The tailored sperm cell

Luis Alvarez

Abstract  Sperm are ubiquitous and yet unique. Genes involved in sexual reproduction are more divergent than most genes expressed in non-reproductive tissues. It has been argued that sperm have been altered during evolution more than any somatic cell. Profound variations are found at the level of morphology, motility, search strategy for the egg, and the underlying signalling mechanisms. Sperm evolutionary adaptation may have arisen from sperm competition (sperm from rival males compete within the female’s body to fertilize eggs), cryptic female choice (the female’s ability to choose among different stored sperm), social cues tuning sperm quality or from the site of fertilization (internal vs. external fertilization), to name a few. Unquestionably, sperm represent an invaluable source for the exploration of biological diversity at the level of signalling, motility, and evolution. Despite the richness in sperm variations, only a few model systems for signalling and motility have been studied in detail. Using fast kinetic techniques, electrophysiological recordings, and optogenetics, the molecular players and the sequence of signalling events of sperm from a few marine invertebrates, mammals, and fish are being elucidated. Furthermore, recent technological advances allow studying sperm motility with unprecedented precision; these studies provide new insights into flagellar motility and navigation in three dimensions (3D). The scope of this review is to highlight variations in motile sperm across species, and discuss the great promise that 3D imaging techniques offer into unravelling sperm mysteries.

Keywords  Sperm morphology · Flagellar beat · Chemotaxis · Klinotaxis · Steering

Introduction

Most species rely on sexual reproduction for the generation of new individuals. For this, male gametes (sperm) and female gametes (eggs) must be transferred from the specialized organs inside the body where they are produced to the fertilization site. Many different strategies have appeared during evolution to ensure the success of this step: Flowering plants, for instance, rely on the directed growth of pollen tubes that carry immotile sperm to the ovule of the female containing mature eggs (Dresselhaus et al. 2016); a process that relies on chemotaxis (Higashiyama et al. 2001). By contrast, in other plants and most animal species, sperm are endowed with the means to move and navigate to the egg by following physical and chemical signals. In the following, I outline the richness of sperm diversity.

Sperm morphology and ultrastructure is diverse

The morphology of motile sperm varies drastically between species (Fig. 1). The structural motifs are so divergent, that sperm morphology has served to delineate the phylogenetic tree of mammals (Tourmente et al. 2011), insects (Dallai et al. 2016; Jamieson et al. 1999), and plants (Renzaglia and Garbary 2001). Nematode model organisms such as Caenorhabditis elegans and Ascaris suum produce sperm that move by crawling on a substrate similar to immune cells or the amoeba Dictyostelium discoideum (Fig. 1b) (Seppenwol et al. 1989). The underlying cytoskeletal structures, however, do not rely on actin, tubulin or myosin,
but on a conserved nematode- and sperm-specific protein (Batchelder et al. 2011; Sepsenwol et al. 1989). Most motile sperm cells use thin appendages named flagella or cilia for motility—in the following referred as flagella. Flagella share a highly conserved structural 9 + 2 motif (Mitchell 2007): a cylindrical arrangement of nine peripheral microtubule doublets crosslinked by dynein motors and a central pair of single microtubules (Fig. 2a) (Roberts et al. 2013). While motile sperm from most animals rely on a single flagellum at the rear of the cell for propulsion (Fig. 1a) (Cohen 1977; Jamieson et al. 1999), sperm from green algae and plants have multiple flagella. For example, sperm from Charophycean algae and plants have multiple flagella. For example, sperm from Charophycean algae and bryophyte (mosses, hornworts, and liverworts) feature two flagella anchored at the head that extend backwards along the sperm body. Ferns and some gymnosperms, such as Ginkgo, have around dozens up to 1000 flagella. The sperm of Zamia (a cycad) can display up to 50,000 motile flagella (Renzaglia and Garbary 2001) (Fig. 1d–f). The length of a flagellum can also greatly vary from the short 1.7 µm of the termite Reticulitermes lucifugus to the 58 mm long sperm from Drosophila bifurca that is about 20 times the size of the male fly (Jamieson et al. 1999) (Fig. 1c). Part of this rich variation in sperm morphology has been attributed to the fertilization site. In particular, sperm from primitive external fertilizers display a rather homogeneous morphology (Cohen 1977). Internal fertilizers, instead, show marked differences in morphology, such as the head shape, even within closely related species (Birkhead and Immler 2007; Cohen 1977) (Fig. 1g, h). Sperm head design could result from sperm competition or interactions with the convoluted epithelium that lines the oviduct of the reproductive female tract. Finally, variations in the axonemal structure are also found that depart from the highly conserved 9 + 2 design (Fig. 2). From the 3 + 0 structure in the parasitic protozoan Diplauxis hatti to the giant axoneme of the dipteran Asphondylia ruebsaameni with 2,500 microtubule doublets (Mencarelli et al. 2001), variations are rich.

