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How the myosalpinx works in gamete and embryo transport

Papel del miosalpinx en el transporte de gametos y embriones

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There are similarities and dissimilarities between the muscular activity of the oviduct in three mammalian species, mouse, rabbit and human. In the rabbit and human oviduct electrical activity becomes disorganized after ovulation and in both species the shape of electrical activity changes. In the rabbit, the number of spikes in a spike burst increases and, in the human, a single wave is replaced by an irregular series of spikes. These changes suggest that the contractile force increases after ovulation. In the rabbit and mouse, the frequency of contractile activity increases as ovum transport progresses. This is observed also in the human oviduct, although to a lesser extent. Ova are found in the front (i.e. on the uterine side) of the disorganized activity in the rabbit and of the organized activity in the mouse. In both species, this borderline progresses towards the uterus. The entry of ova into the uterus requires activation of the whole oviduct. There are indications that this series of events may also occur in the human oviduct but the number of oviducts which have been studied after ovulation is too few to draw any definite conclusion. In the bird oviduct, the ovum itself triggers the activity of the muscular wall of the oviduct, a process which is associated with frequency changes resembling those in the mammals. Thus it seems that, during the evolution, direct regulation of oviductal activity by the ovum itself has been reduced as the size of the ovum has decreased. However, such basic principles as the changes of the frequency and regional activation of the oviduct have been conserved. In mammals, these are regulated more directly by the ovarian hormones. Since ovum transport can be speeded up or retarded by hormonal treatments in various laboratory mammals, and since the oviductal muscular activity changes with the menstrual cycle in the human, it is likely that pathological changes in oviduct function leading to tubal pregnancy are related to hormonal changes (Pulkkinen and Talo, *Clin Obst Gynecol 30:* 164-172, 1987).

INTRODUCTION

The oviduct is an elastic muscular tube filled with mucosal folds. The folds fill the tube so completely that there is hardly any lumen in the isthmus when it is fixed by the method which causes minimal alteration to the tissue (Nilsson and Reinius, 1969). Thus, the isthmus has to be dilated before the eggs and embryos can pas through it. This is particularly evident in the rabbit in which the embryos reach a very large size, about 400 μm in diameter when they become coated in the isthmus with a mucin layer (Greenwald, 1969). The dilatation can result from enhanced fluid secretion, contractile activity interfering with the fluid flow, reduction in mucosal size, and relaxation of the isthmic circular musculature. Whatever mechanisms cause the dilatation propulsive forces are needed to transport the ova into and through the oviduct. Ciliary beat and contractions of the wall musculature provide the forces. I will review experimental and theoretical studies of the muscular activity but only those which are directly relevant to ovum and embryo transport and will omit studies of contractility in which such a relationship has not been established.

METHODOLOGICAL ASPECTS

Two different approaches have provided accurate quantitative information needed to understand the mechanisms of ovum and embryo transport; analysis of the movements of stained ova from cinematographic records (see Verdugo *et al.*,

1976) and the measurement of spread of electrical activity of the circular muscle layer using an array of closely spaced electrodes (Talo, 1974). These methods, together with complementary theoretical work, have been essential for bringing our understanding of the mechanism of ovum transport to the present level. Further progress requires analysis of the smooth muscle function, and of controlling mechanisms, at the cellular and molecular levels.

Methods of recording muscular activity

There are many ways to record muscular activity of the oviduct. Among these are direct recording of wall tension by miniature silicon transducers (Nelsen *et al.*, 1976), measurement of intraluminal pressure through a balloon (Maia and Coutinho, 1970) or through an open ended-catheter (Talo and Brundin, 1971) or contraction by an intraluminal silastic transducer (Blair and Beck, 1976). The wave length of a contraction is much longer than that of the myoelectrical activity since the contraction outlasts the electrical activity. Therefore, even if the sensor is so small that it measures the contraction locally, the measurements of contractile activity have less spatial resolution than measurements of electrical activity. Thus, by measuring mechanical activity it may be difficult to obtain reliable information about sites of initiation and direction and distance of spread of contractions. Such information is needed for understanding the role of the contractile activity in ovum and embryo transport. It can be obtained by recording electrical activity of the wall musculature using a set of electrodes. Of the various electrode types the most convenient is a suction electrode made of flexible polyethylene or silicone tubing by inserting a thin chlorided silver wire into the tube. The electrode is attached by suction onto the surface of the tissue and can be moved to a new place within a couple of seconds. If its size is matched with the size of the oviduct the myoelectrical activity can be recorded from the oviducts of different species. Since the suction electrodes are surface electrodes the musculature of the oviduct has to be exposed. This requires some dissection particularly in the isthmus. The dissection and *in vitro* recording may distort the activity but to what extent does this happen? Althought a direct comparison between *in vivo* and *in vitro* activity can not be made due to the lack of suitable *in vivo* recording methods indirect evidence suggests that the *in vitro* data may not differ much from the undisturbed activity. The *in vitro* data on properties of spread of electrical activity (Talo and Hodgson, 1978, Hodgson and Talo, 1978) match well with filmed *in vivo* movements of ova (Verdugo *et al.*, 1976). Ova recovered from the oviducts after *in vitro* recordings made at various times after ovulation, are located at sites corresponding to those treated in such a way that ova are not displaced by the procedures (Pauerstein *et al.*, 1974). There is a clear correlation between the spread of electrical activity and movements of ovum surrogates (Hodgson *et al.*, 1977), and ovum surrogate transport and real ovum tansport match well when the *in vitro* data are fitted into a simulation model (Portnow *et al.*, 1977a).

Chronically implanted wire electrodes have also been used by various authors to detect oviductal electrical activity. According to my own experience, in the rabbit oviduct, they record more easily the electrical activity of the extraoviductal smooth muscle than of the circular musculature. This is because of the intimate anatomical relation between the circular muscle and the subperitoneal, longitudinally-oriented smooth muscle and by the smallness of the electrical signal originating from the circular muscle compared to that of the subperitoneal smooth muscle layers. The low amplitude of the extracellularly-recorded electrical activity of the circular muscle layer is related to the small conduction velocity (1-4 mm/s). Thus, the length of the oviduct segment undergoing excitation is extremely short and the extracellular potential field generated by it is small. In the extraoviductal smooth muscle, excitation spreads faster and generates a signal which is easily detected by the implanted wire electrodes.

Relationship between electrical and mechanical activity

Like in a majority of muscle types the electrical activity of the oviduct smooth muscle triggers a contraction. Although not established in the smooth muscle of the oviduct, voltage-gated (L-type) calcium channels are opened during the action potential when the membrane potential becomes positive to −40 mV or −30 mV. When the channels are open a steep electrochemical gradient drives calcium ions into the cells. The more spikes there are during a spike burst the more calcium enters the cells and the stronger the contraction becomes since the level of intracellular calcium regulates the extent of contraction.

In the oviduct, the extracellularly-recorded electrical activity correlates well with the mechanical activity recorded as intraluminal pressure through a balloon (Fig. 1, A) or an open-ended catheter (Fig. 1, B) or by a tension transducer (Fig. 1, C). The amount of pressure or tension increases when the number of spikes increases like in other smooth muscle types. The detailed relationship between the characteristics of spike bursts and contractile strength has not, however, been worked out in any species.

