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Models and Speculations

Stretch-activated calcium channels relay fast calcium waves propagated by calcium-induced calcium influx

Lionel F. Jaffe[1]
Marine Biological Laboratory, 7 MBL Street, Woods Hole, MA 02543, U.S.A.

For nearly 30 years, fast calcium waves have been attributed to a regenerative process propagated by CICR (calcium-induced calcium release) from the endoplasmic reticulum. Here, I propose a model containing a new subclass of fast calcium waves which is propagated by CICI (calcium-induced calcium influx) through the plasma membrane. They are called fast CICI waves. These move at the order of 100 to 1000 μm/s (at 20°C), rather than the order of 3 to 30 μm/s found for CICR. Moreover, in this proposed subclass, the calcium influx which drives calcium waves is relayed by stretch-activated calcium channels. This model is based upon reports from approx. 60 various systems. In seven of these reports, calcium waves were imaged, and, in five of these, evidence was presented that these waves were regenerated by CICI. Much of this model involves waves that move along functioning flagella and cilia. In these systems, waves of local calcium influx are thought to cause waves of local contraction by inducing the sliding of dynein or of kinesin past tubulin microtubules. Other cells which are reported to exhibit waves, which move at speeds in the fast CICI range, include ones from a dozen protozoa, three polychaete worms, three molluscs, a bryozoan, two sea urchins, one arthropod, four insects, *Amphioxus*, frogs, two fish and a vascular plant (*Equisetum*), together with numerous healthy, as well as cancerous, mammalian cells, including ones from human. In two of these systems, very gentle local mechanical stimulation is reported to initiate waves. In these non-flagellar systems, the calcium influxes are thought to speed the sliding of actinomyosin filaments past each other. Finally, I propose that this mechanochemical model could be tested by seeing if gentle mechanical stimulation induces waves in more of these systems and, more importantly, by imaging the predicted calcium waves in more of them.

Introduction

Calcium waves were first seen as the calcium tsunami which crosses a fertilizing medaka fish egg (Gilkey et al., 1978). Calcium waves were subsequently seen or inferred to cross a very wide variety of cell parts, cells, tissues and even organs, and to do so at speeds of less than 1 nm/s up to 30 cm/s, and thus a speed range of nearly a billion-fold (I only consider waves which cross cell boundaries in Table or Figures of the present article when their speeds were not substantially slowed by cell-to-cell delays). These fall into four speed-based groups: fast, slow, ultrafast and ultraslow waves (Figure 1).

Fast calcium waves have been thought to be only propagated by CICR (calcium-induced calcium release). This is a ‘travelling’ cycle in which a high level of calcium within some cytosolic zone induces the release of additional calcium stored in the ER (endoplasmic reticulum). This then diffuses to nearby ER channels where it induces the release of yet more calcium – a travelling cycle which can be modulated by the levels of inositol (1,4,5)-trisphosphate within the cytosol (Dumollard et al., 2002).

In the present article, I collate evidence for a second subclass of fast calcium waves which travel at approx. 100 to 1000 μm/s in a wide variety of systems. I also gather evidence that such waves are carried by CICI (calcium-induced calcium influx) through the plasma membrane. Therefore they are named CICI waves, and their place in the calcium-wave spectrum is indicated in Figure 1.

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[1] email ljaffe@mbl.edu

Key words: calcium-induced calcium influx, calcium wave, flagella, metachronal wave, stretch-activated calcium channel.

Abbreviations used: CICI, calcium-induced calcium influx; CICR, calcium-induced calcium release; ER, endoplasmic reticulum.

Figure 1 | Proposed new calcium-wave speed spectrum, including waves propagated by CICI

f, fertilization; fl, flagellar; nfl, non-flagellar. Modified from Figure 1 of Jaffe (2003) (© Portland Press) and Figure 1 of Jaffe (1999) (© John Wiley & Sons, Inc.) with permission, which lacks a CICI category.

Then, I propose a model in which CICI waves are propagated by stretch-sensitive channels in the plasma membrane, and, finally, consider possible tests of these hypotheses.

Lists of proposed CICI waves

In most cases, speeds are taken from the text of the references cited, whereas others are from images taken at successive times during a wave or from the equation

$$v = \lambda f$$

where v is wave velocity, λ is wave length and f is wave frequency. In experiments with mammalian or human preparations, speeds were corrected from the values reported at 20–37 °C.

For flagella, this correction factor was 0.36 (Holwill and Silvester, 1965), whereas for all other systems this factor was 0.50 (Clary-Meinesz et al., 1992). Where possible, the speeds reported for motion along a straight line were corrected for the greater length along the sinuous surfaces which carried the wave.

Table 1 lists the flagellar waves which I propose to be propagated by CICI, whereas Table 2 lists other waves which are proposed to be so propagated. The latter begins with some taken from Alfred Lucas's pioneering study (Lucas, 1931) on molluscan gill cilia and goes forward to many more recent studies. These waves were reported for systems which go from protozoa, such as *Paramecium* and *Stentor*, up to human sperm flagella and human blood neutrophils. In between there is a list of systems, which are presented in the Abstract above. When corrected for temperature and wave pathlength, these speeds generally lie between about 100 and 1000 μm/s.