**Sperm competition and polymorphism**

Due to sexual promiscuity in many species, successful fertilization requires sperm to outcompete rival sperm. This evolutionary pressure has driven many surprising aspects of sperm behaviour and morphology (Fitzpatrick and
Lupold 2014; Lupold et al. 2016). Perhaps the best documented traits determining fertilization success are sperm swimming speed and numbers (Fitzpatrick and Lupold 2014; Gage and Barnard 1996). Yet, other traits such as sperm size, social cues, displacement of sperm from the stores in the female body (spermatheca), and many others exist in nature. Full description of these is beyond the scope of this review, for more detailed account see (Birkhead and Møller 1998). For sake of illustration, however, two examples are worth mentioning.

A perplexing case of sperm traits that originates from male competition is that of sperm trains (Foster and Pizzari 2010; Moore et al. 2002). In order to reach the egg first, sperm from rodents display a distinct behaviour by which hundreds or thousands of cells aggregate to form a train. These sperm trains swim at a speed that is about 50% higher than that of the individual cell. After 60–90 min, individual sperm cells dissociate from the train to make the last run for the egg. Another intriguing example of sperm traits that derive from male–male competition is that found in the squid Loligo bleekeri (Hirohashi et al. 2013; Iwata et al. 2011). In this species, two male types are found that exhibit different reproductive tactics. Large consort males compete with other males and court the female. If successful, these males will place their sperm capsules (spermatophores) inside the female (internal fertilizers). Small males (sneaker males) follow another tactic: these males will rush toward the female and dart their spermatophores into a seminal receptacle located out of the female body (external fertilizers). Sperm from consort and sneaker are morphologically different probably due to the different fertilization site (internal vs. external fertilization). Sperm from the large consort are smaller than that of the sneaker male (Iwata et al. 2011), but even more surprising, sneaker sperm display chemotaxis towards carbon dioxide and exhibit a swarming behaviour. The role of this chemotactic behaviour is unclear, but it has been speculated that CO2 might be used as a chemical signal to locate unfertilized.
Sperm signalling is divergent

For sensory cells such as photoreceptors, olfactory neurons and taste cells, signalling components are fairly well conserved. By contrast, the repertoire of proteins involved in sexual reproduction in general, and those making up sperm in particular, have been subject of extensive modifications during evolution (Birkhead and Immler 2007; Swanson and Vacquier 2002; Torgerson et al. 2002). As a result, signalling molecules controlling sperm motility are as diverse as sperm shape (Bönigk et al. 2009; Fechner et al. 2015; Kaupp and Strünker 2017; Strünker et al. 2015). The sperm-specific Ca\(^{2+}\) channel, CatSper, is an example that illustrates this signalling diversity. The CatSper channel complex is the most complex ion channel that has been identified so far. It features four pore-forming subunits and up to five auxiliary subunits, depending on the species. The channel probably appeared early in evolution before the branching of eukaryotes into the unikonts and bikonts (Cai et al. 2014; Chung et al. 2017). Although the control of CatSper by membrane potential and intracellular pH is conserved from sea urchins (Seifert et al. 2015) to mammals (Kirichok et al. 2006), the signalling mechanisms that eventually activate CatSper differ greatly. The female hormone progesterone, for instance, activates CatSper in humans (Lishko et al. 2011; Strünker et al. 2011), but not in mouse (Strünker et al. 2011). In human sperm, progesterone released by cumulus cells activates CatSper via an unconventional endocannabinoid mechanism (Miller et al. 2016); this progesterone-induced Ca\(^{2+}\) influx has been implicated in sperm chemotaxis (Oren-Benaroya et al. 2008; Publicover et al. 2008). Furthermore, chemicals as diverse as steroids, prostaglandins, odorants, and endocrine disrupting chemicals (EDCs) also activate human CatSper (Schiffer et al. 2014). It has been proposed that, for human sperm, CatSper serves as polymodal ‘stimulus integrator’, translating the chemical, hydrodynamic, and topographical microenvironment of the genital tract into a spatio-temporal pattern of Ca\(^{2+}\) signals (Brenker et al. 2012). In sea urchin sperm, CatSper activation involves a different signalling pathway initiated by the binding of a chemoattractant molecule to a chemoreceptor guanylate cyclase followed by the activation of two different ion channels and a Na\(^+\)/H\(^+\) exchanger (Kaupp and Alvarez 2016). These signalling events produce changes in membrane potential and intracellular pH that are required for CatSper opening. Finally, even though sperm motility from the zebrafish Danio rerio is controlled by Ca\(^{2+}\) (Fechner et al. 2015), these species lack the genes for the CatSper channel (Cai and Clapham 2008).