In the studies of electrical activity, an assumption has been made that when electrical activity is recorded from one point of a circumferential segment of the oviduct the whole circumference works in

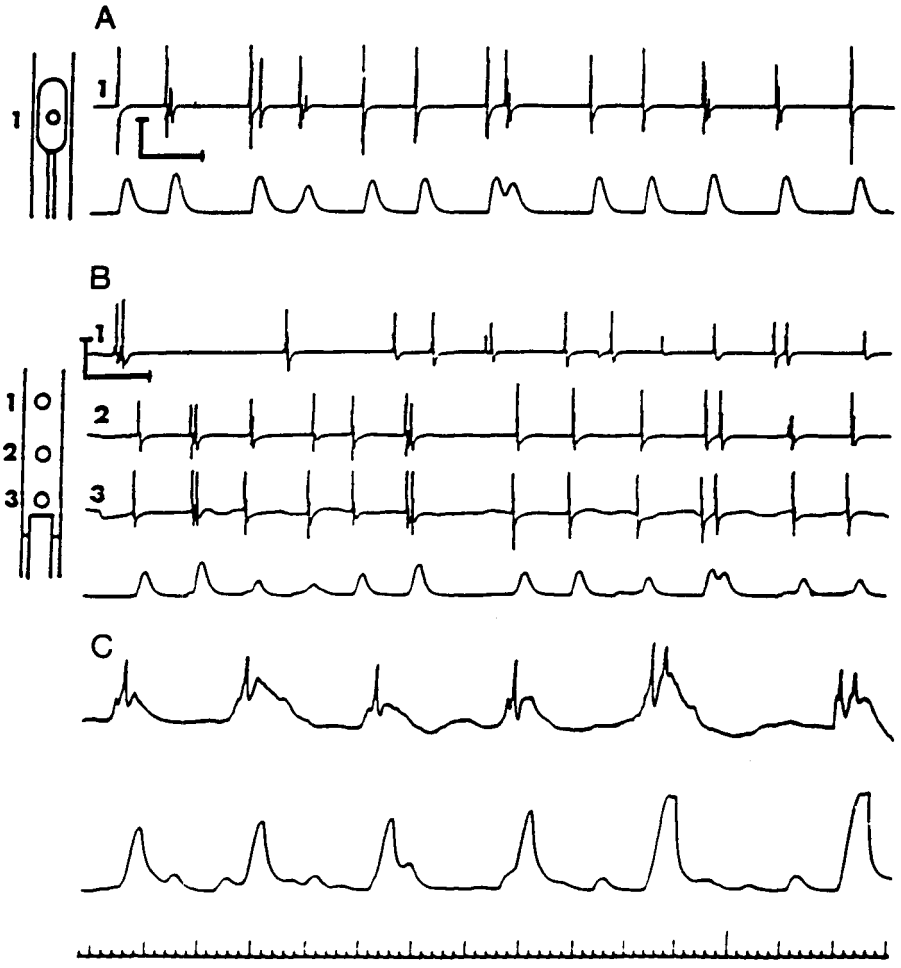

Fig. 1: A recording of electrical activity with a simultaneous measurement of intraluminal pressure by a balloon (Panel A), or by an open-ended catheter (Panel B) or measurement of tension of the muscle strip of the ampulla (Panel C). Rabbit oviduct.

synchrony. This may not always be the case since my unpublished observations indicate that there might be various degrees of asynchrony between points in the same circumference, or lack of activity in some points when other points are active. This may not be a serious problem when activity is recorded during ovum transport since the spread of electrical activity and movements of ovum surrogates are closely correlated (Hodgson, *et al.*, 1977).

Spread of electrical activity vs movements of ova or ovum surrogates

The relationship between spread of electrical activity and movements of ovum surrogates or ova has been studied in the rabbit ampulla (Hodgson *et al.*, 1977) and mouse oviduct (Talo, 1980). Correlation between electrical activity and ovum transport has been studied also in the bird, Japanese quail (Talo and Kekäläinen, 1976, Arjamaa and Talo, 1983).

The ovum surrogates used to study this relationship in the rabbit were of the size (400 μm diameter) which is transported approximately at the same speed as rabbit ova (Hodgson *et al.*, 1976). Fig. 2 shows 6 short segments (A-F) of a recording from a study of Hodgson *et al.* (1977). The recording was made in the ampulla near the ampullary-isthmic juction (AIJ) with 7 small suction electrodes. The distances (in mm) between the centers of the electrodes are marked on the right. Arrows indicate spread of activity. The location of one or two surrogates before the event and their new location after the event is shown by a shaded and open circle. The events were selected to illustrate general rules of the relationship between spread of electrical activity and movements of surrogates. These are: i) Surrogates are displaced only by contractions occuring in their immediate vicinity but not by contractions appearing at a distance which exceeds a few millimeters. In Panel A, the event which starts under electrode 2 and spreads to electrodes 1 and 3 does not move the ovum surrogate located between electrodes 5 and 6. The distance from which the contraction moves the ovum surrogate may not be defined simply since it depends on the amount of fluid in the lumen, on the lenght to which the contraction spreads and on the distensibility of the wall. Thus, if other factors were identical the distance would be longer in the isthmus than in

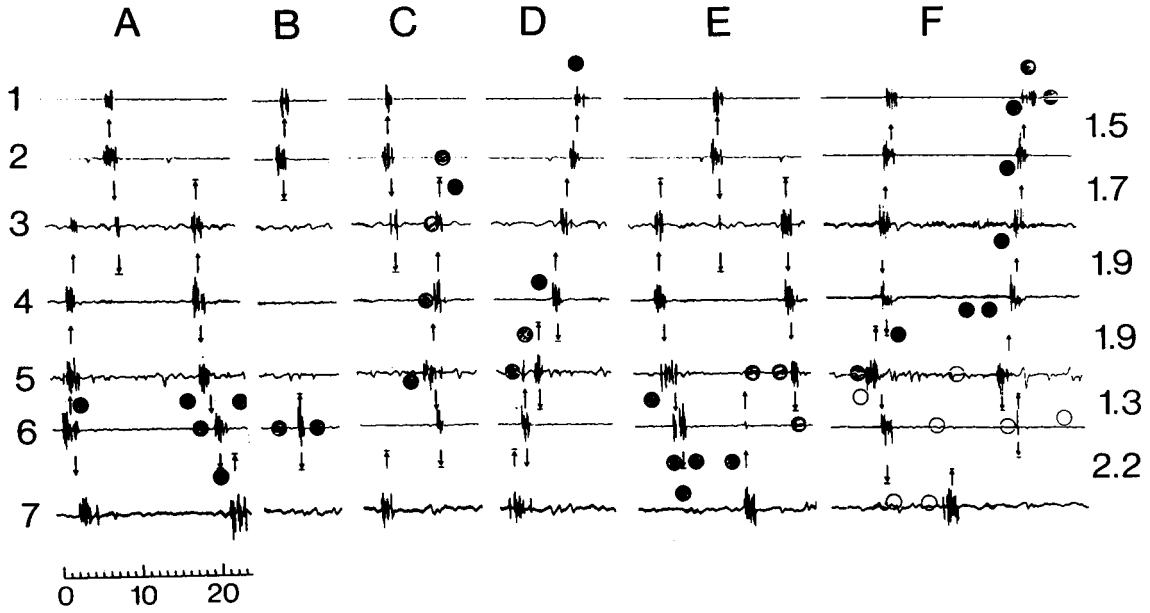

Fig. 2: Six short segments (A-F) of recording of electrical activity, made with 7 suction electrodes, in the rabbit ampulla near the AIJ at 68 h after ovulatory injection of hCG. The distances between the centers of the electrodes (in mm) are shown in the right. Locations of one or two 400 μm ovum surrogates before and after individual events are shown by a shaded and open circle. From Hodgson *et al.*, 1977.

the ampulla since it has a thicker, less elastic wall. ii) The direction and distance of displacement of the ovum surrogate is directly proportional to the distance of spread of contractions. (Panels B, C, D). Local contractions may cause a small net movement or no net displacement since the surrogate may return to its original position when the contraction ceases (Panel B). After a longer displacement there is often a small backward movement caused by backward fluid flow when the contraction subsides (Panels C and F). In Panel D, the ovum surrogate is moved into the ovarian direction, first by an activity initiating under electrode 6 and spreading only to electrode 5. The next activity is local, appearing only at electrode 5 but it shifts the surrogate slightly further, past the electrode 4. The third event, which starts under electrode 4, spreads to electrode 1 and displaces the surrogate past electrode 1. iii) It follows from [ii] that surrogates are displaced from the area where contractions initiate and spread. They move back and forth in the areas in which contractions propagating toward each other die out. An example of this is shown in Panel E in which the ovum surrogate moves in the vicinity of electrode 6. In Panel F, two surrogates are initially close to each other. They are first separated by an event which initiates between them. The second event, appearing under electrode 7, brings the surrogate marked by the open circle again near electrode 5. Then they are again separated when the next event moves the surrogate, indicated by the filled circle, past electrode 1. This series of events illustrates one aspect of the random nature of ovum transport. As the result of a difference in position of a fraction of a millimeter ova may be moved in opposite directions. It also emphasizes that the effects of contractions on the movements of ova are very local.

