Doing more with less: the flagellar end piece enhances the propulsive effectiveness of spermatozoa

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Abstract

Spermatozoa self-propel by propagating bending waves along an active elastic flagellum. The structure in the distal flagellum is likely incapable of actively bending, and as such is largely neglected. Through elastohydrodynamic modeling we show that an inactive distal region confers a significant propulsive advantage when compared with a fully active flagellum of the same length. The optimal inactive length, typically 2–5% (but up to 37% in extremes), depends on both wavenumber and viscous-elastic ratio. Potential implications in evolutionary biology and clinical assessment are discussed.
Spermatozoa, alongside their crucial role in sexual reproduction, are a principal motivating example of inertialess propulsion in the very low Reynolds number regime. The time-irreversible motion required for effective motility is achieved through the propagation of bending waves along the eukaryotic axoneme, which forms the active elastic internal core of the slender flagellum. While sperm morphology varies significantly between species [1–6], there are clear conserved features which can be seen in humans, most mammals, and also our evolutionary ancestors [7]. In gross structural terms, sperm comprise (i) the head, which contains the genetic cargo; (ii) the midpiece of the flagellum, typically a few microns in length, containing the ATP-generating mitochondria; (iii) the principal piece of the flagellum, typically 40–50 µm in length (although much longer in some species [8]), the core of which is a “9+2” axoneme, producing and propagating active bending waves through dynein-ATPase activity [9]; and (iv) the end piece, typically a few microns in length, which consists of singleton microtubules only [10]. Lacking the predominant “9+2” axonemal structure it appears unlikely that the end piece is a site of molecular motor activity. Since the end piece is unactuated, we will refer to it as ‘inactive’, noting however that this does not mean it is necessarily ineffective. Correspondingly, the actuated principal piece will be referred to as ‘active’. A detailed review of human sperm morphology can be found in [11, 12].

While the end piece can be observed through transmission electron and atomic force microscopy [2, 13], live imaging to determine its role in propelling the cell is currently challenging. Furthermore, because the end piece has been considered to not have a role in propelling the cell, it has received relatively little attention. However, we know that waveform has a significant impact on propulsive effectiveness, and moreover changes to the waveform have an important role in enabling cells to penetrate the highly viscous cervical mucus encountered in internal fertilization [14]. This leads us to ask: does the presence of a mechanically inactive region at the end of the flagellum help or hinder the cell’s progressive motion?

The emergence of elastic waves on the flagellum can be described by a constitutively linear, geometrically nonlinear filament, with the addition of an active moment per unit length $m$, which models the internal sliding produced by dynein activity, and a hydrodynamic term $f$ which describes the force per unit length exerted by the filament onto the fluid. Many sperm have approximately planar waveforms, especially upon approaching and collecting at surfaces [15, 16]. As such, their shape can be fully described by the angle made between
the tangent and the head centreline, denoted $\theta$, as shown in Fig. 1. Following [17, 18] we parameterize the filament by arclength $s$, with $s = 0$ corresponds to the head-flagellum joint and $s = L^*$ to the distal end of the flagellum, and apply force and moment free boundary conditions at $s = L^*$ to get

$$E(s) \partial_s \theta(s, t) - e_3 \cdot \int_s^{L^*} \partial_{s'} X(s', t) \times \left( \int_{s'}^{L^*} f(s'', t) ds'' \right) ds' - \int_s^{L^*} m(s', t) ds' = 0, \quad (1)$$

with the elastic stiffness given, following [11], by

$$E(s) = \begin{cases} (E^* - E^*_d) \left( \frac{s - s^*_d}{s^*_d} \right)^2 + E^*_d & s \leq s^*_d, \\ E^*_d & s > s^*_d. \end{cases} \quad (2)$$

where parameters $E^*_p = 8 \times 10^{-21} \text{Nm}^2$, $E^*_d = 2.2 \times 10^{-21} \text{Nm}^2$ and $s^*_d = 39 \mu \text{m} = 3.9 \times 10^{-5} \text{m}$ have been chosen to model the tapering structure of mammalian sperm flagella and match to experimental stiffness measurements [19, 20]. The position vector $X = X(s, t)$ describes the flagellar waveform at time $t$, so that $\partial_s X$ is the tangent vector, and $e_3$ is a unit vector pointing perpendicular to the plane of beating. Integrating by parts leads to the elasticity integral equation

$$E(s) \partial_s \theta(s, t) + e_3 \cdot \int_s^{L^*} (X(s', t) - X(s, t)) \times f(s', t) ds' - \int_s^{L^*} m(s', t) ds' = 0. \quad (3)$$