Although Ca\(^{2+}\) signalling is ubiquitous in animals and plants, phylogenetic studies argue that the kit of Ca\(^{2+}\) channels and exchangers found in the different kingdoms differs extensively (Cai et al. 2014; Nagata et al. 2004; Wheeler and Brownlee 2008). For example, some land plants, such as Arabidopsis thaliana, are lacking the CatSper channel, four-domain voltage-dependent Ca\(^{2+}\) channels, and transient receptor potential channels. It would be interesting to enlarge the number of plant species in these studies to corroborate this finding. Interestingly, several cyclic nucleotide-gated channels (CNGC) have been identified in Arabidopsis (20) and the moss Physcomitrella patens (8), suggesting that this type of channels are abundant among plants. CNGC are key players in chemotaxis of sperm from sea urchins (Bönigk et al. 2009) and motility of Zebrafish (Fechner et al. 2015) and control Ca\(^{2+}\) entry in sperm. It would interesting to find which Ca\(^{2+}\) channels play a role in sperm chemotaxis among plants, and if CNGCs are involved.

In summary, signalling of sperm in most species involves changes in Ca\(^{2+}\), but the channels and the mechanisms of activation implicated differ greatly between species.

The advent of 3D sperm imaging

Despite the fact that fertilization often takes place in three dimensions (3D), most of our knowledge on sperm motility and navigation is restricted to two dimensions (2D). The main reason for this lack of information is technological: When compared to crawling cells such as immune cells or Dictyostelium, most sperm move at speeds that are two to three orders of magnitude higher. Sea urchin sperm, for example, swim at speeds of about 200 \(\mu\)m/s (Jikeli et al. 2015). Dendritic cells or CD8\(^{+}\) T lymphocytes, by comparison, move at characteristic speeds of about 0.2 \(\mu\)m/s (Solanes et al. 2015). For this reason, tracking sperm in three dimensions (3D) with conventional imaging methods is challenging. Despite the technical difficulties, the 3D motion of sperm has been addressed for sea urchins and mammals, but very little is known for sperm from other animals such as insects or plants. Such lack of knowledge is striking, as insects represent by far the majority of species on our planet (Mora et al. 2011), and some of our current understanding of 3D sperm motility and navigation was first gathered from plants (Brokaw 1958). An influential and pioneering study of animal sperm motility in 3D was presented by Hugh Crenshaw (Crenshaw 1990). Using two dark-field microscopes with perpendicular views of an observation chamber, Crenshaw followed sea urchin sperm while swimming freely in 3D. This study provided
experimental evidence for a mechanism of navigation called ‘helical klinotaxis’, by which microorganisms moving along a helical path align with a stimulus gradient by simply adjusting the cell rotation velocity as a function of the stimulus (Crenshaw 1996). After Crenshaw’s seminal contribution, imaging of sperm in 3D has not seen much progress until recently. Several studies have investigated sperm motility by following the 3D motion of the head (Corkidi et al. 2008; Di Caprio et al. 2014; Jikeli et al. 2015, Su et al. 2013, 2012) and the flagellum (Bukatin et al. 2015; Silva-Villalobos et al. 2014; Wilson et al. 2013), to list a few. In the following, I will discuss some insights provided by these studies into sperm motility, navigation, and steering using 3D methods.

Sperm steering

A key aspect in flagellar motility concerns steering. Sperm propulsion involves a break of symmetry—the flagellar travelling wave moves in one preferential direction. For most animals, wave moves from the head to the tip of the flagellum. Sperm steering requires an additional symmetry break to change direction. Two mechanisms have been proposed to break this symmetry: an average flagellar curvature (Elgeti et al. 2010; Friedrich et al. 2010; Geyer et al. 2016) or a buckling instability (Bukatin et al. 2015; Gadêlha et al. 2010). In principle, both mechanisms involve bending of the flagellum into one preferential direction. The first mechanism assumes that bending is produced along the flagellum in a smooth manner. The second mechanism involves an abrupt bending that arises from strong mechanical flagellar compression along the axoneme. Bukatin and his co-workers used a novel method to examine the 3D flagellar beat of human sperm in a flow (Bukatin et al. 2015). Using common bright-field microscopy, the authors calculated the position of the flagellum along the axis normal to the focal plane from the broadening of the flagellum along its arc-length. This study describes several interesting aspects of human sperm motility: first, most human sperm produce a rolling motion along its longitudinal axis. Second, rolling is invariably counter-clockwise when observing the cell head-on towards the tip. Third, the cell population falls into two groups: those turning left and those turning right. Finally, turning direction correlates with bending of the flagellar midpiece: cells turning left feature an approximately zero average curvature, whereas cells turning right display a preferential flagellar bending to the right when observed from above. As pointed out by the authors, a preferential direction of bending cannot result from an average flagellar curvature, because due to rolling, the direction of bending should alternate from right to left. From this insight, the authors hypothesize that steering might be achieved by a dynamical buckling instability. While this study argues that a mean flagellar curvature is not sufficient to explain human sperm steering, the underlying mechanism remains to be shown experimentally. We expect new exciting surprises in this respect.