IS THE OVIDUCT A CHAIN OF OSCILLATORS?

Electrical activity of the rabbit oviduct is not stable. Activity initiates independently in many areas and the points where the activities initiate shift. The direction, distance and apparent velocity of the spread of excitation also vary. This variation is clearly illustrated in Figure 3 which is from an unpublished study by the author (18 h after ovulatory injection of (hCG) human Chorionic Gonadotropin. In the beginning of Panel A the activities of electrodes 1 and 2, 3 and 4 and 5 and 6 are coupled. In the center of Figure 3A, activity under electrode 3 becomes coupled with that of 1 and 2 breaking the coupling between electrodes 3 and 4. A moment later (Panel B), the activity starting under electrode 2 spreads to electrode 4 or 5 and at that time the coupling between 5 and 6 breaks. At the end of Panel B, the activity again becomes disrupted. This kind of behaviour could be explained if the oviduct is assumed to consist of a chain of narrow segments each acting as a relaxation oscillator like the small intestine (Sarna *et al.*, 1971). Each segment has its own inherent excitability cycle regulated by ovarian hormones and other regulatory mechanisms. If there is no influence from the neighbouring segments the segment maintains its own cycle. Sensitivity to influence from the neighbouring segment appears to depend on the phase of the excitability cycle. It is highest just before and after the moment when the segment would become active spontaneously. According to my unpublished observations, in the rabbit and human oviduct, the cycle length is not stable. Spontaneous variations and/or influence from the neighbouring segments change the cycle length and alter the timing of the activity. Thus, adjacent segments which were out of phase may suddenly get back in phase and the activity spreads from one to the next, starting from the segment which happens to become active first. This point would be defined as a temporary pacemaker. This variation of the cycle length is a very important factor causing shifting of (apparent) pacemaker location and altering the direction of spread of contractions in the rabbit oviduct. In the human oviduct, its effects are less pronounced because of the long distance between the pacemaker areas. The

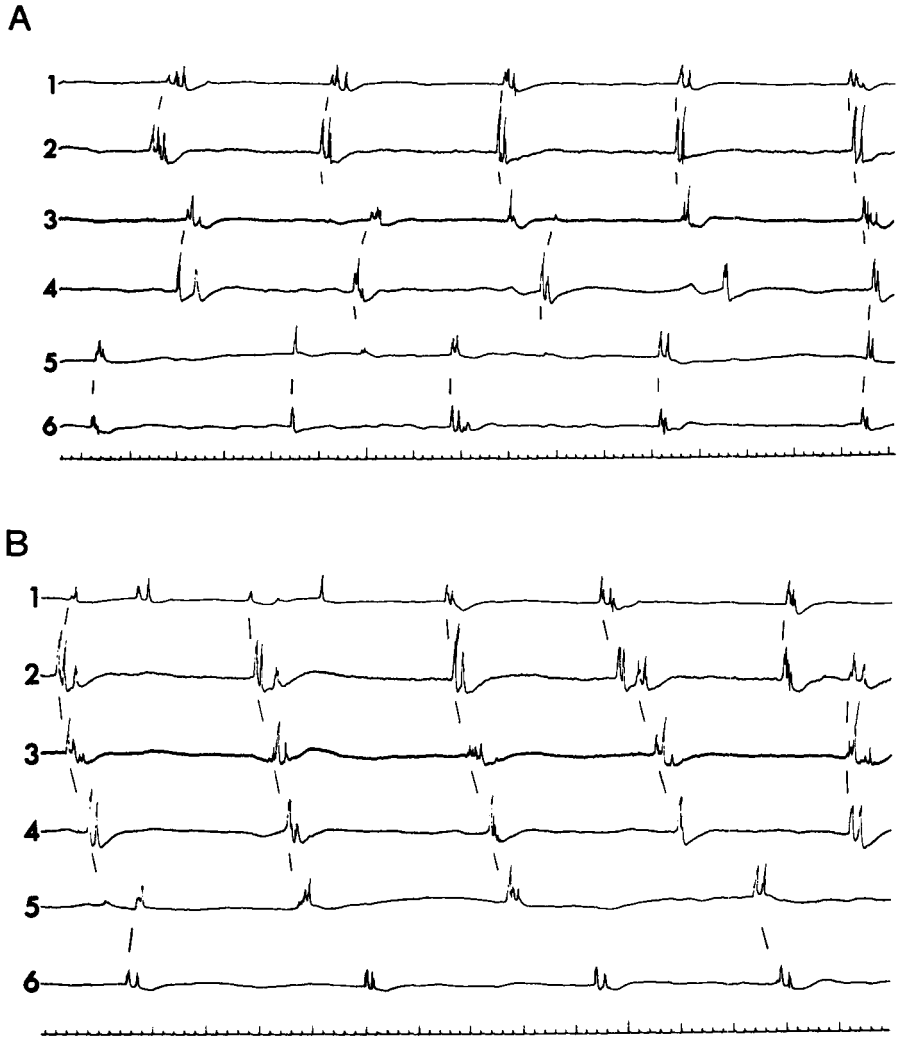

Fig. 3: Two short segments (A and B) from a recording from a postovulatory (18 h after HCG) rabbit ampulla, near the AIJ. The interelectrode distances are about 2 mm. Time marked in seconds. This is an example in variation of coupling between the nearby segments.

only effect of the temporary shortening or lengthening of the cycle in one pacemaker is the shifting of the area where the spreading activities meet. In the rabbit oviduct, the pacemaker areas are just a few millimeters apart. Thus even a small alteration of the cycle length of about 20s may have an effect since the activity spreads a distance of 2 mm in one or two seconds.

In the rabbit oviduct and in the ampulla of the human oviduct, regularity of spread is disrupted and the pattern of electrical activity becomes more disorganized after ovulation compared to the oestrous or follicular phase, respectively. This could be a direct consequence of an enhanced tendency to become active spontaneously and could be related to depolarization of the membrane potential by progesterone (Nozaki and Ito, 1987).

ACTIVITY ALONG THE WHOLE OVIDUCT

When it had been established that there was a good correlation between the spread of electrical activity and movements of ovum surrogates the question arose: Is it possible to analyse the electrical activity along the whole oviduct to such a degree of accuracy

that it would be possible to understand such characteristics of ovum transport as its delay (or slowing down) at the AIJ, the slow transport through the isthmus and the timing of the entry of embryos into the uterus? To this aim, the electrical activity was analysed along the whole oviduct at different intervals after ovulation and after hormonal treatments aimed at accelerating or delaying the ovum transport in the rabbit (Talo and Hodgson, 1978, Hodgson and Talo, 1978).