In seven of the listed cases, the waves were directly seen to be calcium ones, and in five of these evidence is presented that they are regenerative calcium waves. Moreover, in five of the other cases, they were inferred to be calcium waves for various reasons which are presented below. Thus the 70 μm/s calcium waves, which were reported to traverse fish keratocytes by Brust-Mascher and Webb (1998) (Table 2), were absent in low-calcium medium and were stopped by calcium-channel blockers – observations which directly support CICI as a wave-propagation mechanism in these cells (Bressac et al., 1991). Figure 2 shows the number of listed cases of non-flagellar and flagellar waves versus wave speed. Two distinct, if overlapping curves, can be observed.

Finally, I would like to note that CICI waves may prove to explain gliding and swimming by cyanobacteria, and thus extend the range of CICI waves to prokaryotes. There are three studies which argue for surface waves as driving such movement. Specifically, Ehlers et al. (1996) speculated on theoretical grounds that their speed would be 160 μm/s (a speed at the centre of the proposed CICI range); calcium entry is required for the motility of the cyanobacterium *Synechoccus* (Pitta et al., 1997); and quick-freeze electron microscopy of *Synechoccus* reveals an array of spicules which extend into the medium and could act as oars to propel it (Samuel et al., 2001). Moreover, 'the strongest argument for their existence is that one cannot think of any other viable mechanism' (personal communication, H. Berg). When one adds that cyanobacteria lack an endoplasmic reticulum, one may well wonder if CICI propels cyanobacteria.

Evidence that the listed waves are calcium waves which are supported by an influx of calcium ions

The strongest evidence that 60–200 μm/s waves are calcium waves which require an influx of calcium ions has been provided by seven studies of seeing them as calcium waves; moreover, in five of these cases they were dependent upon external calcium or a calcium influx.

First, Charles et al. (1996) observed 100–200 μm/s intercellular calcium waves in primary cultured mouse cortical neurons; waves which were abolished in medium which lacked calcium. It is interesting that they wrote of being puzzled by the mechanism of calcium waves which moved at this speed.

Table 1 | Speeds of fast waves which move along flagella or cilia

System	Speed (μm/s)	Reference
Sperm flagella		
Equisetum (vascular plant)	600	Bilderback et al. (1973)
Myzostomum (polychaete)	800	Ishijima et al. (1994)
Arenicola (polychaete)	340	Pasey et al. (1994)
Turritella (marine snail) (swimming forward)	900	Ishijima et al. (1999)
Corbicula (clam)	1200	Howard et al. (2004)
Psammechinus (sea urchin)	900	Gray and Hancock (1955)
Lytechinus (sea urchin)	900	Brokaw (1972)
Tripneustes (sea urchin)	1000	Gibbons (1980, 1982)
Bacillus (arthropod)		Baccetti et al. (1973a)
Short wave	800	
Long wave	600	
Cricket	100	Rikmenspoel (1978)
Drosophila	150	Bressac et al. (1991)
Other fruit fly (swimming forward)	100	Baccetti et al. (1989)
Tenebrio (beetle) (long wave)	400	Baccetti et al. (1973b)
Aleochara (beetle)	200	Werner et al. (2002)
Eel	1300	Wooley (1998)
Hamster		Ishijima et al. (2002)
Capacitated	700	
Activated	700	
Hyperactivated	400	
Acrosome-reacted	200	
Rat epididymal	100	Lindemann et al. (1987)
	300	Jeulin et al. (1996)
Ram epididymal	200	Chevrier and Dacheaux (1992)
Macaque		Ishijima et al. (2006)
Activated	400	
Hyperactivated	100	
Human	500	Serres et al. (1991)
	500	Mortimer et al. (1997)
Flagellates: flagella or cilia		
Peranema	300	Lowndes (1941)
Menoidium	500	Lowndes (1941)
Euglena	500	Lowndes (1941)
	400	Lowndes (1944)
Monas	500	Lowndes (1945)
Stentor	900	Sleigh (1960)
Polytoma	600	Brokaw (1963)
Ceratium	500	Brokaw and Wright (1963)
Strigomonas	500	Holwill (1965)
Crithidia	500	Sugrue et al. (1988)
Chlamydomonas	200	Hyams and Borisy (1978)
	500	Holland et al. (1997)
Dunaliella	900	Schoevaert et al. (1988)