The active moment density can be described to a first approximation by a sinusoidal traveling wave $m(s, t) = m^* \cos(k^*s - \omega^*t)$, where $k^*$ is wavenumber and $\omega^*$ is radian frequency. The inactive end piece can be modeled by taking the product with a Heaviside function, so that $m(s, t) = m^* \cos(k^*s - \omega^*t) H(\ell^* - s)$ where $0 < \ell^* \leq L^*$ is the length of the active tail segment.

At very low Reynolds number, neglecting non-Newtonian influences on the fluid, the hydrodynamics are described by the Stokes flow equations

$$- \nabla p + \mu^* \nabla^2 u = 0, \quad \nabla \cdot u = 0, \quad (4)$$

where $p = p(x, t)$ is pressure, $u = u(x, t)$ is velocity and $\mu^*$ is dynamic viscosity. These equations are augmented by the no-slip, no-penetration boundary condition $u(X(s, t), t) = \partial_t X(s, t)$, i.e. the fluid in contact with the filament moves at the same velocity as the filament. A convenient and accurate numerical method to solve these equations for biological flow problems with deforming boundaries is based on the ‘regularized stokeslet’
FIG. 1. Schematic of an idealized sperm cell. The flagellum is described by a time-varying curve \( X(s,t) \) where \( s \in [0,L^*] \) denotes arclength along the flagellum. For \( s \in [0,\ell^*] \) the flagellum is considered active (shown in yellow), with the remaining distal region \( s \in [\ell^*,L^*] \) considered inactive (shown in black). The shape of the flagellum is described via the evolving tangent angle \( \theta(s,t) \). The head is modeled by an ellipsoidal surface \( \partial H \), with the head-flagellum joint denoted by \( X_0(t) \).

\[21, 22\], i.e. the solution to the exactly incompressible Stokes flow equations driven by a spatially-concentrated but smoothed force

\[- \nabla p + \mu^* \nabla^2 u + \psi_\varepsilon(x,y)e_3 = 0, \quad \nabla \cdot u = 0, \tag{5}\]

where \( \varepsilon \ll 1 \) is a regularization parameter, \( y \) is the location of the force, \( x \) is the evaluation point and \( \psi_\varepsilon \) is a smoothed approximation to a Dirac delta function. The choice

\[ \psi_\varepsilon(x,y) = 15 \varepsilon^4 / r_\varepsilon^7, \tag{6}\]

leads to the regularized stokeslet \[22\]

\[ S_{ij}^\varepsilon(x,y) = \frac{1}{8\pi\mu} \left( \delta_{ij} \left( r^2 + 2\varepsilon^2 \right) + r_i r_j \right) / r_\varepsilon^3, \tag{7}\]

where \( r_i = x_i - y_i, r^2 = r_i r_i, r_\varepsilon^2 = r^2 + \varepsilon^2. \]

The flow \( u_j(x,t) \) produced by a filament \( X(s,t) \) exerting force per unit length \( f(s,t) \) is then given by the line integral \( \int_0^{L^*} S_{jk}^\varepsilon(x,X(s,t)) f_k(s,t) \, ds \). The flow due to the surface of the sperm head \( \partial H \), exerting force per unit area \( \varphi(Y,t) \) for \( Y \in \partial H \), is given by the surface integral \( \iint_{\partial H} S_{jk}^\varepsilon(x,Y) \varphi_k(Y) \, dS_Y \), yielding the boundary integral equation \[23\] for the hydrodynamics, namely

\[ u_j(x,t) = \int_0^{L^*} S_{jk}^\varepsilon(x,X(s,t)) f_k(s,t) \, ds + \iint_{\partial H} S_{jk}^\varepsilon(x,Y) \varphi_k(Y,t) \, dS_Y. \tag{8}\]

The position and shape of the cell can be described by the location \( X_0(t) \) of the head-flagellum join and the waveform \( \theta(s,t) \), so that the flagellar curve is

\[ X(s,t) = X_0(t) + \int_0^s [\cos \theta(s',t), \sin \theta(s',t), 0]^T \, ds'. \tag{9}\]
Differentiating with respect to time, the flagellar velocity is then given by

\[ u(X(s, t), t) = \dot{X}_0(t) + \int_0^s \partial_t \theta(s', t)[-\sin \theta(s', t), \cos \theta(s', t), 0]^T ds'. \] (10)