Sperm are ambidextrous

Nodal cilia, found in embryos, represent an important exception to the 9 + 2 axonemal motif. These short appendages (about 5 µm long) are key to breaking the left–right symmetry of our body during embryogenesis and lack the central microtubule pair (9 + 0 motif). Their motion, in contrast to that of other motile cilia and flagella, is circular instead of roughly planar. This difference in beat planarity has been attributed to the absence of the central pair (Brokaw 2005; Hirokawa et al. 2009). However, other structures linking specific microtubule doublets might be involved as well (Lin et al. 2012). An essential feature of nodal ciliary beat is the sense of rotation. It has been observed that the circling motion is always in a single direction: clockwise - when observing these cilia from the cell base toward the tip (Hirokawa et al. 2009). This beat chirality is required for nodal cilia to break the left–right asymmetry formation during development of the embryo, and has been attributed to the underlying chirality of the axoneme itself: By design, dynein arms point in a clockwise direction from one doublet to the next (Fig. 2a) (Brokaw 2005; Hilfinger and Jülicher 2008; Hirokawa et al. 2009). Using holographic methods and sperm from malaria parasites as a simple flagellar model system to study sperm motility in 3D, Laurence Wilson revealed that, despite the intrinsic flagellar structural chirality, malaria sperm produce ambidextrous flagellar waveforms (Fig. 3a–c) (Wilson et al. 2013), i.e. the flagellar beat is left (Fig. 3a) or right handed (Fig. 3b), and handedness alternates at the frequency of the beat (Fig. 3c). This study represents a primary example on how knowledge about the mechanisms of action of the axoneme can be inferred for observations of the flagellar beat in 3D. As an aside, theoretical studies show that by tuning internal cellular parameters, such as structural elements or motor properties, a cilium could produce clock-wise and counter-clockwise beating. However, the probability of observing a specific turning direction is higher when the underlying structure is chiral (Brokaw 2005; Hilfinger and Jülicher 2008). Taken together, chiral rotation in nodal cilia and ambidextrous beating in sperm has been shown by experiments and predicted by theory.

Sperm use a deterministic navigation strategy

Many cells and organisms exploit physical and chemical cues to navigate in complex environments to search for mates, food or, more generally, better life conditions.
Although crucially important, navigation principles along well-defined chemical gradients in three dimensions (3D) have been revealed only for bacteria. In his pioneering study (Berg and Brown 1972), Howard Berg revealed the stochastic navigation principle of bacterial chemotaxis that lead to the run-and-tumble model of chemotaxis (Fig. 4a) (Berg 1993). It took almost another half century of technological advances in several fields to address anew this complex and challenging question for a eukaryotic microswimmer. Using holographic microscopy, optochemical techniques, and computational models, Jan Jikeli et al. examined 3D navigation of sea urchin sperm while swimming in defined 3D gradients of chemoattractant (Jikeli et al. 2015). The navigation principle in 3D is characterized by several key features. First, and consistent with previous reports (Corkidi et al. 2008; Crenshaw 1990), sperm swim along a helical path (Fig. 3d). Second, during chemotaxis, the helical swimming path bends in a deterministic fashion to align with the chemical gradient (Figs. 3e, f, 4b). Fourth, sperm respond to fast and slow components of the chemoattractant stimulus: A fast periodic component that results from...
the periodic component of helical swimming provides sperm with a local map of the gradient; it is used to steer in the right direction. Slow changes of the average stimulus level allow sperm to monitor its success and to trigger emergency steering responses in case sperm are veering off course (Fig. 3e). Finally, the mechanism of Ca$^{2+}$ signalling underlying emergency steering responses, and the principle by which sperm detect increases and decreases of chemoattractant concentration were revealed, thereby, linking cellular signaling to cell behavior (Jikeli et al. 2015). Of note, emergency steering responses while swimming down the gradient have been also reported for sperm from algae, indicating that this cellular behaviour might be general (Kinoshita et al. 2017). The biflagellated sperm from these algae use their posterior flagellum for drastic turning. It would be interesting to know if the underlying signalling mechanism is conserved.