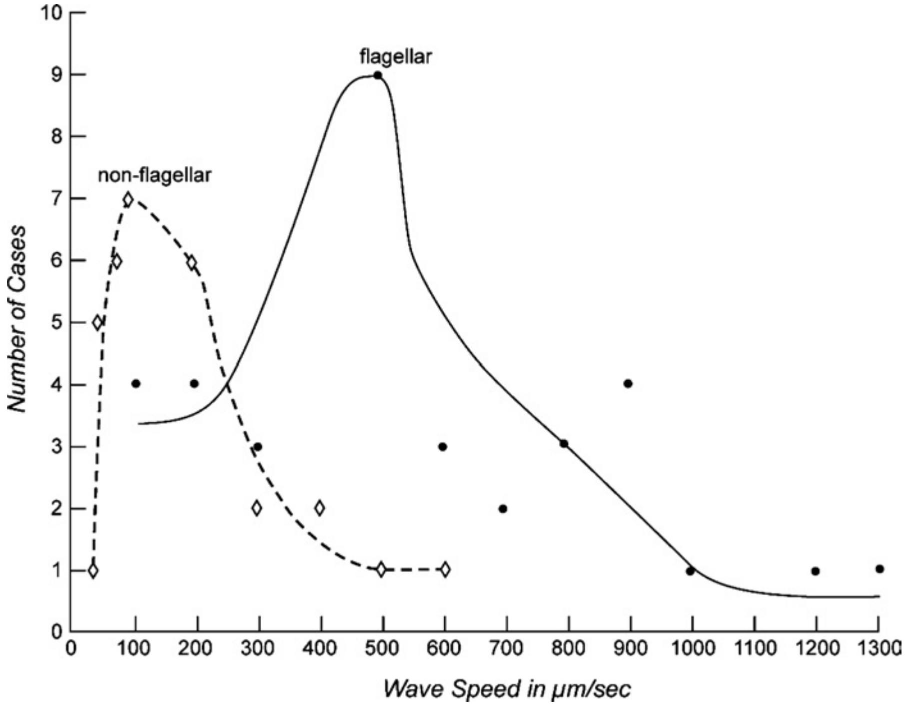
Table 2 | Speeds of non-flagellar waves

System	Speed (μm/s)	Reference
Protozoa		
Opalina body: metachronal	500	Okajima (1953)
Stentor peristomial region: metachronal	600	Sleigh (1956)
Paramecium oral groove: metachronal	300	Machemer (1972)
Koruga's whole surface: undulatory and metachronal	200	Cleveland and Cleveland (1966)
	400	Tamm (1999)
Polychaete sperm body		
Myzostomum	400	Ishijima et al. (1994)
Mollusc gill cilia		Lucas (1931)
Modiolus: metachronal		
Laterofrontal	60	
Lateral	200	
Bryozoan cilia: metachronal		
Plumatella	200	Riisgard et al. (2004)
Amphioxus larval cilia	300	Stokes and Holland (1995)
Vertebrates		
Frog palate epithelium: metachronal	100	Spungin and Silberberg (1984)
	150	Eshel and Priel (1987)
Frog cultured oesophagus: metachronal	100	Gheber and Priel (1987)
Fish keratocyte	60	Brust-Mascher and Webb (1998)
Rat cortical astrocyte	40	Guthrie et al. (1999)
Rat lung myocyte	100	Featherstone et al. (2005)
Rodent heart myocyte	80	Kaneko et al. (2000)
In situ	90	Takamatsu et al. (1991)
Isolated	60	Lipp and Nigglii (1994)
	80	Cheng et al. (1996)
	100	Wussling and Salz (1996)
	80	Ishide et al. (1990)
	100	Trafford et al. (1995)
	60	Wussling and Mair (1999)
Rodent heart endothelial cell	60	Isshiki et al. (2004)
Mammalian cancer cell line		
HT 1080 fibrosarcoma	100	Huang et al. (2004)
HeLa carcinoma	80	Rintoul and Bainbridge (2003)
Human blood neutrophil	100	Kindzelskii and Petty (2003)
Ferret retina	200	Feller et al. (1997)
Cultured mouse neuron	200	Charles et al. (1996)
PC12 neurite	80	Reber and Schindelholz (1996)

Secondly, Reber and Schindelholz (1996) observed 80 μm/s calcium waves moving along PC12 neurites towards the growth cone. Although they did not investigate the role of calcium influxes, these neurites are only approx. 2 μm thick, which precludes release from the only known source of internal calcium release, namely the ER.

Thirdly, Brust-Mascher and Webb (1998) observed 60 μm/s calcium intracellular waves moving along fish keratocytes; waves which were not inducible in

Figure 2 | **Wave speeds as shown in Tables 1 and 2**
Each of the values shown in the Tables are shown as a point in this figure. Most of the non-flagellar values are of speeds which lie between 60 and 400 μm/s, whereas most of the flagellar values are of speeds between 200 and 1000 μm/s.



medium which contained the calcium-channel blockers cobalt ions or verapamil.

Fourthly, in a truly remarkable paper, Kindzelskii and Petty (2003) observed 90 μm/s subsurface calcium waves moving around human blood neutrophil cells. Some moved clockwise, as seen from the basal-to-apical surface, whereas some moved counterclockwise. All of these waves occurred in medium containing normal blood levels of calcium, but the clockwise ones did not occur in zero-calcium medium.

Fifth, Rintoul and Bainbridge (2003) observed 80 μm/s intracellular calcium moving across HeLa cells. Although intracellularly applied EGTA or BAPTA reduced the speeds of the calcium waves by approximately half, the effects of changes in extracellular calcium were not reported.

Sixth, Huang et al. (2004) observed 100 μm/s intracellular calcium waves moving across cells from a line of human fibrosarcoma cells. These waves were blocked by the calcium-channel blockers gadolinium ions or mibrafredil.

Seventh, Isshiki et al. (2004) reported seeing 60 μm/s subsurface intracellular calcium waves in rodent heart endothelial cells. These waves which occurred in 1.2 mM Ca^{2+}, but not in zero-free-calcium medium.

In addition, further evidence that 100–1000 μm/s flagellar waves are calcium waves is provided by four lines of evidence, as follows.

First, the flagellate *Koruga* [from termite (*Mastotermes darwiniensis*) gut] exhibits synchronous 200 μm/s front-to-back synchronous waves of both indentation and of metachronous ciliary bending. By indentation waves, I mean ones that look like the much slower ones which move along many eggs (Jaffe and Créton, 1998) and are illustrated in Jaffe (1999). More detailed study of these waves in *Koruga* showed that the indentation waves induce the metachronal ones (Cleveland and Cleveland, 1966). Then, 33 years later, Tamm (1999) reported that these waves are stopped within minutes by the addition to the medium of 1 mM Ni^{2+}, a blocker of calcium channels. One may wonder why *Koruga* cells are the only ones known to show fast CICI waves of surface indentation. Perhaps, this is because they actually lack indentation waves within the acidic and anaerobic hindguts of termites where they live naturally, so the observed indentation waves may be artifacts of their observation in medium at a neutral pH and abundant oxygen. In any case, if one considers the studies by Cleveland and Cleveland (1966) and Tamm (1999) together, it is hard to avoid the inference that the *Koruga* ones are mechanically driven subsurface ones.