Modeling the head as undergoing rigid body motion around the head-flagellum joint, the surface velocity of a point \( Y \in \partial H \) is given by

\[ u(Y, t) = \dot{X}_0(t) + \partial_t \theta(0, t) e_3 \times (Y - X_0). \] (11)

Eqs. (10) and (11) couple with fluid mechanics (Eq. (8)), active elasticity (Eq. (3)), and total force and moment balance across the cell to yield a model for the unknowns \( \theta(s, t), X_0(t), f(s, t) \) and \( \varphi(Y, t) \). Non-dimensionalising with lengthscale \( L^* \), timescale \( 1/\omega^* \) and force scale \( \mu^* \omega^* L^*^2 \) yields the equation in scaled variables (dimensionless variables denoted with ^)

\[ \partial_{\hat{s}} \hat{\theta}(\hat{s}, \hat{t}) + e_3 \cdot S^4 \int_{\hat{s}}^1 (\hat{X}(\hat{s}', \hat{t}) - \hat{X}(\hat{s}, \hat{t})) \times \hat{f}(\hat{s}', \hat{t}) d\hat{s}' - \mathcal{M} \int_{\hat{s}}^1 \cos(\hat{k}\hat{s}' - \hat{t}) H(\ell - \hat{s}') d\hat{s}' = 0, \] (12)

where \( S = L^*(\mu^*\omega^*/E^*)^{1/4} \) is a dimensionless group comparing viscous and elastic forces (related, but not identical to, the commonly-used ‘sperm number’), \( \mathcal{M} = m^*_0 L^*^2 / E^* \) is a dimensionless group comparing active and elastic forces, and \( \ell = \ell^*/L^* \) is the dimensionless length of the active segment. Here \( E^* \) is the stiffness at the distal tip of the flagellum (\( \hat{s} = 1 \)) and the dimensionless wavenumber is \( \hat{k} = k^* L^* \).

The problem is numerically discretised as described by Hall-McNair \textit{et al.} \[18\], accounting for non-local hydrodynamics via the method of regularized stokeslets \[22\]. This framework is modified to take into account the presence of the head via the nearest-neighbor discretisation of Gallagher & Smith \[24\]. The head-flagellum coupling is enforced via the dimensionless moment balance boundary condition

\[ \partial_{\hat{s}} \hat{\theta}(0, \hat{t}) - e_3 \cdot S^4 \int_{\partial H} (\hat{Y}(\hat{t}) - \hat{X}_0(\hat{t})) \times \hat{\varphi}(\hat{Y}, \hat{t}) dS_Y = 0. \] (13)

Note that for the remainder of this letter we will work with the dimensionless model but drop the ^ notation used to represent dimensionless variables for clarity. The initial value problem for the flagellar trajectory, discretised waveform and force distributions is solved in MATLAB\textsuperscript{®} using the built-in solver \texttt{ode15s}. At any point in time, the sperm cell’s position and shape can be reconstructed completely from \( X_0(t) \) and \( \theta(s, t) \) through equation (9).
Results. The impact of the length of the inactive end piece on propulsion is quantified by the swimming speed and efficiency. Velocity along a line (VAL) is used as a measure of swimming speed, calculated via

\[
\text{VAL}(j) = \|X_0^{(j)} - X_0^{(j-1)}\|/T,
\]

where \(T = 2\pi\) is the period of the driving wave and \(X_0^{(j)}\) represents the position of the head-flagellum joint after \(j\) periods. Lighthill efficiency [25] is calculated as

\[
\eta^{(j)} = \left( \text{VAL}(j) \right)^2 / \overline{W^{(j)}},
\]

where \(\overline{W^{(j)}} = \left\langle \int_0^1 u \cdot f \, ds \right\rangle\) is the average work done by the cell over the \(j^{th}\) period. In the following, \(j\) is chosen sufficiently large so that the cell has established a regular beat before its statistics are calculated (\(j = 3\) is sufficient for what follows).