**Discussion**

Sperm offer a unique example of evolutionary adaptation. These cells have been so extensively tailored that sperm from different species each merit their own studies. Variations in sperm morphology, ultrastructure, signalling, navigation principles, and behaviours are myriad. Our knowledge about sperm is vast, yet mostly compartmentalized, and does not cross interdisciplinary borders. For example, even though sperm chemotaxis has been described across most kingdoms (Yoshida et al. 2013), a comprehensive quantitative picture of sperm navigation and the underlying signalling mechanism has been advanced for only few model systems, such as marine invertebrates (Guererro et al. 2010; Hirohashi et al. 2013; Kaupp and Alvarez 2016; Yoshida and Yoshida 2011; Zimmer and Riffell 2011), mammalian sperm (Bukatin et al. 2015; Eisenbach...
and Giojalas 2006; Kaupp and Strünker 2017; Miki and Clapham 2013), some fish (Fechner et al. 2015; Yanagimachi et al. 2013), and bracken fern (Brokaw 1958, 1973). For insects, most studies have addressed only morphological and evolutionary aspects. Sperm motility in insects has been only addressed sparsely and has remained for the most part descriptive. Despite the fact that some indications of sperm chemotaxis among insects have been reported (Grodner and Steffens 1978), no insect model for chemotaxis has been established. Males from some insects inject sperm trough a wound inflicted into the females abdomen (hypodermic insemination). These sperm must reach the females reproductive organs for fertilization (Jamieson et al. 1999). It would be interesting to study if chemotaxis plays a role into assisting sperm to find the spermatheca. In nematodes, it has been reported that sperm are able to perform chemotaxis (Sepsenwol CIL:44001). The role, mechanisms, and molecules involved are, however, still unknown. It is also perplexing, that although chemotaxis of plant sperm is firmly stablished, and these sperm cells are lacking a characteristic cell wall, fluorescent indicators have not been exploited to delineate the sequence of signalling events underlying chemotaxis in plants.

During the last decade, a number of studies using 3D techniques have tackled fundamental questions of sperm motility. Protozoa and insect sperm offer a unique opportunity to investigate axoneme architectures that depart from the prototypical 9 + 2 structural motif. Additionally, 3D imaging could be exploited to investigate sperm navigation in plants or algae. It would be interesting to see if mechanisms other than helical klinotaxis have evolved for these sperm species. Finally, sperm from most animals display a single flagellum that is used both for propulsion and as a rudder. Biflagellated sperm from algae (Kinoshita et al. 2017, 2016) and the liverwort Marchantia polymorpha (Miyamura et al. 2002) display flagellar waveforms that are different for each flagellum, and steering/propulsion can be adjusted differentially using both flagella. The beat of the posterior flagellum in Marchantia displays a more three-dimensional beat pattern than that of the anterior flagellum (Miyamura et al. 2002), indicating that possibly the posterior flagellum has an important role for 3D swimming. Algae sperm propel using both flagella, but steer by using the posterior flagellum as a rudder during chemotaxis (Kinoshita et al. 2017). The underlying signalling mechanism for differential beat patterns during chemotaxis of biflagellated sperm is unknown. More complex sperm, such as that of Zamia featuring up to 50,000 flagella could coordinate flagellar beating in a similar fashion as that found in the multicellular alga Volvox (Drescher et al. 2010; Ueki et al. 2010). It would be interesting to understand how multiflagellated plant sperm orchestrate 3D flagellar motion for directed motility.

Acknowledgements Open access funding provided by Max Planck Society. The author greatly acknowledges Drs. Karen Renzaglia, Romano Dallai, Sol Sepsenwol, Tokushiro Takaso, Stephan Irser, Simone Immler, and Tim Birkhead for their spectacular sperm pictures, Drs. U. Benjamin Kaupp, Sol Sepsenwol, and Reinhard Seifert for careful reading of the manuscript and discussions, and Dr. René Pascal for his assistance preparing figures. The author also thanks Drs. Katsuyuki Yamato and Kazuyuki Kuchitsu for their invitation to write this review.

Conflict of interest The author declares no competing interests. This work was done with the financial support from the Deutsche Forschungsgemeinschaft via the priority program SPP 1726 “Microswimmers”.

Open Access This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.