Secondly, the 80 μm/s waves that move along HeLa cells, which were studied by Rintoul and Bainbridge (2003), were greatly inhibited by exposing the cells to the membrane-permeant calcium-chelators EGTA-AM or BAPTA-AM.

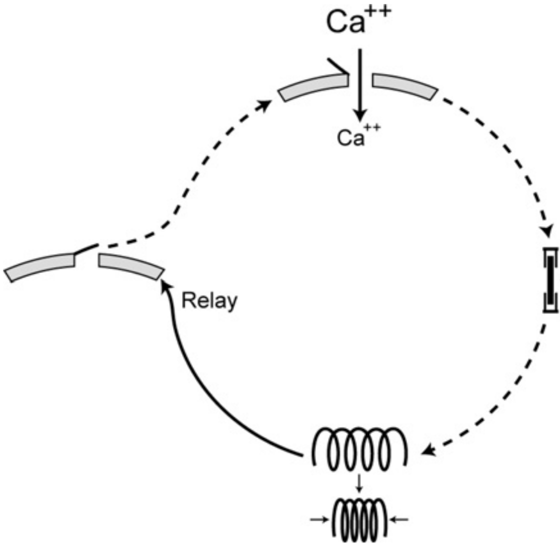
Thirdly, there are numerous reports that the direction of sperm swimming and therefore flagellar wave direction are reversed by sudden changes in extracellular calcium levels, e.g. the studies by Ishijima et al. (1999) on marine snail (*Turritella communis*) sperm and by Schmidt and Eckert (1976) on *Chlamydomonas*.

Fourthly, four studies report striking changes that occur in the beating patterns of de-membranated flagella or cilia when the calcium level rises above 1 μM in the following organisms: *Paramecium* (Naitoh and Kaneko, 1972); trypanosome (Holwill and MacGregor, 1976); *Chlamydomonas* (Wakabayashi et al., 1997); and sea urchin (Bannai et al., 2000).

Altogether, although the role of calcium in fast CICI wave propagation has been little studied, the available results establish, indicate or suggest that certain of these waves are, indeed, calcium ones.

Figure 3 | Cycle that may propagate fast CICI calcium waves, as well as slow calcium waves

Starting at the top and going clockwise: calcium ions enter the cell; subsurface filaments slide past each other so as to shorten; the cell membrane is stretched so as to pull on the nearby membrane; nearby calcium channels open to relay the wave; calcium ions enter etc.



Proposed mechanisms

In our model, fast CICI waves are propagated by stretch-activated calcium channels. Thus they are propagated by a travelling cycle in which stretching a cell's membrane at one point opens nearby stretch-activated calcium channels (Martinac, 2004), and the resultant influx of calcium ions causes subsurface filaments to slide past each other and thereby stretch the nearby membrane and in this way relay the wave. These filaments would be actinomyosin in non-flagellar systems, and microtubule–dynein or microtubule–kinesin filaments in flagellar systems (Satir, 1968; Cosson, 1992). Action via actinomyosin would be as in the nine studies of calcium waves in isolated rodent heart myocytes listed in Table 2 and, more generally, in the well-known control of muscle contraction by calcium. Figure 3 shows this model, whereas Figure 2 indicates the different speeds to be expected of waves with propagation mechanisms that ultimately depend upon entirely different sliding filaments.

We do so since most such waves have gross visible mechanical components. Thus they include the bending waves that occur along active flagella, the waves of ciliary bending which define metachronal waves, the undulatory waves reported to cross the bodies of two species of flagellates (Tamm, 1999) and the waves along the sperm body of the polychaete *Myzostomum* (Ishijima et al., 1994). Moreover, many of the examples listed in Table 2 involve heart cells, which are well known to be dependent upon stretch to function (Hu and Sachs, 1997). Moreover, there are two studies of fast CICI waves which report that they can be initiated by gentle local mechanical stimulation: Charles et al. (1996) who gently poked some monolayers of cultured cortical neurons, and Guthrie et al. (1999) who dropped tiny (30 to 50 μm) glass beads on to monolayers of cultured astrocytes and reported that 'When thousands of beads are dropped throughout a single culture, thousands of such waves are simultaneously initiated and subsequently propagated throughout the culture'. Such mechanical wave initiation provides further evidence for the proposed mechanochemical cycle.

One objection to the proposal is that the propagation of slow calcium waves, which move approximately one thousand times slower than CICI ones, has been implicitly attributed to the same travelling cycle (Jaffe and Cretón, 1998). However, the speed of a mechanochemical wave will depend upon the response speed and the calcium conductance of the particular channel which is opened by stretch. Indeed, mechanosensitive channels have been proposed to mediate the submillisecond responses of hair cells in the vertebrate ear (Corey et al., 2004).

Another objection is that metachronal waves are generally believed to be propagated by hydrodynamic coupling between cells, and that intercellular or intracellular events do not regulate their propagation (Machemer, 1974; Sleigh, 1974; personal communication, M. Sanderson). However, hydrodynamic coupling will surely exert mechanical forces on the cell membrane; therefore we see no reason why CICI waves cannot be driven by mechanically propagated calcium waves. {Moreover, Tamm (1999) reported that in a swimming flagellate (*Koruga*) the 400 μm/s undulatory waves along its surface precede the metachronal ciliary waves moving at this same speed along its surface and do so by about 10 μm. Moreover, the 10 μm high undulatory waves can be stopped rapidly by the addition of 1 mM nickel ion to the medium. So we would infer that they are mechanically propagated calcium waves}.