Characterization of electrical activity along the whole oviduct was done, later on, also in the mouse (Talo, 1980) and the human (Talo and Pulkkinen, 1982). In addition to these three mammalian species, a comparable study has been done in the oviduct of a bird (Japanese quail) (Talo and Kekäläinen, 1976, Arjamaa and Talo, 1983).

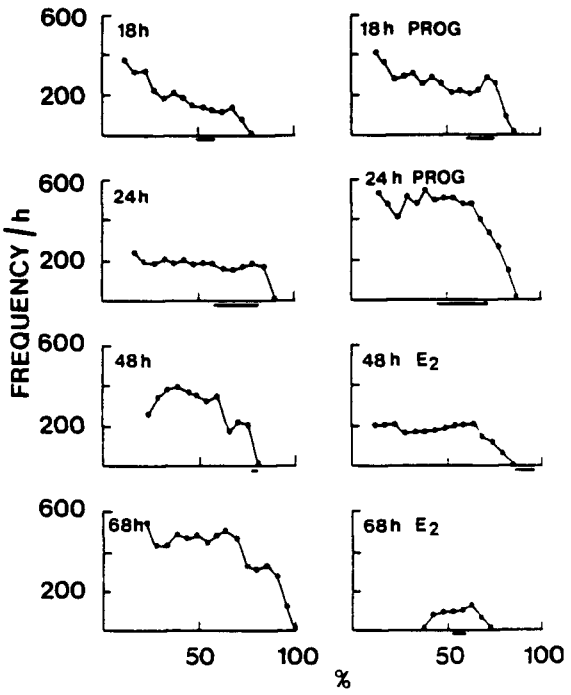

Fig. 4: Profiles of the mean frequency of spike bursts along the rabbit oviduct in control animals at 18 h, 24 h, 48 h, and 68 h after ovulatory injection of hCG and at 18 h and 24 h after accelerating ovum transport by treatment with progesterone or estradiol (at 48 h) and, at 68 h. after "tube locking" by estrogen treatment. The line under the abscissa indicates the range of locations of oviductal ova. From: Talo and Hodgson, 1978; Hodgson and Talo, 1978.

Rabbit oviduct

At 18 h after ovulatory injection fo hCG, electrical activity could be recorded in the whole ampulla and in 60% of the isthmus. About 40% of the isthmus, on the uterine side, was inactive. That the inactivity was real and not due to faulty recording was confirmed by exciting the inactive region with carbacholine. During the carbacholine effect, activity appeared in the electrodes which had previously recorded no activity. The inactive region becomes shorter with time and, at 68 h, when ova were found even in the uterus the activity was present throughout the isthmus (Fig. 4). Thus, during ovum transport, ova are first in the active area. Later on, they are found at the borderline of active and inactive regions. The forward progress of the ova depends on a progressive shift of the borderline towards the uterus. The entry of the ova into the uterus ensues when the region which is most proximal to the uterus also becomes active. The inactivity may not be total *in vivo* since small spheres (100 or 200 μm in diameter) are transported much faster into the uterus than ova or ovum-size spheres (Hodgson *et al.*, 1976).

An increase in the frequency is a prominent feature of activity during the postovulatory period (Talo, 1974, Talo and Hodgson, 1978, Hodgson and Talo, 1978). Hormonal treatments which either accelerate or delay ovum transport affect the frequency and the length of the inactive isthmic segment (Fig. 4). When ovum transport is accelerated by progesterone the rise in frequency takes place earlier than in the control oviducts (Hodgson and Talo, 1978). However, the frequency drops when ovum transport is accelerated with estradiol. A high dose of estradiol (250 μg) which causes so-called tube blocking and stops ovum transport for a long time (Greenwald, 1961) does so by inhibiting the oviductal activity. No electrical or contractile activity was detected in many oviducts and, when present, it was localized to the region around the ampullary-isthmic junction. These data show that although the frequency increases during ovum transport its role is not crucial in determining the speed of ovum transport. Bias, length of the

spread and length of the actively contracting region are the important factors.

Considering the high degree of variability of electrical activity and the influence of small differences of location of the surrogate ova on their movements (Fig. 2F), it is obvious that ovum transport in the rabbit contains a large random component. This was elegantly pointed out by Verdugo *et al.* (1976) on the basis of accurate analysis on ovum movements. Due to the random component it is not possible to predict the detailed course of movements of the ova even if the characteristics of the contractility were known. Actually, there is no need to do so. As pointed out above, ova and embryos spend a period of time in the actively contracting area but then enter the inactive region. The entry to the uterus is determined by activation of the inactive segment near the uterine end of the isthmus. It has been shown that even if the movements of ova were completely random, they would be transported through the oviduct (Portnow *et al.*, 1977a). This happens if two requirements are filled. One; there is a reflecting barrier in the ovarian end of the oviduct, i.e. once the ova enter the oviduct they are never expelled back into the abdominal cavity. Two; there is an absorbing barrier in the isthmus and, finally, in the uterus from which the ova do not return to the rest of the oviduct. These requirements are both filled. The contractile activity is weak in the fimbrial end of the oviduct but the ova are transported effectively into the uterine direction by the unidirectional ciliary beat. Thus, the fimbrial end acts as the reflecting barrier, always returning ova back to the rest of the oviduct if they happen to be pushed there by the contractile activity. The inactive isthmic region and, finally, the uterus act as the absorbing barrier since the embryos cannot return from the inactive region to the actively contracting region unless a segment on their uterine side becomes active. The speed of transport under conditions in which movements are random (random walk is critically dependent on the step size (diffusion coefficient) and less on the frequency of the steps. Lengthening of the steps speeds up the transport. In the rabbit oviduct the electrical activity spreads for short distances. The majority of the electrical waves spread less than 2 mm (Fig. 5), i.e. less than 2% of the oviduct length. Thus, the transport consists of short steps throughout the oviduct. The fre-

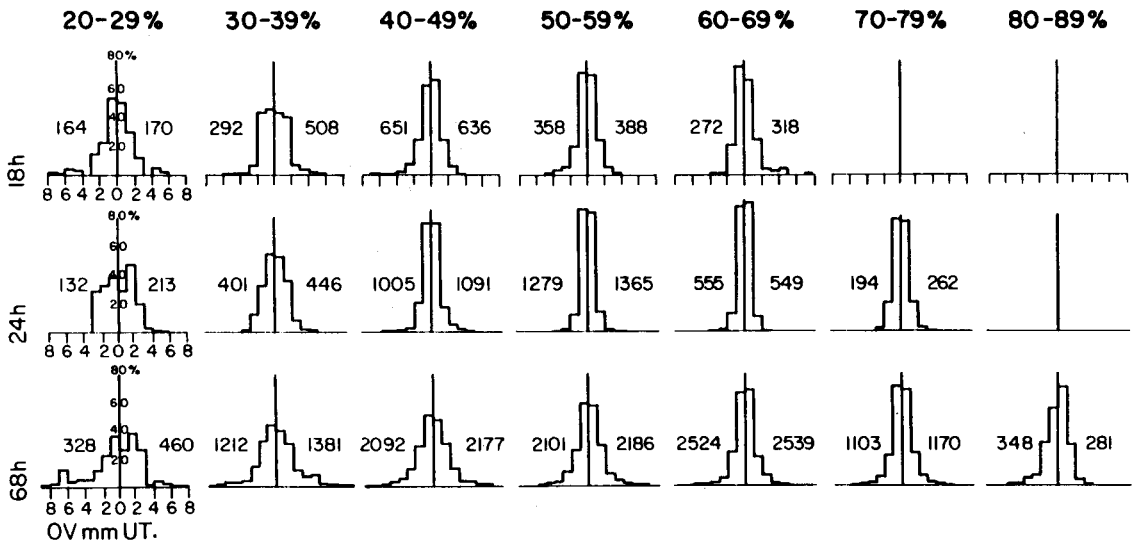

Fig. 5: Frequency histograms of the distance of spread of electrical activity in ovarian (OV) and uterine (UT) direction, in different oviductal segments representing 10% of the length of the rabbit oviduct. Recording performed at 18 h, 24 h and 68 h after ovulatory injection of hCG. From: Talo and Hodgson, 1978.

quency of movements increases during the transport. Thus, it would ensure that embryos enter the absorbing barrier in time. Also, if the activity were random the decline in frequency from the ampulla towards the uterus would be an effective factor guarantying the transport of ova in the uterine direction.