References

Alvarez L, Friedrich BM, Gompper G, Kaupp UB (2014) The computational sperm cell. Trends Cell Biol 24:198–207
Batchelder EL, Holloper G, Campillo C, Mezanges X, Jorgensen EM, Nasso P, Sens P, Plastino J (2011) Membrane tension regulates motility by controlling lamellipodium organization. Proc Natl Acad Sci USA 108:11429–11434
Berg HC (1993) Random walks in biology. Princeton University Press, Princeton
Berg HC, Brown DA (1972) Chemotaxis in Escherichia coli analysed by three-dimensional tracking. Nature 239:500–504
Birkhead TR, Møller AP (1998) Sperm competition and sexual selection. Academic, San Diego
Bönigk W, Loogen A, Seifert R, Kashikar ND, Klemm C, Krause E, Hagen V, Kremmer E, Strünker T, Kaupp UB (2009) An atypical CNG channel activated by a single cGMP molecule controls sperm chemotaxis. Sci Signal 2:ra68
Bremer C, Goodwin N, Weyand I, Kashikar ND, Naruse M, Krahl- ing M, Müller A, Kaupp UB, Strünker T (2012) The CatSper channel: a polymodal chemosensor in human sperm. EMBO J 31:1654–1665
Brokaw CJ (1958) Chemotaxis of bracken spermatozoids. J Exp Biol 35:197–212
Brokaw CJ (1973) Calcium and flagellar response during the chemotaxis of bracken spermatozoids. J Cell Physiol 83:151–158
Brokaw CJ (2005) Computer simulation of flagellar movement IX. Oscillation and symmetry breaking in a model for short flagella and nodal cilia. Cell Motil Cytoskeleton 60:35–47
Bukatin A, Kukhtevich I, Stoop N, Dunkel J, Kantsler V (2015) Specific gene loss and rapid evolution of a sperm-specific ion channel complex: CatSpers and CatSperbeta. PloS One 3:e3569
Cai X, Clapham DE (2008) Evolutionary genomics reveals lineage-specific gene loss and rapid evolution of a sperm-specific ion channel complex: CatSpers and CatSpermBeta. PLoS One 3:e3569
Cai X, Wang X, Clapham DE (2014) Early evolution of the eukaryotic Ca2+ signaling machinery: conservation of the CatSper channel complex. Mol Biol Evol 31:2735–2740
Iwata Y, Shaw P, Fujiwara E, Shiba K, Kakiuchi Y, Hirohashi N (2011) Why small males have big sperm: dimorphic squid sperm linked to alternative mating behaviours. BMC Evol Biol 11:236

Jamieson BGM, Dallai R, Azfelius BA (1999) Insects. Their spermatozoa and phylogeny. Science, Enfield

Jikeli JF, Alvarez L, Friedrich BM, Wilson LG, Paskal R, Colin R, Pichlo M, Rennhack A, Brenker C, Kaupp UB (2015) Sperm navigation along helical paths in 3D chemoeffector landscapes. Nat Commun 6:7985

Kaupp UB, Alvarez L (2016) Sperm as microswimmers—navigation and sensing at the physical limit. Eur Phys J Spec Top 225:2119–2139

Kaupp UB, Stränker T (2017) Signaling in sperm: more different than similar. Trends Cell Biol 27:101–109

Kinosita N, Nagasato C, Tanaka A, Motomura T (2016) Chemotaxis in the anisogamous brown algae *Mutimo cylindricus* (Cutleriaceae, Tiliopteridales). Phycologia 55:359–364

Kinosita N, Nagasato C, Motomura T (2017) Chemotactic movement in sperm of the oogamous brown algae, *Saccharina japonica* and *Fucus distichus*. Protoplasma 254:547–555

Kirichok Y, Navarro B, Clapham DE (2006) Whole-cell patch-clamp measurements of spermatozoa reveal an alkaline-activated Ca2+ channel. Nature 439:737–740

Lin JF, Heuser T, Song KK, Fu X, Nicastro D (2012) One of the nine doublet microtubules of eukaryotic flagella exhibits unique and partially conserved structures. PLoS One 7(10):e46494

Lisko PV, Botchkina IL, Kirichok Y (2011) Progesterone activates the principal Ca2+ channel of human sperm. Nature 471:387–391

Lupold S, Manier MK, Puniamoorthy N, Schoff C, Starmer WT, Luepold SHB, Belote JM, Pitnick S (2016) How sexual selection can drive the evolution of costly sperm ornamentation. Nature 533:535–538

Mencarelli C, Lupetti P, Rosetto M, Mercati D, Heuser J, Dallai R (2001) Molecular structure of dynein and motility of a giant sperm axoneme provided with only the outer dynein arm. Cell Motil Cytoskeleton 50:129–146

Miki K, Clapham DE (2013) Rheotaxis guides mammalian sperm. Curr Biol 23:443–452

Miller MR, Mannowitz N, Iavarone AT, Safavi R, Gracheva EO, Smith JF, Hill RZ, Bautista DM, Kirichok Y, Lisko PV (2016) Unconventional endocannabinoid signaling governs sperm activation via sex hormone progesterone. Science 352:555–559

