GASTRULATION AND FORMATION OF SOMITES IN AMPHIBIA AND BIRDS

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The talk first gave an exposition of primary and secondary waves [5], and then extended the ideas from amphibia to birds. We give here a brief summary.

Differentiation is an embryo refers to regions that are initially alike and subsequently become different; in other words cells in those regions follow divergent paths of development in the space of states of a cell. Divergence implies a cusp catastrophe over space-time, and genericity requires that the cusp axis be inclined to the time axis. This implies a wave of cell determination which we call a primary wave, and which eventually slows to rest, forming the frontier between the two regions. The primary wave may be hidden, in the sense that the changes in each cell may be too delicate to detect at the time, but the cell may manifest some visible secondary effect after a delay of several hours. Although this secondary effect may be purely intracellular, nevertheless since it has been programmed by the primary wave, it will appear as a visible secondary wave. Furthermore, if the secondary wave causes morphogenesis, then the wavefronts may themselves be geometrically distorted by the morphogenesis. Consequently any tertiary effect will produce a tertiary wave that may appear as somewhat mysterious because it will have to follow the distorted pre-programmed wavefronts.

Amphibia. In [5] these ideas were applied to the differentiation between ectoderm and mesoderm in amphibia. The hidden primary wave of mesoderm determination results in a secondary wave of invagination, causing gastrulation, and a tertiary wave of adhesiveness, causing the formation of notochord. Furthermore, in a model worked out jointly with Jonathan Cooke [2,3,5], the formation of somites can also be explained by superimposing a smooth clock during the passage of the primary wave. The clock allows the primary wave to move smoothly along the dorsal axis, but laterally causes it to move periodically in jerks. Therefore the resulting tertiary wave of adhesiveness causes the notochord to grow continuously along the dorsal axis, but laterally causes periodic groups of cells to adhere to one another, thus forming the somites. One advantage that this model has over previous models is that it permits regulation of somites, up to the observed precision.

Experiments. Subsequent experiments with frogs stimulated by the wave + clock model have produced results compatible with the model. Cooke has grown frogs in heavy water, which apparently slows the clock but not the wave, thus producing slightly fewer larger somites. Elsdale, Pearson and Whitehead [4] have momentarily interrupted the clock, but not the wave, by raising the temperature (from 25° to 37° for 5 minutes) during the primary wave determining somites; then when the somites form 6 hours later two or three of them are meshed together, while earlier and later somites are unaffected in position or timing.

Birds. I am indebted to Ruth Bellairs for explaining the development of birds to me (see [1], Chapters 4,5,6). The morphogenesis of birds is not so easy to understand as that of amphibia, because the bird

embryo, instead of floating freely in 3-dimensions as the amphibian embryo, is crushed down onto the 2-dimensional surface of the yolk. Nevertheless a similar wave + clock model would seem to fit the observed facts, and it would be interesting to test the model by repeating and developing the above experiments with chicks.

In Figures 1-6 we sketch the model applied to the gastrulation of chicks. Figure 1 shows the hidden primary wave of mesoderm determination beginning at the embryonic shield and travelling across the area pellucida, through the presumptive mesoderm, which consists of presumptive notochord and somites. We have symbolically drawn eight wave-fronts to indicate successive positions of the primary wave; the even spacing indicates the regularity of the wave at this stage, before any morphogenesis has taken place (regulated by diffusion prior to cleavage). When the primary wave approaches wavefront number 8 it slows to rest, and forms the frontier between mesoderm and ectoderm.

We assume that the secondary effect causes cells to invaginate, thus producing the primitive streak and causing gastrulation. We also assume that the mesodermal sheet retains it topological integrity (apart from the temporary contact of the two sides of each wavefront as it rolls through the streak). Figure 2 shows wavefront 1 rolling through the streak, with the embryonic shield already folded underneath. Figure 3 shows[*] wavefront 5 rolling through the streak, with wavefronts 1-4 already folded underneath, and shown dotted. Figure 4 shows the end of gastrulation, with the secondary wave coming to a halt, and the rolling through the streak halted at wavefront 8.