A further objection is that flagellar waves can be seen in de-membranated flagella; a fact that would seem to argue against propagation by calcium waves in the flagellar membrane. There are many reports of such waves, most recently by Ho et al. (2002) and Linhart et al. (2002). Indeed, on the basis of the observations of waves along de-membranated flagella, a sliding filament model of flagellar waves was proposed some time ago (Brokaw, 1972). Nevertheless, it seems impossible to assess the significance of these reports for our calcium-wave model, since, to our knowledge, none of them provide the speeds of flagellar wave propagation, as opposed to the speeds of sperm movement.

Finally, we would like to point out that the angle between the axis of a structure, such as a flagellum or a cell, and the direction of mechanical propagation along it will be controlled by the angle between the subsurface actinomyosin fibrils or microtubules and this axis. Thus the proposed mechanical mechanism would provide an explanation in principle for such phenomena as spiral metachronal waves along cells and spiral contractile waves along flagella.

Why should CICI rather than CICR determine calcium-wave speeds along flagella etc.?

A qualitative explanation lies in the absence of an ER in flagella and cilia. A semi-quantitative theory that holds more widely is supported by the higher surface-to-volume ratios within the relatively thin or flat cell regions or cells that make up most of the non-flagellar cases listed in Table 2. Thus the first case in Table 2 is that of the parasitic ciliate *Opalina*, which has a body that is less than 10 μm thick, whereas the fifth case is that of a polychaete sperm's body which is only approx. 1.5 μm thick. Also, Table 2 shows the cases of certain fish keratocytes, which are only 1 μm thick, and PC12 neurites, which are only approx. 2 μm thick.

Proposed tests of this proposal

This model predicts that calcium waves move at predictable rates along various undulating flagella and along many other cells. This could be tested by using fluorescent calcium indicators; alternatively, one could introduce one of the luminescent calcium reporters called aequorins and then observing the system with an ultralow-light imaging device (Sala-Newby et al., 2000; Chiesa et al., 2001; Créton and Jaffe, 2001; Rogers et al., 2005). It predicts that such waves should depend upon calcium influx which is an easily tested prediction. It also predicts that many of these waves could be initiated by gentle localized poking and could be suppressed by mechanical constraints with appropriate gels or viscogens.

Above all, pursuit of this model calls for efforts in the imaging of calcium waves.

Summary

We have assembled approx. 60 reports of waves which move at the order of 100 to 1000 μm/s. Surely, these call for consideration. In seven of these, calcium waves were imaged. Surely, this suggests that many of the 100–1000 μm/s waves are calcium waves.

However, these waves fall into two distinct groups: those that move along flagella and those that move along other systems. All of the calcium waves were seen in these latter non-flagellar systems. So the most important, if most demanding, future test of our proposal is to image the spatiotemporal patterns of calcium in flagella.

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References

Baccetti, B., Burrini, A.G., Dallai, R., Pallini, V., Pereiti, P., Piantelli, F., Rosati, F. and Selmi, G. (1973a) Structure and function in the spermatozoan of *Bacillus rossius.* The spermatozoon of arthropoda. XIX. J. Ultrastruct. Res. Suppl. **12**, 5–73

Baccetti, B., Burrini, G., Dallai, R., Giusti, F., Mazzini, M., Renieri, T., Rosati, F. and Selmi, G. (1973b) Structure and function in the spermatozoan of *Tenebrio molitor* (the spermatozoon of Arthropoda. XX). J. Mechanochem. Cell Motil. **2**, 149–161

Baccetti, B., Gibbons, B.H. and Gibbons, I.R. (1989) Bidirectional swimming in spermatozoa of Tephritid flies. J. Submicrosc. Cytol. Pathol. **21**, 619–625

Bilderback, D.E., Bilderback, D.E., Jahn, T.L. and Fonseca, J.R. (1973) The release mechanism and locomotor behavior of *Equisetum* sperm. Am. J. Bot. **60**, 796–801

Bannai, H., Yoshimura, M., Takahashi, K. and Shingyoji, C. (2000) Calcium regulation of microtubule sliding in reactivation sea urchin sperm flagella. J. Cell Sci. **113**, 831–839

Bressac, C., Joly, D., Devaus, J., Serres, C., Feneux, B. and Lachaise, D. (1991) Comparative kinetics of short and long sperm in sperm dimorphic *Drosophila* species. Cell Motil. Cytoskeleton **19**, 269–274

Brokaw, C.J. (1963) Movement of the flagella of *Polytoma uvella.* J. Exp. Biol. **40**, 149–156

Brokaw, C.J. (1972) Flagellar movement: a sliding filament model. Science **178**, 455–462

Brokaw, C.J. and Wright, L. (1963) Bending waves of the posterior flagellum of *Ceratium*. Science **142**, 116–170

Brust-Mascher, I. and Webb, W.W. (1998) Calcium waves induced by large voltage pulses in fish keratocytes. Biophys. J. **75**, 1669–1678

Charles, A.C., Kodali, S.K. and Tyndale, R.F. (1996) Intercellular calcium waves in neurons. Mol. Cell Neurosci. **7**, 337–353