The effects of varying the dimensionless active tail length on sperm swimming speed and efficiency for three choices of dimensionless wavenumber \(k\) are shown in Fig. 2. Here \(\ell = 1\) corresponds to an entirely active flagellum and \(\ell = 0\) to an entirely inactive flagellum. Values \(0.5 \leq \ell \leq 1\) are considered so that the resulting simulations produce cells that are likely to be biologically realistic. Higher wavenumbers are considered as they are typical of mammalian sperm flagella in higher viscosity media [14]. Results are calculated by taking \(m_0^* = 0.01 \mu^* \omega^* L^2 k / S\) (\(k\) dimensionless, \(m_0^*\) dimensional) and hence \(M = 0.01 k S^3\), the effect of which is to produce waveforms of realistic amplitude across a range of values of \(k\) and \(S\).

Optimal active lengths for swimming speed, \(\ell_{\text{VAL}}\), and efficiency, \(\ell_{\eta}\), occur for each parameter pair \((S, k)\); crucially, in all cases considered in Fig. 2 the optima are less than 1, indicating that by either measure some length of inactive flagellum is generally always better than a fully active flagellum. Values of \(\ell_{\text{VAL}}\) and \(\ell_{\eta}\) for the \((S, k)\) parameter pairs considered in Fig. 2 are given in Table I. Typically \(\ell_{\text{VAL}} \neq \ell_{\eta}\) for a given swimmer. For each metric, optimum active length remains approximately consistent regardless of the choice of \(S\) when \(k = 3\pi\) or \(4\pi\). When \(k = 5\pi\), much higher variability in optimum active length is observed.

In Fig. 3 the relationship between optimum active flagellum length and each of VAL and \(\eta\) is further investigated by simulating cells over a finer gradation in \(S \in [9, 18]\). When \(k = 3\pi\) and \(4\pi\), we again observe that a short inactive distal region is beneficial to the cell regardless of \(S\). For \(k = 5\pi\), there is a clear sensitivity of \(\ell_{\text{VAL}}\) to \(S\), which is not observed between \(\ell_{\eta}\) and \(S\). In all cases, the optimum values \(\ell_{\text{VAL}}\) and \(\ell_{\eta}\) are strictly less than 1.
FIG. 2. The effect of the inactive end piece length on swimming speed and efficiency of propulsion at various wavenumbers, along with velocity-optimal waveforms and example data for human sperm. (column 1) Velocity along a line (VAL) versus active length $\ell$ for viscous-elastic parameter choices $S = 18, 13.5, 9,$ and wavenumbers $k = 3\pi, 4\pi, 5\pi$; (column 2) Lighthill efficiency versus active length $\ell$ for the same choices of $S$ and $k$; (column 3) velocity-optimal cell waveforms for each $S$ and $k$; (column 4) experimental data showing the instantaneous waveform of a human sperm in high viscosity medium, with centerline plotted in purple (tracked with FAST [26]), scale bar denotes 5$\mu$m.

The waveform and velocity field associated with flagella that are fully-active and optimally-inactive for propulsion are shown in Fig. 4. The qualitative features of both waveform and the velocity field are similar, however the optimally-inactive flagellar waveform has reduced curvature and tangent angle in the distal region, and increased velocity in both ‘oblique’ regions (i.e. where $\theta \approx \pm \pi/4$).

Discussion. In simulations, we observe that spermatozoa which feature a short, inactive region at the end of their flagellum swim faster and more efficiently than those without. For $k = 3\pi$ and $k = 4\pi$, cell motility is optimized when $\approx 5\%$ of the distal flagellum length is
TABLE I. The optimum dimensionless active tail length (a) $\ell_{\text{VAL}}$ for swimming speed VAL, and (b) $\ell_\eta$ for Lighthill efficiency $\eta$, for each parameter pair $(S, k)$.

| $S$ | $k$ | $\ell_{\text{VAL}}$ | $\ell_\eta$ |
|-----|-----|---------------------|-------------|
| 18  | $3\pi$ | 0.9833 0.9500 0.6333 | 0.9833 0.9333 0.5833 |
| 13.5 | $4\pi$ | 0.9833 0.9500 0.7500 | 0.9500 0.9500 0.6167 |
| 9 | $5\pi$ | 0.9333 0.9333 0.9167 | 0.9500 0.9833 0.8333 |

FIG. 3. Normalized VAL (top row) and normalized Lighthill efficiency (bottom row) values for varying $0.5 \leq \ell \leq 1$ and $9 \leq S \leq 18$, for three values of dimensionless wavenumber $k$. Values in each subplot are normalized with respect to either the maximum VAL or maximum $\eta$ for each $k$.

inactive, regardless of $S$. Experimental measurements of human sperm indicate an average combined length of the midpiece and principal piece of $\approx 54 \mu m$ and an average end piece length of $\approx 3 \mu m$ [7], suggesting that the effects uncovered here are biologically important.