Although it seemed that even a completely random activity was capable of transporting ova, it was not clear that the contractile activity is random. At least, during short periods of recording (10 min), there are regions in which spread was strongly biased (Fig. 6). Regions of high pro-uterine bias alternate with those of pro-ovarian bias. To be able to assess whether the differences in the bias could explain such observations as delay in ovum transport at the ampullary-isthmic junction, the data obtained by analysing the electrical activity along the whole oviduct at different times following hCG injection were fitted into a Monte Carlo simulation model (Portnow *et al.*, 1977b). Some simplifications were made, e.g. the length of the steps was fixed at 1% of the oviduct length, and the frequency of steps was taken to be similar for each 5% long segment. This frequency was the average of at least 10 oviducts for each segment. The simulated ovum transport closely mimicked normal transport with back and forth movements and gradual pro-uterine progress. Interestingly, the transport did not continue through the AIJ when the data of 18 h after hCG was fed into the computer. On the other hand, when the 68 h data were used the ova were transported through the AIJ and reached the borderline between active and inactive regions. At this time donor eggs are transported through the AIJ and rapidly catch up with the native eggs in the rabbit (Tsutsumi *et al.*, 1975). These data suggest that the contractile activity alone is capable of transporting ova in the oviduct and that the differences in bias can effect the transport speed, particularly in the AIJ. However, there may be other gating mechanisms in this region (Gomez and Croxatto, 1977, Weinberg and Pauerstein, 1980). The effect of bias on the transport velocity is understood by considering that if in two adjacent segments the probability of pro-uterine spread (P) is 0.1 in only one case out of 100 the sequence of contractions is such that ova would get transported through both segments. As can be seen from Fig. 6, regions of pro-uterine bias alternate with those of pro-ovarian bias. Thus, regions of pro-ovarian bias are found a few millimeters apart.

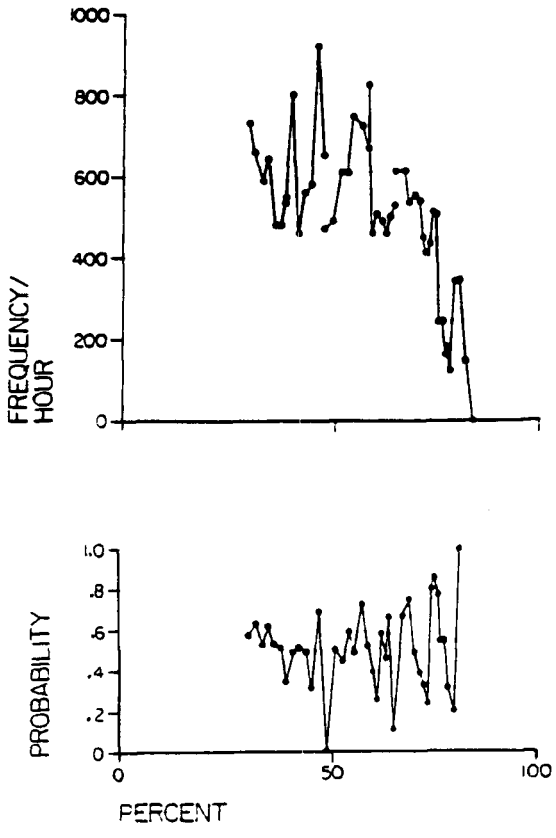

Fig. 6: Variation of frequency and probability of spread of electrical activity in the uterine direction along the rabbit oviduct at 68 h after injection of hCG. The sites of initiation of activity are represented as percent of total oviduct length. From Talo and Hodgson, 1978.

The ciliary beat in the ampulla transports ova effectively into the uterine direction. This transport is linear and fast in the absence of contractile activity (Halbert *et al.*, 1976). This linear force ensures that ova are rapidly transported to the AIJ. Thus, even if the isthmic activity were completely random it would have time to move fertilized ova to the borderline between activity and inactivity. The most advanced theoretical work which com-

bines ciliary and contractile activity is that of Verdugo *et al.* (1980).

Mouse oviduct

The very complex stochastic contractile activity of the rabbit oviduct during ovum and embryo transport may not have a counterpart in other mammals. In the mouse and human oviduct the pacemaker sites remain more stable and their number is much fewer than in the rabbit. The electrical activity spreads regularly and there is much less randomness in the activity pattern (Fig. 7). When ova are in the ampulla of the mouse, electrical activity initiating over the ova spreads in both directions but dies out before it reaches the AIJ. A separate activity which initiates at the pacemaker located in the isthmus near the AIJ spreads toward the ovary but does not reach the AIJ. Thus, the ova in a bolus of fluid swing back and forth without any net movement. Presumably, there is a period during which contractions spread from the ampulla to the isthmus through the AIJ and displace the ova into the isthmus but I did not capture that moment. Later on, when the ova are in the isthmus near the AIJ (Fig. 8) the contractions initiate in the ampulla, spread through the AIJ and die out in the isthmus. With time, the activity spreads progressively further towards the uterus. There is a segment of inactivity or of a low frequency next to the ova on their uterine side, but slightly further towards the uterus, there is a separate pacemaker from which activity propagates towards the ova (Figs. 7 and 8). Thus, ova bounce back and forth within a bolus of fluid at the region where contractions die out. When the transport progresses, the pacemaker which is located on the uterine side of the ova shifts towards the uterus but the one near the AIJ remains stable. My observations indicate that when the contractions propagating in the uterine direction push the oviductal fluid forward into the segment in which the ova are located they are not capable of dilating the closed segment on their uterine side. Thus, fluid begins to flow backwards at a high speed under the contraction while it continues to propagate in the uterine direction. When the contraction then dies out, the fluid and ova return to their original segment. It is not clear whether the inability of the fluid to dilate the segment on the uterine side of the ova is because of a sustained contracture of this region or because of the other, often simultaneous, contractions propagating in the opposite direction (Fig. 7). Since the region in which the ova are confined shifts towards the uterus it must be accompanied by a progressive relaxation of the closed isthmic segment and/or progressive shift of the pacemaker located on the

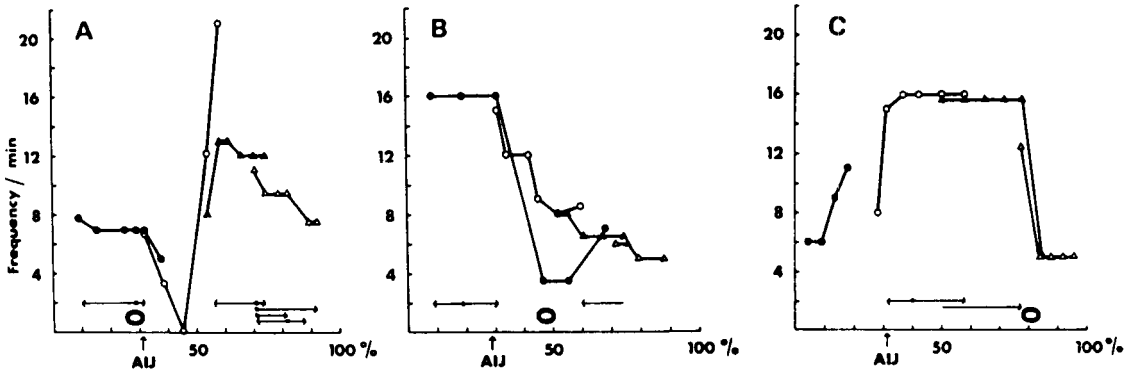

Fig. 7: Frequency profiles of the electrical activity along the mouse oviduct when ova (indicated by an ovoid are located in the ampulla (A), proximal isthmus (B) or distal isthmus (C). Arrows indicate direction and distance of spread of electrical activity from the pacemakes marked by a dot. Each symbol represents a different array of electrodes. From Talo, 1980.