Cheng, H., Lederer, M.R., Lederer, W.J. and Cannell, M.B. (1996) Calcium sparks and [Ca^{2+}]i waves in cardiac myocytes. Am. J. Physiol. **270**, C148–C159

Chevrier, C. and Dacheux, J.-L. (1992) Evolution of the flagellar waveform of ram spermatozoa in relation to the degree of epididymal maturation. Cell Motil. Cytoskeleton **23**, 8–18

Chiesa, A., Rapizzi, E., Tosello, V., Pinton, P., de Virgilio, M., Fogarty, K.E. and Rizzuto, R. (2001) Recombinant aequorin and green flluorescent protein as valuable tools in the study of cell signalling. Biochem. J. **355**, 1–12

Clary-Meinesz, C.F., Cosson, J., Huitorel, P. and Blaive, B. (1992) Temperature effect on the ciliary beat frequency of human nasal and trachael ciliated cells. Biol. Cell **76**, 335–338

Cleveland, L.R. and Cleveland, B.T. (1966) The locomotory waves of *Koruga, Deltotrichonympha* and *Mixotricha*. Arch. Protistenkd. **109**, 39–63

Corey, D.P., Garcia-Anoveros, J., Holt, J.R., Kwan, K.Y., Lin, S.Y., Vollrath, M.A., Amalfitano, A., Cheung, E.L., Derfler, B.H., Duggan, A., Geleoc, G.S., Gray, P.A., Hoffman, M.P., Rehm, H.L., Tamasauskas, D. and Zhang, D.S. (2004) TRPA1 is a candidate for the mechanosensitive transduction channel of vertebrate hair cells. Nature **432**, 723–729

Cosson, J. (1992) The covalent oscillator: a paradigm accounting for the sliding/bend mechanism and wave propagation in cilia and flagella. Biol. Cell **76**, 319–327

Créton, R. and Jaffe, L.F. (2001) Chemiluminescence microscopy as a tool in biomedical research. Biotechniques **31**, 1098–1105

Dumollard, R., Carroll, J., Dupont, G. and Sardet, C. (2002) Calcium wave pacemakers in eggs. J. Cell Sci. **115**, 3557–3564

Ehlers, K.M., Samuel, A.D.T., Berg, H.C. and Montgomery, R. (1996) Do cyanobacteria swim using surface waves? Proc. Natl. Acad. Sci. U.S.A. **93**, 8340–8343

Eshel, D. and Priel, Z. (1987) Characterization of metachronal wave of beating cilia on frog's palate epithelium in tissue culture. J. Physiol. **388**, 1–8

Featherstone, N.C., Jesudason, E.C., Connell, M.G., Fernig, D.G., Wray, S., Losty, P.D. and Burdyga, T.V. (2005) Spontaneous propagating calcium waves underpin airway peristalsis in embryonic rat lung. Am. J. Respir. Cell Mol. Biol. **33**, 153–160

Feller, M.B., Butts, D.A., Aaron, H.L., Rokhsar, D.S. and Shatz, D.J. (1997) Dynamic processes shape spatiotemporal properties of retinal waves. Neuron **19**, 293–306

Gheber, L. and Priel, Z. (1987) Extraction of cilium beat parameters by the combined application of photoelectric measurements and computer simulation. Biophys. J. **72**, 449–462

Gibbons, I.R. (1980) Intermittent swimming in live sea urchin sperm. J. Cell Biol. **84**, 1–12

Gibbons, I.R. (1982) Sliding and bending in sea urchin sperm flagella. Symp. Soc. Exp. Biol. **35**, 225–287

Gilkey, J.C., Jaffe, L.F., Ridgway, E.B. and Reynolds, G.T. (1978) A free calcium wave traverses the activating egg of the medaka, *Oryzias latipes*. J. Cell Biol. **76**, 448–466

Gray, J. and Hancock (1955) The propulsion of sea-urchin spermatozoa. J. Exp. Biol. **32**, 802–814

Guthrie, P.B., Knappenberger, J., Segal, M., Bennett, M.V.L., Charles, A.C. and Kater, S.B. (1999) ATP released from astrocytes mediates glial calcium waves. J. Neurosci. **19**, 520–528

Ho, H.-C., Granish, K.A. and Suarez, S.S. (2002) Hyperactivated motility of bull sperm is triggered at the axoneme by Ca^{2+} and not cAMP. Dev. Biol. **250**, 208–217

Holland, E.M., Hartmann, H., Uhl, R. and Hegemann, P. (1997) Control of phobic behavioral responses by rhodopsin-induced photocurrents in *Chlamydomona*s. Biophys. J. **73**, 1395–1401

Holwill, M.E.J. (1965) The motion of *Strigomonas oncopelti*. J. Exp. Biol. **42**, 125–137

Holwill, M.E.J. and Silvester, N.R. (1965) The thermal dependence of flagellar activity in *Strigomonas oncopelti.* J. Exp. Biol. **42**, 537–544

Holwill, M.E.J. and McGregor, J.L. (1976) Effects of calcium on flagellar movement in the trypanosome *Crithidia oncopelti*. J. Exp. Biol. **65**, 229–242

Howard, D.R., Trantow, C.M. and Thaler, C.D. (2004) Motility of a biflagellate sperm: waveform analysis and cyclic nucleotide activatrion. Cell Motil. Cytoskeleton **59**, 120–130

Hu, H. and Sachs, F. (1997) Stretch-activated ion channels in the heart. J. Mol. Cardiol. **29**, 1511–1523