Mitchell DR (2007) The evolution of eukaryotic cilia and flagella as motile and sensory organelles. In: Back N, Cohen IR, Lajtha A, Lambrds JD, Paolelli R (eds) Eukaryotic membranes as motile and sensory organelles. In: Back N, Cohen IR, Lajtha A, Lambrds JD, Paolelli R (eds) Eukaryotic membranes and cytoskeleton: origins and evolution. Springer, New York, pp 130–140

Miyamura S, Matsunaga S, Hori T (2002) High-speed video microscopic analysis of the flagellar movement of *Marchantia polymorpha* sperm. Bryol Soc Jpn 8:79–83

Moore H, Dvoráková K, Jenkins N, Breed W (2002) Exceptional sperm cooperation in the wood mouse. Nature 418:174–177

Mora C, Tittensor DP, Adl S, Simpson AGB, Worm B (2011) How many species are there on earth and in the ocean? Plos Biol 9(8):e1001127

Movassaghi T, Bui KH, Sakakibara H, Oiwa K, Ishikawa T (2010) Chlamydomonas flagellar beat. Curr Biol 20:R314–R316

Gadêlha H, Gaffney EA, Smith DJ, Kirkman-Brown JC (2010) Non-linear instability in flagellar dynamics: a novel modulation mechanism in sperm migration? JR Soc. Interface 7:1689–1697

Hirohashi N, Okada Y, Tanaka Y (2009) Fluid Dynamic mechanism responsible for breaking the left-right symmetry of the human body: the nodal flow. Annu Rev Fluid Mech 41:53–72

Chung JJ, Miki K, Kim D, Shim SH, Shi HF, Hwang JY, Cai X, Iseri Y, Zhuang X, Clapham DE (2017) CatSper regulates the structural continuity of sperm Ca2+ signaling domains and is required for normal fertility. eLife 6:e23082

Crenshaw HC (1996) A new look at locomotion in microorganisms: rotating and translating. Am Zool 36:608–618

Corkidi G, Taboada B, Wood CD, Guerrero A, Darszon A (2008) Tracking sperm in three-dimensions. Biochem Biophys Res Commun 373:125–129

Crenshaw HC (1996) Helical orientation - a novel mechanism for the orientation of microorganisms. In: Alt W, Hofmann G (eds) Lecture Notes in Biomathematics. Springer, Berlin, pp 361–386

Cohen J (1977) Reproduction. Butterworths & Co., London

Chung JJ, Miki K, Kim D, Shim SH, Shi HF, Hwang JY, Cai X, Iseri Y, Zhuang X, Clapham DE (2017) CatSper regulates the structural continuity of sperm Ca2+ signaling domains and is required for normal fertility. eLife 6:e23082

Crenshaw HC (1996) Helical orientation - a novel mechanism for the orientation of microorganisms. In: Alt W, Hofmann G (eds) Lecture Notes in Biomathematics. Springer, Berlin, pp 361–386

Cohen J (1977) Reproduction. Butterworths & Co., London

Chung JJ, Miki K, Kim D, Shim SH, Shi HF, Hwang JY, Cai X, Iseri Y, Zhuang X, Clapham DE (2017) CatSper regulates the structural continuity of sperm Ca2+ signaling domains and is required for normal fertility. eLife 6:e23082

Crenshaw HC (1996) Helical orientation - a novel mechanism for the orientation of microorganisms. In: Alt W, Hofmann G (eds) Lecture Notes in Biomathematics. Springer, Berlin, pp 361–386