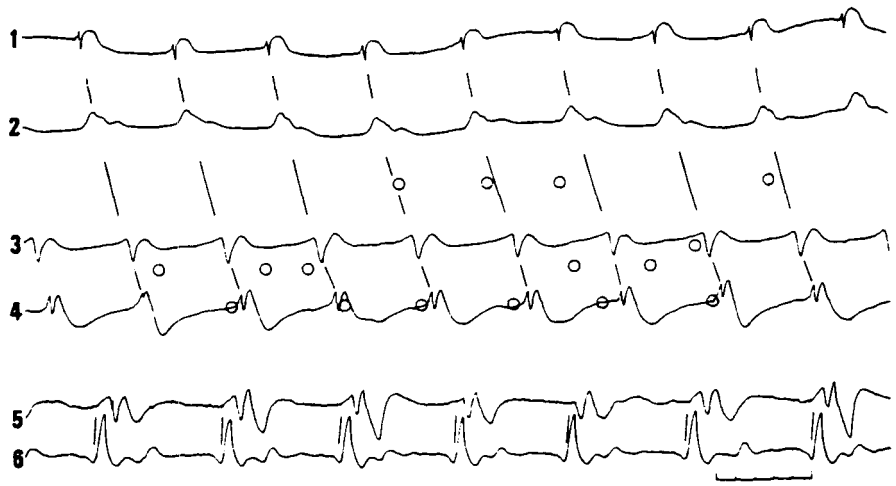

Fig. 8: Spread of electrical activity in the mouse oviduct *in vitro*. Electrode N° 1 is located at the AIJ, and N° 6 is at the TUJ. The distances between the traces are proportional to the interelectrode distances. Locations of ova at given moments are indicated by open circles. The spread from electrode 1 ceases in the region between electrodes 4 and 5. Another activity which has a slightly lower frequency spreads from electrode 6 to 5.

uterine side of the ova. At the early stage of the isthmic transport, when the ova are close to the AIJ, there can be more than one pacemaker in the isthmus between the ova and the tubo-uterine junction. Entry of ova into the uterus would, in the mouse, be associated with the spread of contractions from the AIJ to the uterine end of the isthmus.

The transparency of the isthmus and the relatively large volume of fluid filling the isthmus make observations of the fluid flow and movements of ova more readily available in the mouse than in the rabbit oviduct. Whether also in the rabbit isthmus fluid is pushed against a closed segment at the borderline of the active and inactive regions of the isthmus is not known.

Human oviduct

The pattern of contractile activity of the human oviduct resembles more that of the mouse than of the rabbit oviduct. The number of pacemakers is low and the spread of activity is regular except after ovulation in the ampulla (Talo and Pulkkinen, 1982). The pattern and wave form change during the menstrual cycle. When the activity in both oviducts of women were compared they were surprisingly similar. The same holds true for different women at the same phase of the cycle. Before ovulation (day 12 of the cycle) most of the electrical activity begins in two pacemakers, one located at the uterine end of the isthmus and the other near the ovarian end of the ampulla. The contractions spread towards the middle region of the oviduct. The area where they meet is around the ampullary-isthmic junction (Fig. 9). This kind of activity would be capable of transporting ova and spermatozoa towards each other. In the postovulatory oviduct the ampullary activity is more disorganized than during other phases of the cycle and a single wave changes to an irregular burst of spikes. This change of the wave form occurs later on in the isthmus. The spreading activity often begins in the ampulla a short distance from the AIJ and propagates in the uterine direction (Fig. 10). The distance of propagation is variable and, occasionally at least, there is an independent focus of activity on the uterine side of this activity. In this respect, there is a resemblance between the mouse and human oviduct.

INTERACTION BETWEEN THE MUSCULAR LAYERS OF THE OVIDUCT

The ampulla of the oviduct consists of a circular muscle layer but the isthmus also has an inner longitudinal muscle layer

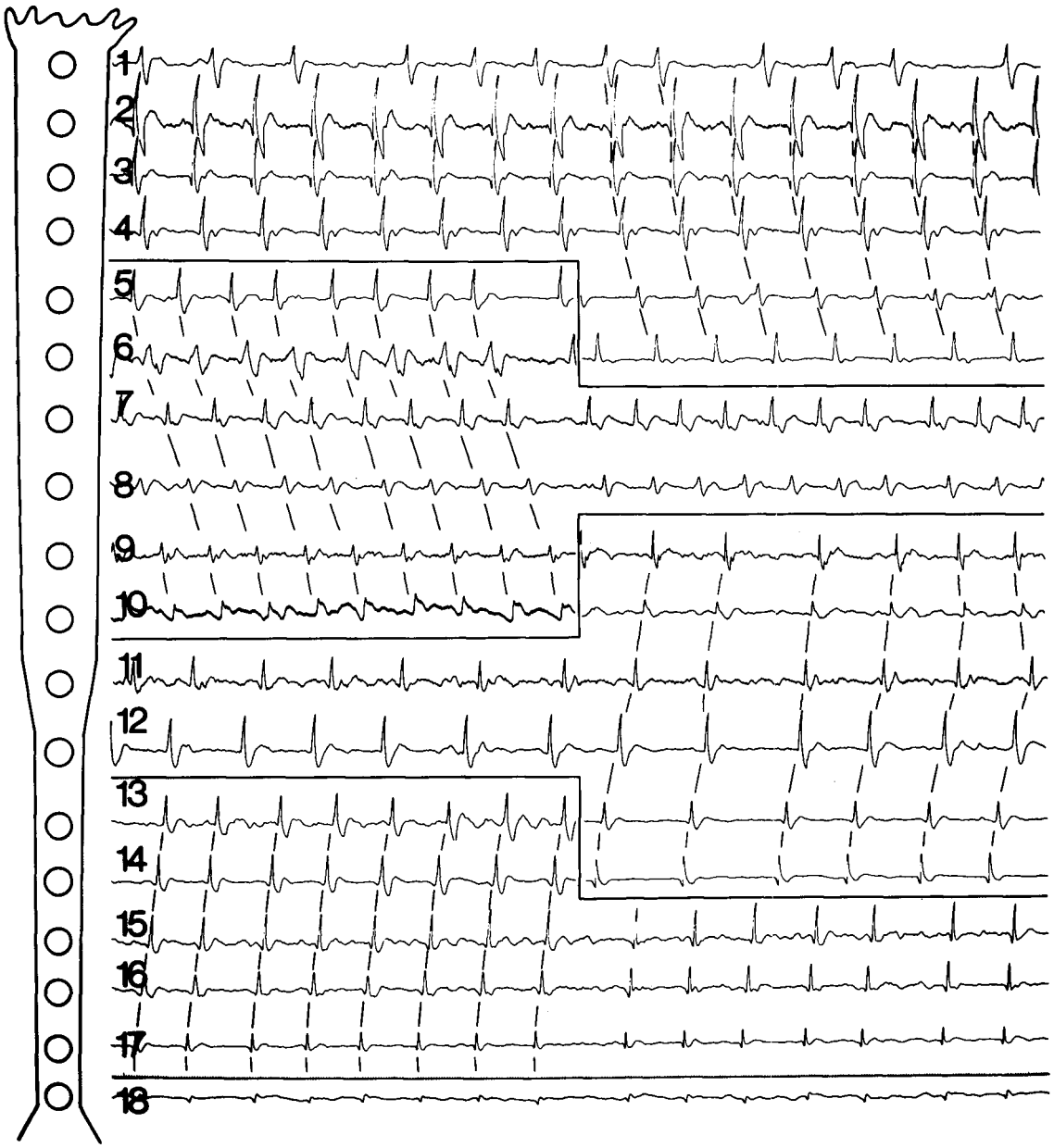

Fig. 9: Spread of electrical activity in the human oviduct on day 12 of the menstrual cycle. The locations of suction electrodes are illustrated on the left. Activity which initiates at or near the ends of the tube spreads towards the center.