Huang, J.-B., Kindzelskii, S.L., Clark, A.F. and Petty, H. (2004) Identification of calcium channels promoting calcium waves in HT1080 tumor cells. Cancer Res. **64**, 2482–2489

Hyams, J.S. and Borisy, G.G. (1978) Isolated flagellar apparatus of *Chlamydomonas*: characterization of forward swimming and alteration of waveform and reversal of motion by calciuim ions *in vitro*. J. Cell Sci. **33**, 235–253

Ishide, N., Urayama, T., Inoue, K.-I., Komaru, T. and Takashima, T. (1990) Propagation and collision characteristics of calcium waves in rat myocytes Am. J. Physiol. **259**, H940–H950

Ishijima, S., Ishijima, S.A. and Afzelius, B.A. (1994) Movement of *Myzostomium* spermatozoa: calcium ion regulation of swimming direction. Cell Motil. Cytoskeleton **28**, 145–142

Ishijima, S., Ishijima, S.A. and Afzelius, B.A. (1999) Movement of *Turritella* spermatozoa: direction of propagation and chirality of flagellar bends. Cell Motil. Cytoskeleton **44**, 85–95

Ishijima, S., Baba, S.A., Mohri, H. and Suarez, S.S. (2002) Quantitative analysis of flagellar movement in hyperactivated and acrosome-reacted golden hamster spermatozoa. Mol. Reprod. Dev. **61**, 376–384

Ishijima, S., Mohri, H., Overstreet, J.W. and Yudin, A.I. (2006) Hyperactivation of monkey spermatozoa is triggered by Ca^{2+} and completed by cAMP. Mol. Reprod. Dev. **73**, 1129–1139

Isshiki, M., Mutoh, A. and Fujita, T. (2004) Subcortical Ca^{2+} waves sneaking under the plasma membrane in endothelial cells. Circ. Res. **95**, e11–e21

Jaffe, L.F. (1999) Organization of early development by calcium patterns. BioEssays **21**, 657–667

Jaffe, L.F. (2003) The propagation speeds of calcium action potentials are remarkably invariant. Biol. Cell **95**, 343–355

Jaffe, L.F. and Créton, R. (1998) On the conservation of calcium wave speeds. Cell Calcium **24**, 1–8

Jeulin, C., Lewin, L.M., Chevrier, C. and Schoevaert-Brossault, D. (1996) Changes in flagellar movement of rat spermatozoa along the length of the epididymis: manual and computor-aided image analysis. Cell Motil. Cytoskeleton **35**, 147–161

Kaneko, T., Tanaka, H., Oyamada, M., Kawata, S. and Takamatsu, T. (2000) Three distinct types of Ca^{2+} waves in Langendorff-perfused rat heart revealed by real-time confocal microscopy. Circ. Res. **86**, 1093–1099

Kindzelskii, A.L. and Petty, H.R. (2003) Intracellular calcium waves accompany neutrophil polarization, formylmethylleucyl-phenylalanine stimulation and phagocytosis: a high speed microscopy study. J. Immunol. **170**, 64–72

Lindemann, C.B., Goltz, J.S. and Kanous, K.S. (1987) Regulation of activation state and flagellar wave form in epididymal rat sperm: evidence for the involvement of both Ca^{2+} and cAMP. Cell Motil. Cytoskeleton **8**, 324–332

Linhart, O., Cosson, J., Mims, S.D., Selton, W.L. and Rodina, M. (2002) Effects of ions on the motility of fresh and demembranated paddle fish (*Polyodon spathula*) spermatozoa. Reproduction **124**, 713–719

Lipp, P. and Niggli, E. (1994) Modulation of Ca^{2+} release in cultured neonatal cardiac myocytes. Circ. Res. **74**, 979–990

Lowndes, A.G. (1941) On flagellar movement in unicellular organisms. Proc. Zool. Soc. London **111**, 111–134

Lowndes, A.G. (1944) On the swimming of uniflagellate organisms. Proc. Zool. Soc. London **113A**, 99–197

Lowndes, A.G. (1945) Swimming of *Monas stigmata.* Nature **155**, 579

Lucas, A.M. (1931) An investigation of the nervous system as a possible factor in the regulation of ciliary activity of the lamellibranch gill. J. Morphol. Physiol. **51**, 147–185

Machemer, H. (1972) Temperature influences on ciliary beat and metachronal coordination in *Paramecium.* J. Mechanochem. Cell Motil. **1**, 57–66

Machemer, H. (1974) In Ciliary activity and metachronism in protozoa. In Cilia and Flagella (Sleigh, M.A., ed.), pp. 199–286, Academic Press, London

Martinac, B. (2004) Mechanosensitive ion channels: molecules of mechanotransductin. J. Cell Sci. **117**, 2449–2460

Mortimer, S.T., Schoevaert, D., Swan, M.A. and Mortimer, D. (1997) Quantitative observations of flagellar motility of capacitating human spermatozoa. Hum. Reprod. **12**, 1006–1012

Naitoh, Y. and Kaneko, H. (1972) Reactivated Triton-extracted models of *Paramecium*: modification of ciliary movement by calcium ions. Science **176**, 523–524

Okajima, A. (1953) Studies on the metachronal wave in *Opalina* I. Electrical stimulation with the microelectrode. Jpn. J. Zool. **10**, 87–100

Pasey, A.A., Cosson, J.C. and Bentley, M.G. (1994) Intermittent swimming in the spermatozoa of the lugworm *Arenicola marina* (L.) (annelida: polychaeta). Cell Motil. Cytoskeleton **29**, 186–194

