathog. submitted
[26] Machin K E 1958 Wave propagation along flagella J. Exp. Biol. 35 796
[27] Wiggins C H and Goldstein R E 1998 Flexible and propulsive dynamics of elastica at low Reynolds number Phys. Rev. Lett. 80 3879
[28] Lauga E 2007 Floppy swimming: viscous locomotion of actuated elastica Phys. Rev. E 75 041916
[29] Gauger E M, Downton M T and Stark H 2009 Fluid transport at low Reynolds number with magnetically actuated artificial cilia Eur. Phys. J. E 28 231
[30] Zaburdaev V, Uppaluri S, Pfohl T, Engstler M, Friedrich R and Stark H 2011 Langevin dynamics deciphers the motility pattern of swimming parasites Phys. Rev. Lett. 106 208103
[31] Reddig S and Stark H 2011 Cross-streamline migration of a semiflexible polymer in a pressure driven flow J. Chem. Phys. 135 165101
[32] Gompper G, Ihle T, Kroll D M and Winkler R G 2009 Multi-particle collision dynamics: a particle-based mesoscale simulation approach to the hydrodynamics of complex fluids Adv. Polym. Sci. 221 1
[33] Malevanets A and Kapral R 1999 Mesoscopic model for solvent dynamics J. Chem. Phys. 110 8605
[34] Malevanets A and Kapral R 2000 Solute molecular dynamics in a mesoscale solvent J. Chem. Phys. 112 7260
[35] Malevanets A and Yeomans J M 2000 Dynamics of short polymer chains in solution Europhys. Lett. 52 231
[36] Kapral R 2008 Multiparticle collision dynamics: simulation of complex systems on mesoscales Adv. Chem. Phys. 140 89
[37] Noguchi H, Kikuchi N and Gompper G 2007 Particle-based mesoscale hydrodynamic techniques Europhys. Lett. 78 10005
[38] Götze I O, Noguchi H and Gompper G 2007 Relevance of angular momentum conservation in mesoscale hydrodynamics simulations Phys. Rev. E 76 046705
[39] Noguchi H and Gompper G 2008 Transport coefficients of off-lattice mesoscale-hydrodynamics simulation techniques Phys. Rev. E 78 016706
[40] Noguchi H and Gompper G 2005 Dynamics of fluid vesicles in shear flow: effect of membrane viscosity and thermal fluctuations Phys. Rev. E 72 011901

New Journal of Physics 14 (2012) 085012 (http://www.njp.org/)
[41] Noguchi H and Gompper G 2005 Shape transitions of fluid vesicles and red blood cells in capillary flows Proc. Natl Acad. Sci. USA 102 14159
[42] Noguchi H and Gompper G 2004 Fluid vesicles with viscous membranes in shear flow Phys. Rev. Lett. 93 258102
[43] Götze I O and Gompper G 2010 Mesoscale simulations of hydrodynamic squirmer interactions Phys. Rev. E 82 041921
[44] Babu S B and Stark H 2011 Dynamics of semi-flexible tethered sheets Eur. Phys. J. E 34 136
[45] Yang Y, Elgeti J and Gompper G 2008 Cooperation of sperm in two dimensions: synchronization, attraction and aggregation through hydrodynamic interactions Phys. Rev. E 78 066103
[46] Elgeti J, Kaupp U B and Gompper G 2010 Hydrodynamics of sperm cells near surfaces J. Biophys. 99 1018
[47] Reid D A P, Hildenbrandt H, Padding J T and Hemelrijk C K 2012 Fluid dynamics of moving fish in a two-dimensional multiparticle collision dynamics model Phys. Rev. E 85 021901
[48] Uppaluri S, Nagler J, Stellamanns E, Heddergott N, Herminghaus S, Engstler M and Pfohl T 2011 Impact of microscopic motility on the swimming behavior of parasites: straighter trypanosomes are more directional PLoS Comput. Biol. 7 e1002058
[49] Allen M P and Tildesley D J 1991 Computer Simulation of Liquids (Oxford: Clarendon)
[50] Padding J T and Louis A A 2008 Interplay between hydrodynamic and Brownian fluctuations in sedimenting colloidal suspensions Phys. Rev. E 77 011402
[51] Padding J T and Louis A A 2006 Hydrodynamic interactions and Brownian forces in colloidal suspensions: coarse-graining over time and length scales Phys. Rev. E 74 031402
[52] Padding J T, Wysocki A, Lowen H and Louis A A 2005 Stick boundary conditions and rotational velocity auto-correlation functions for colloidal particles in a coarse-grained representation of the solvent J. Phys.: Condens. Matter 17 S3393
[53] Ihle T and Kroll D M 2001 Stochastic rotation dynamics: a Galilean-invariant mesoscopic model for fluid flow Phys. Rev. E 63 020201
[54] Ihle T and Kroll D M 2003 Stochastic rotation dynamics. I. Formalism, Galilean invariance, and Green–Kubo relations Phys. Rev. E 67 066705
[55] Dhont J K G 1996 An Introduction to Dynamics of Colloids (Amsterdam: Elsevier)