Cohen J (1977) Reproduction. Butterworths & Co., London
Oren-Benaroya R, Orvieto R, Gakamsky A, Pinchasov M, Eisenbach M (2008) The sperm chemoattractant secreted from human cumulus cells is progesterone. Hum Reprod 23:2339–2345
Publicover SJ, Giojalas LC, Teves ME, de Oliveira GS, Garcia AA, Barratt CL, Harper CV (2008) Ca2+ signalling in the control of motility and guidance in mammalian sperm. Front Biosci 13:5623–5637
Renzaglia KS, Garbary DJ (2001) Motile gametes of land plants: Diversity, development, and evolution. Crit Rev Plant Sci 20:107–213
Renzaglia KS, Dengate SB, Schmitt SJ, Duckett JG (2002) Novel features of Equisetum arvense spermatozoids: insights into pteridophyte evolution. New Phytol 154:159–174
Roberts AJ, Kon T, Knight PJ, Sutoh K, Burgess SA (2013) Functions and mechanics of dynein motor proteins. Nat Rev Mol Cell Biol 14:713–726
Schiffer C, Müller A, Egeberg DL, Alvarez L, Brenker C, Rehfeld A, Frederiksen H, Kaupp UB, Balbach M, Wachen D, Skakkebaek NE, Almstrup K, Strünker T (2014) Direct action of endocrine disrupting chemicals on human sperm. EMBO Rep 15:758–765
Seifert R, Flick M, Bönigk W, Alvarez L, Trotschel C, Poetsch A, Müller A, Goodwin N, Pelzer P, Kashikar ND, Kremmer E, Jikeli J, Timmermann B, Kuhl H, Fridman D, Windler F, Kaupp UB, Strünker T (2015) The CatSper channel controls chemosenescation in sea urchin sperm. EMBO J 34:379–392
Sepsenwol S, Taft SJ (1988) (CIL:44001) Cell Image Library. http://www.cellimagelibrary.org/images/44001
Sepsenwol S, Ris H, Roberts TM (1989) A unique cytoskeleton associated with crawling in the amoeboid sperm of the nematode, Ascaris suum. J Cell Biol 108:55–66
Silva-Villalobos F, Pimentel JA, Darson A, Corkidi G (2014) Imaging of the 3D dynamics of flagellar beating in human sperm. Conf Proc IEEE Eng Med Biol Soc 2014:190–193
Solanes P, Heuze ML, Maurin M, Breton M, Lautenschlaeger F, Mairui P, Terriac E, Thouleuze MI, Launay P, Piel M, Vargas P, Lennon-Dumenil AM (2015) Space exploration by dendritic cells requires maintenance of myosin II activity by IP3 receptor 1. EMBO J 34:798–810
Strünker T, Goodwin N, Brenker C, Kashikar ND, Weyand I, Seifert R, Kaupp UB (2011) The CatSper channel mediates progesterone-induced Ca2+ influx in human sperm. Nature 471:382–386
Strünker T, Alvarez L, Kaupp UB (2015) At the physical limit - chemosensation in sperm. Curr Opin Neurobiol 34:110–116
Su TW, Xue L, Ozcan A (2012) High-throughput lensfree 3D tracking of human sperms reveals rare statistics of helical trajectories. Proc Natl Acad Sci U S A 109:16018–16022
Su TW, Choi I, Feng JW, Huang K, McLeod E, Ozcan A (2013) Sperm trajectories form chiral ribbons. Sci Rep 3:1664
Swanson WJ, Vacquier VD (2002) The rapid evolution of reproductive proteins. Nat Rev Genet 3:137–144
Takaso T, Kimoto Y, Owens JN, Kono M, Mimura T (2013) Secretions from the female gametophyte and their role in spermatozoid induction in Cycas revoluta. Plant Reprod 26:17–23
Torgerson DG, Kulathinal RJ, Singh RS (2002) Mammalian sperm proteins are rapidly evolving: evidence of positive selection in functionally diverse genes. Mol Biol Evol 19:1973–1980
Tourmente M, Gomendio M, Roldan ERS (2011) Sperm competition and the evolution of sperm design in mammals. BMC Evol Biol 11:12
Ueki N, Matsunaga S, Inouye I, Hallmann A (2010) How 5000 independent rowers coordinate their strokes in order to row into the sunlight: Phototaxis in the multicellular green alga Volvox. BMC Biol 8
Wargo MJ, Smith EF (2003) Asymmetry of the central apparatus defines the location of active microtubule sliding in Chlamydomonas flagella. Proc Natl Acad Sci USA 100:137–142
Wheeler GL, Brownlee C (2008) Ca2+ signalling in plants and green algae-changing channels. Trends Plant Sci 13:506–514
Wilson LG, Carter LM, Reece SE (2013) High-speed holographic microscopy of malaria parasites reveals ambidextrous flagellar waveforms. Proc Natl Acad Sci USA 110:18769–18774
Yanagimachi R, Cherr G, Matsubara T, Andoh T, Harumi T, Vines C, Pillai M, Griffin F, Matsubara H, Weatherby T, Kaneshiro K (2013) Sperm attractant in the micropyle region of fish and insect eggs. Biol Reprod 88:47
Yoshida M, Yoshida K (2011) Sperm chemotaxis and regulation of flagellar movement by Ca2+. Mol Hum Reprod 17:457–465
Yoshida M, Hiradate Y, Sensui N, Cosson J, Morisawa M (2013) Species-specificity of sperm motility activation and chemotaxis: a study on ascidian species. Biol Bull 224:156–165
Zimmer RK, Riffee JA (2011) Sperm chemotaxis, fluid shear, and the evolution of sexual reproduction. Proc Natl Acad Sci USA 108:13200–13205