Pitta, T.P., Sherwood, E.E., Kobel, A.M. and Berg, H.C. (1997) Calcium is required for swimming by the nonflagellated cyanobacterium *Synechoccus* strain WH8113. J. Bacteriol. **179**, 2524–2528

Reber, B.F.X. and Schindelholz, B. (1996) Detection of a trigger zone of bradykinin-induced fast calcium waves in PC12 neurites. Pflügers Arch. **432**, 893–903

Rikmenspoel, R. (1978) The equation of motion for sperm flagella. Biophys. J. **23**, 177–205

Riisgard, H.U., Nielsen, K.K., Fuchs, J., Rasmussen, B.F., Obst, M. and Funch, P. (2004) Ciliary feeding structures and particle capture mechanism in the freshwater bryozoan *Plumatella repens* (Phylactolaemata). Invertebr. Biol. **123**, 156–167

Rintoul, G.L. and Bainbridge, K.G. (2003) Effects of calcium buffers and calbindin D-28k upon histamineinduced calcium oscillations and calcium waves in HeLa cells. Cell Calcium **34**, 131–144

Rogers, K.L., Stinnakre, J., Agulhon, C., Jublot, D., Shorte, S.L., Kremer, E.J. and Brulet, P. (2005) Visualization of local Ca^{2+} dynamics with genetically encoded bioluminescent reporters. Eur. J. Neurosci. **21**, 597–610

Sala-Newby, G.B., Badminton, M.N., Evans, W.H., George, C.H., Jones, H.E., Kendall, J.M., Ribiero, A.R. and Campbell, A.K. (2000) Targeted bioluminescence indicators in living cells. Methods Enzymol. **305**, 479–498

Samuel, A.D.T., Petersen, J.D. and Reese, T.S. (2001) Envelope structure of *Synechoccus sp*. WH8113, a nonflagellated swimming cyanobacterium. BMC Microbiol. **1**, 4

Satir, P. (1968) Studies on cilia III. Further studies on the cilium tip and a ‘sliding filament’ model of ciliary motility. J. Cell Biol. **39**, 77–94

Schmidt, J.A. and Eckert, R. (1976) Calcium couples flagellar reversal to photostimulation in *Chlamydomonas Reinhardttii.* Nature **262**, 713–715

Schoevaert, D., Krishnashwamy, S., Couturier, M. and Marano, F. (1988) Ciliary beat and cell motility of *Dunaliella*: computer analysis of high speed microcinematography. Biol. Cell **62**, 229–240

Serres, C., Feneux, D. and Berthon, B. (1991) Decrease of internal free calcium and human sperm movement. Cell Motil. Cytoskeleton **18**, 228–240

Sleigh, M.A. (1956) Metachronism and frequency of beat in the peristomal cilia of *Stentor*. J. Exp. Biol. **33**, 15–28

Sleigh, M.A. (1960) The form of beat in cilia of *Stentor* and *Opalina*. J. Exp. Biol. **37**, 1–10

Sleigh, M.A. (1974) Metachronism of cilia of metazoa. In Cilia and Flagella (Sleigh, M.A., ed.), pp. 287–304, Academic Press, London

Spungin, B. and Silberberg, A. (1984) Stimulation of mucus secretion, ciliary activity, and transport in frog palate epithelium. Am. J. Physiol. **247**, C299–C308

Stokes, M.D. and Holland, N.D. (1995) Ciliary hovering in larval lancelets (Amphioxus). Biol. Bull. **188**, 231–233

Sugrue, P., Hirons, M.R., Adam, J.U. and Holwill, M.E.J. (1988) Flagellar wave reversal in the kinetoplastid flagellate *Crithidia oncopelti*. Biol. Cell **63**, 127–131

Takamatsu, T., Minamikawa, T., Kawachi, H. and Fujita, S. (1991) Imaging of calcium wave propagation in guinea pig ventricular cell pairs by confocal laser scanning microscopy. Cell Struct. Funct. **16**, 341–346

Tamm, S.L. (1999) Locomotory waves of *Koruga* and *Deltotrichonympha:* flagella wag the cell. Cell Motil. Cytoskeleton **43**, 145–158

Trafford, A.W., Lipp, P., O'Neill, Niggli, E. and Eisner, D.A. (1995) Propagating calcium waves initiated by local caffeine application in rat ventricular myocytes. J. Physiol. **489**, 319–326

Wakabayashi, K.-i, Yagi, T. and Kamiya, R. (1997) Ca^{2+} dependent waveform conversion in the flagellar axoneme of *Chlamydomonas* mutants lacking the central-pair/radial spoke system. Cell Motil. Cytoskeleton **38**, 22–28

Werner, M., Tscheulin, T., Speck, T., Zissler, D. and Peschke, K. (2002) Ultrastructure and motility pattern of the spermatozoa of *Aleochara curtula* (coleoptera, staphylinidae). Arthropod Struct. Dev. **31**, 243–254

Wooley, D.M. (1998) Studies on the eel sperm flagellum. 2. The kinematics of normal motility. Cell Motil. Cytoskeleton **39**, 233–245

Wussling, M. and Mair, T. (1999) Calcium waves in rat cardiac myocytes underlie the principles of selforganization in excitable media. Lect. Notes Phys. **532**, 151–163

Wussling, M.H.P. and Salz, H. (1996) Nonlinear propagation of spherical calcium waves in rat cardiac myocytes. Biophys. J. **70**, 1144–1153

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