Results for waveforms that are characteristic of those in higher viscosity fluids indicate that in some cases ($k = 5\pi$) much longer inactive regions are optimal, up to $\approx 22 \mu m/57 \mu m$ or $\approx 37\%$ of the flagellum – substantially longer than the end piece observed of human spermatozoa. Sperm move through a variety of fluids during migration, in particular encountering a step change in viscosity when penetrating the interface between semen and
FIG. 4. Comparison of the normalized flow fields around the end of a simulated sperm for (a) a fully active flagellum, and (b) a flagellum featuring an inactive distal region of length $1 - \ell_{VAL}$. The active part of the flagellum is drawn in red and the inactive region in black. Fluid velocity is scaled against the maximum velocity across both frames, with magnitude indicated by the colorbar and direction by the field lines. Here, $k = 4\pi$, $S = 13.5$ and $\ell_{VAL} = 0.95$.

cervical mucus, and having to swim against physiological flows [27]. Cells featuring an optimally-sized inactive end piece may form better candidates for fertilization, being able to swim faster and for longer when traversing the female reproductive tract [28].

The basic mechanism by which the flagellar wave produces propulsion is through the interaction of segments of the filament moving obliquely through the fluid [29]. Analysis of the flow field (Fig. 4) suggests that the lower curvature associated with the inactive end piece enhances the strength of the interaction between the obliquely moving region and the fluid.

At high viscous-elastic ratio and wavenumber, a ‘normal’ flagellar waveform can be produced by a relatively large inactive region of around one wavelength (Fig. 2). This effect may have physiological relevance in respect of biochemical energy transport requirements from the mitochondria, which are situated in the midpiece.

An inactive region of flagellum is not a feature unique to human gametes - its presence can also be observed in the sperm of other species [2], as well as other microorganisms. In particular, the axomenal structures of the bi-flagellated algae *chlamydomonas reinhardtii* deplete at the distal tips [30], suggesting the presence of an inactive region. The contribution to swimming speed and cell efficiency due to the inactive distal section in these cases remains unknown. By contrast, the tip of the “9+2” cilium is a more organized “crown” structure [31], which will interact differently with fluid than the flagellar end piece mod-
eled here. Understanding this distinction between cilia and flagella, as well as the role of the inactive region in other microorganisms, may provide further insight into underlying biological phenomena, such as chemotaxis\cite{32} and synchronization\cite{33,34}. Further work should investigate how this phenomenon changes when more detailed models of the flagellar ultrastructure are considered, taking into account the full “9+2” structure\cite{35}, sliding resistance associated with filament connections\cite{36}, and the interplay of these factors with biochemical signalling in the cell\cite{37}.

The ability to qualitatively assess and model the inactive end piece of a human spermatozoon could have important clinical applications. In live imaging for diagnostic purposes, the end piece is often hard to resolve due to its depleted axonemal structure. Lacking more sophisticated imaging techniques, which are often expensive or impractical in a clinical environment, modeling of the end piece combined with flagellar tracking software, such as FAST\cite{26}, could enable more accurate sperm analysis, and help improve cell selection in assisted reproductive technologies. Furthermore, knowledge of the function of an inactive distal region has wider applications across synthetic microbiology, particularly in the design and fabrication of artificial swimmers\cite{38} and flexible filament microbots used in targeted drug delivery\cite{39}.

**Summary and Conclusions.** In this letter, we have revealed the propulsive advantage conferred by an inactive distal region of a unipolar “pusher” actuated elastic flagellum, characteristic of mammalian sperm. The optimal inactive flagellum length depends on the balance between elastic stiffness and viscous resistance, and the wavenumber of actuation. The optimal inactive fraction mirrors that seen in humans sperm (≈ 3 µm/57 µm, or ≈ 5%). These findings have a range of potential applications. They motivate the development of new methodology for improving the analysis of flagellar imaging data; by model fitting the experimentally visible region it may be possible to resolve the difficult to image distal segment. Inclusion of an inactive region may be an interesting avenue to explore when improving the efficiency of artificial microswimmer design. Finally, important biological questions may now be posed, for example does the presence of the inactive end piece confer an advantage to cells penetrating highly viscous cervical mucus?

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