(Pauerstein *et al.*, 1970). In the isthmus the circular layer is in close association with the smooth muscle of the oviductal ligaments. In the ampulla this association varies between species. In the rabbit it is intimate but in the human the circular muscle is separated from the smooth muscle layers of the ligaments. Due to the intimate anatomical relationship between these muscle layers there is a possibility for functional interaction. Relatively little attention has been paid to this. The character of electrical activity of the ligaments of the oviduct is different from that of the oviduct circular layer in the rabbit (Talo and Brundin, 1973). Long bursts appearing with a low frequency are usually recorded in the ligaments while the bursts are of shorty duration and have a higher frequency in the oviduct. During the study of

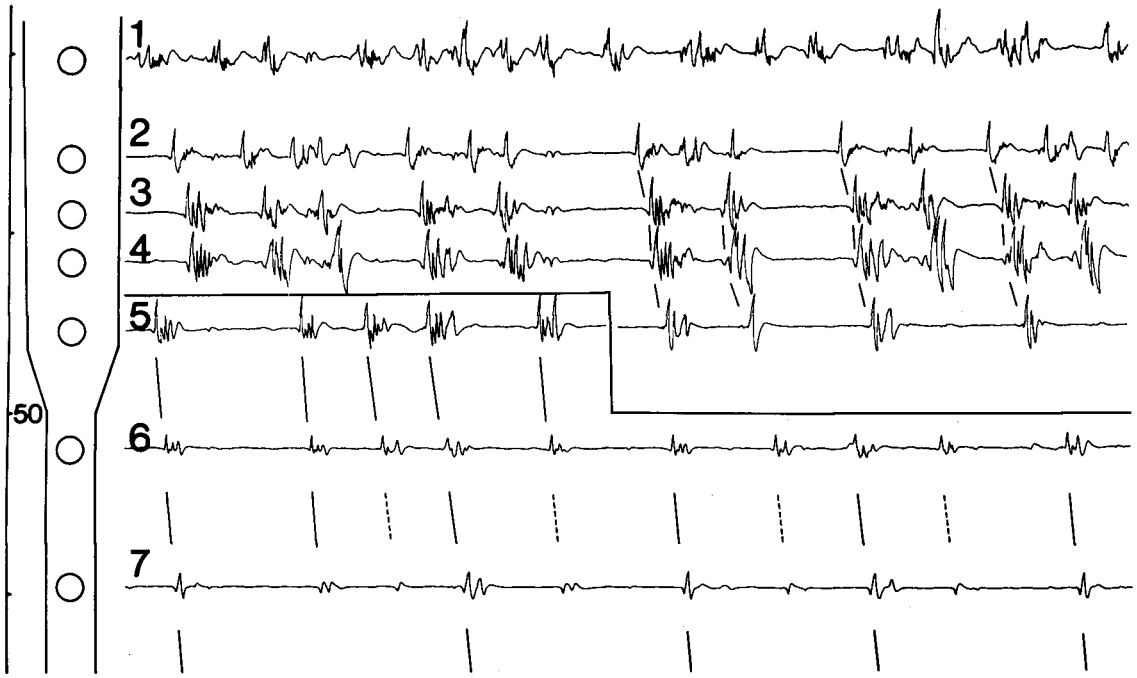

Fig. 10: Spread of electrical activity in the human oviduct shortly after ovulation.

electrical activity of the rabbit oviduct (Talo and Hodgson, 1978; Hodgson and Talo, 1978) we also paid attention to the possible interaction between the oviductal and ligamental activity. In only one rabbit out of dozens did we find indications of interaction in the isthmus. When this region was processed histologically there was a clear continuation from the smooth muscle bundles of the ligaments to those of the isthmus. Thus, although the majority of the data suggests that there is little or no spread of excitation between the ligaments and the oviduct circular layer this possibility cannot be ruled out completely.

Another interesting question is a possible functional interaction between the inner longitudinal and circular muscle layer of the isthmus. Could it be that there is a somewhat similar functional arrangement between these layers as between the two muscular layers of the intestine (Sanders, 1989). Although not pointed out in the publications, indications of an interaction between the isthmic muscle layers have been observed in estrogen-treated castrated rabbits (Talo and Brundin, 1973), and in estrogen treated (250 μg given at 24 h after ovulatory injection of hCG) rabbits (Hodgson and Talo, 1978). Fig. 11, shows an example of this. At regular intervals a small spike initiates under electrode 2 or 3 and spreads in both directions. Some of these small spikes are followed by a higher spike. The high spike originates from the circular muscle layer. The small size of the first signal could indicate that it originates from a layer which is beneath the circular muscle layer, *i.e.* from the inner longitudinal layer. This suggests that the circular layer activity may only periodically be coupled to that of the longitudinal layer. If that were true, an organization resembling that of the small intestine could perhaps operate in the isthmus.

The possible interaction between the inner longitudinal and circular muscle layer is being studied presently in the human oviduct by the author and Dr. B. Lindblom in collaboration. The preliminary data suggest that, when dissected partly free from the circular layer, the inner longitudinal muscle layer has a higher spontaneous frequency than the circular muscle layer. It may have a high frequency also when in association with the circular layer or else its frequency is low coinciding with that of the circular layer. This sug-

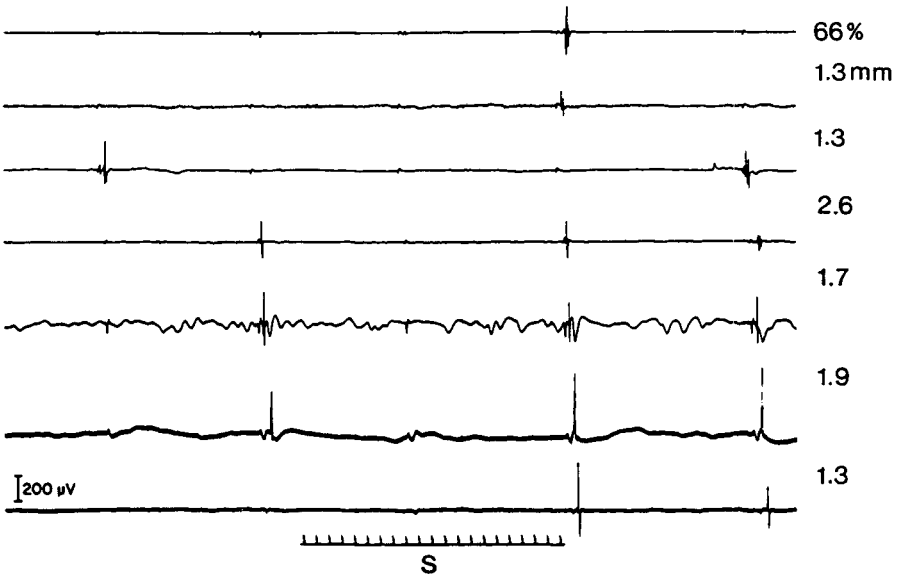

Fig. 11: Spread of low amplitude electrical activity in the isthmus of a rabbit, injected with 250 µg estradiol cyclopentylpropionate 24 h after an ovulatory injection of hCG, and studied at 48 h after hCG injection. Small spikes initiate at a region of the electrodes 2 and 3 and spread to electrodes 1 and 7. Some, but not all of these, are followed at various intervals in different electrodes by a higher spike. The location of electrode 1 is at 66% of the oviduct length.

gests that there can be various degrees of coupling between these two isthmic muscle layers.

REFERENCES

ARJAMAA, O.; TALO, A. (1983) Smooth muscle of the quail oviduct acts as a stretch receptor during ovum transport. *Biol. Reprod. 29:* 472-478.

BLAIR, W.D.; BECK, L.R. (1976) A system for measurement of oviductal motility and contractility and chronic changes in luminal diameter. In: *Ovum transport and Fertility Regulation.* World Health Organization Symposium. Edited by Harper, M.J.K.; Pauerstein, C.J.; Adams, C.E.; Coutinho, E.M.; Croxatto, H.B.; Paton, D.M. Scriptor, Copenhagen, pp. 41-74.

GOMEZ, C.V.; CROXATTO, H.B. (1977). A study of the time course of egg retention activity in the rabbit oviduct. *J. Reprod. Fert. 50:* 69-73.

GREENWALD, S. (1961) A study of transport of ova through the rabbit oviduct. *Fert. Steril. 12:* 80-95.

GREENWALD, G.S. (1969) Endocrinology of oviductal secretions. In: *The Mammalian Oviduct, Comparative Biology and Methodology*, Eds. Hafez, E.S.E.; Blandau, R.J. University of Chicago Press, Chicago, pp. 183-201.

HALBERT, S.A.; TAM, P.Y.; ADAMS, R.J.; BLANDAU, R.J. (1976) An analysis of the mechanisms of egg transport in the ampulla of the rabbit oviduct. *Gynecol. Invest. 7:* 306-320.

HODGSON, B.J.; CROXATTO, H.B.; VARGAS, M.I.; PAUERSTEIN, C.J. (1976) Effect of particle size on the time course of transport of surrogate ova through the rabbit oviduct. *Obst. Gynecol. 47:* 213-217.

HODGSON, B.J.; TALO, A. (1978) Spike bursts in rabbit oviduct. II. Effects of estrogen and progesterone. *Am. J. Physiol. 234:* E439-E443.

HODGSON, B.J.; TALO, A.; PAUERSTEIN, C.J. (1977) Oviductal ovum surrogate movement: Interrelation with muscular activity. *Biol. Reprod. 16:* 394-396.

MAIA, H.S.; COUTINHO, E.M. (1970) Peristalsis and antiperistalsis of the human fallopian tube during menstrual cycle. *Biol. Reprod. 2:* 305-314.

NELSEN, T.S.; NUNN, T.A.; ANGELL, J.B. (1976) Microminiature transducers for oviductal motor function. In: *Ovum Transport and Fertility Regulation.* World Health Organization Symposium. Edited by Harper, M.J.K.; Pauerstein, C.J.; Adams, C.E.; Coutinho, E.M.; Croxatto, H.B.; Paton, D.M. Scriptor, Copenhagen, pp. 75-98.

NILSSON, O.; REINIUS, S. (1969) Light and electron microscopic structure of the oviduct. In: *The Mammalian Oviduct, Comparative Biology and Methodology.* Eds. Hafez, E.S.E.; Blandau, R.J. University of Chicago Press, Chicago, pp. 57-83.

NOZAKI, M.; ITO, Y. (1987) Changes in physiological properties of rabbit oviduct by ovarian steroids. *Am. J. Physiol. 252:* R1059-R1065.

PAUERSTEIN, C.J.; ALEXANDER, R.W.; MOBLEY, M.A.; FREMMING, B.D. (1970) Comparative anatomy of the inner longitudinal muscle layer of the oviduct isthmus. *Obst. Gynecol. 35:* 504-512.

PAUERSTEIN, C.J.; ANDERSON, V.; CHATKOFF, M.L.; HODGSON, B.J. (1974) Effect of estrogen and progesterone on the time-course of tubal ovum transport in the rabbit. *Am. J. Obst. Gynecol. 120:* 299-308.

PORTWNOW, J.; TALO, A.; HODGSON, B.J. (1977a) A random walk model of ovum transport. *Bull. Mathem. Biol. 39:* 349-357.

PORTNOW, J.; HODGSON, B.J.; TALO, A. (1977b)

Simulation of oviductal ovum transport. *Can. J. Physiol. Pharmacol. 55:* 972-974.

PULKKINEN, M.O.; TALO, A. (1987) Tubal physiologic consideration in ectopic pregnancy. *Clin. Obst. Gynecol. 30:* 164-172.

SANDERS, K.M. (1989) Colonic electrical activity: Concerto for two pacemakers. *New Physiol. Sci. 4:* 176-181.

SARNA, S.K.; DANIEL, E.E.; KINGMA, Y.J. (1971) Simulation of electrical activity of small intestine. *A. J. Physiol. 221:* 166-175.

TALO, A. (1974) Electric and mechanical activity of the rabbit oviduct *in vitro* before and after ovulation. *Biol. Reprod. 11:* 335-345.

TALO, A. (1980) Myoelectrical activity and transport of unfertilized ova in the oviduct of the mouse *in vitro. J. Reprod. Fert. 60:* 53-58.

TALO, A.; BRUNDIN, J. (1971) Muscular activity in the rabbit oviduct: A combination of electric and mechanic recordings. *Biol. Reprod. 5:* 67-77.

TALO, A.; BRUNDIN, J. (1973) The functional connections and contractile function of the upper reproductive tract in female rabbits. *Biol. Reprod. 9:* 142-148.

TALO, A.; HODGSON, B.J. (1978) Spike bursts in rabbit oviduct. I. Effect of ovulation. *Am. J. Physiol. 234:* E430-E438.

TALO, A.; KEKALAINEN, R. (1976) Ovum promotes its own transport in the oviduct of the Japanese quail. *Biol. Reprod. 14:* 186-189.

TALO, A.; PULKKINEN, M.O. (1982) Electrical activity in the human oviduct during the menstrual cycle. *Am. J. Obst. Gynecol. 142:* 135-147.

TSUTSUMI, Y.; OGURI, N.; HAFEZ, E.S.E. (1975) Rapid transport of alien eggs transplanted 66 hours post coitum in the oviduct of the rabbit. *J. Reprod. Med. 14:* 62-63.

VERDUGO, P.; BLANDAU, R.J.; TAM, P.Y.; HALBERT, S. (1976) Stochastic elements in the development of deterministic models of egg trnsport. In: *Ovum Transport and Fertility Regulation.* World Health Organization Symposium. Edit by Harper, M.J.K.; Pauerstein, C.J.; Adams, C.E.; Coutinho, E.M.; Croxatto, H.B.; Paton, D.M. Scriptor, Copenhagen. pp. 126-137.

VERDUGO, P.; LEE, W.I.; HALBERT, S.A.; BLANDAU, R.J.; TAM, P.Y. (1980) A stochastic model for oviductal egg transport. *Biophys. J. 29:* 257-270.

WEINBERG, L.; PAUERSTEIN, C.J. (1980) Transport of ova transferred to rabbit oviducts at varying intervals after human chorionic gonadotropin injection. *Fert. Steril. 33:* 77-81.