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[*] We have not shown what is happening to the surrounding area opaca, because it is not clear whether the mesoderm tears away or remains attached. If it remains attached along the boundary 0 then a tongue of endoderm will be pulled out of the area opaca underneath the mesoderm, and move in an anterior direction parallel to the streak.
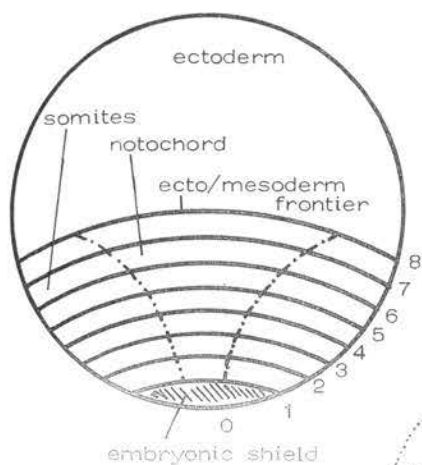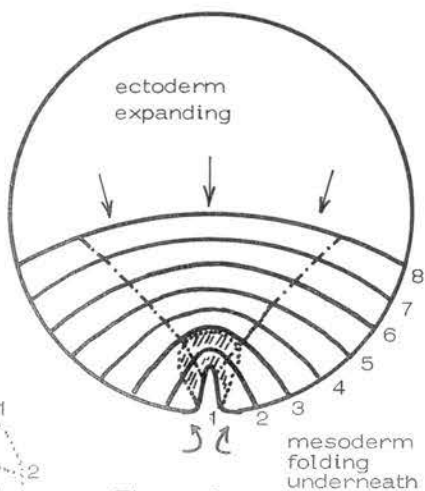
Figure 1.
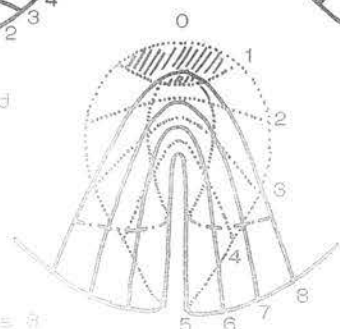AREA PELLUCIDA

Figure 2
SHORT PRIMITIVE STREAK
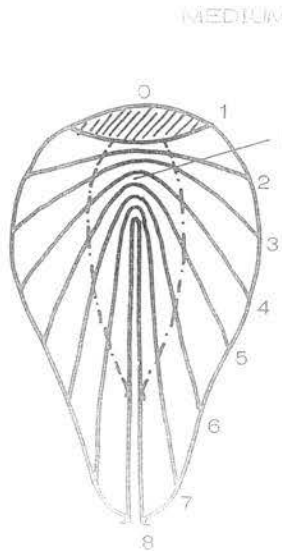
Figure 3
MEDIUM PRIMITIVE STREAK
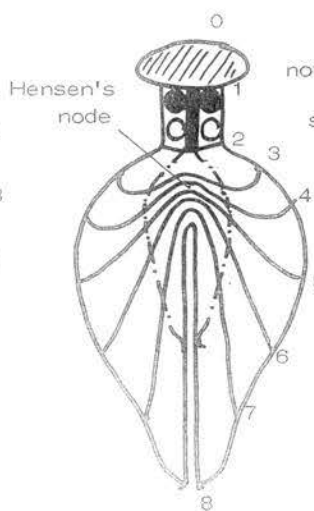
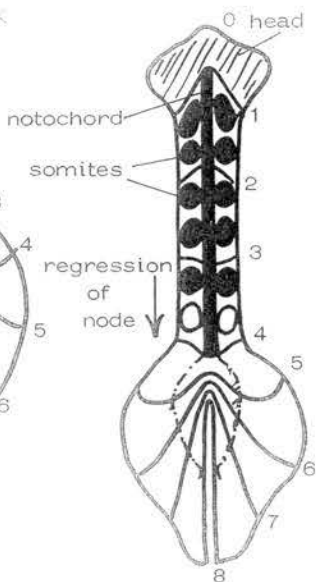Figure 4
END PRIMITIVE
STREAK

Figure 5
HENSEN'S NODE

Figure 6
FORMATION OF
NOTOCHORD AND
SOMITES

By now the whole mesoderm has folded underneath, and so in Figure 4 we have drawn it in black lines rather than dotted. We can gain some idea of the geometric distortion of both mesodermal and ectodermal sheets at this stage by imagining the original disk of area pellucida folded along wavefront 8 into a semi-disk, and then pulled into a disk by bringing the two ends of the fold together. Such a process would stretch the perimeter and compress the centre. The resulting bulge at the centre is called Hensen's node. Meanwhile all the earlier wavefronts have been distorted and bunched together at the node, as shown in Figure 4.

We now assume that the tertiary effect causes each cell to become adhesive and increase its contact with its neighbours. Thus we have a tertiary wave of adhesiveness following the distorted wavefronts. Figure 5 shows the cells of the central region between wavefronts 1 and 2 adhering together to form the beginning of the notochord. At the same time the tertiary wave moves in jerks across the lateral regions to form the first few somites (we have symbolically drawn 2 pairs). The resulting contraction of wavefront 2 causes further bulging of the material between wavefronts 2 and 4, thus enhancing the bulge of Hensen's node. Figure 6 shows the tertiary wave reaching wavefront 4, having caused the notochord to grow continuously, and the next few somites to form. The contraction of wavefront 4 now causes bulging of the material between wavefronts 4 and 6, and so Hensen's node begins to regress. Meanwhile the sideways contraction of material into the notochord causes the latter to elongate, pushing the head process forward, and Hensen's node backwards, accelerating its regression.

Thus our assumption of a primary wave together with secondary and tertiary effects suffice to explain the whole geometry of embryonic axis. In particular Hensen's node is merely the bulge where the tissue has been

forced to thicken by the way that the secondary wave caused it to infold through the streak, and this bulge contains the distorted pre-programmed wavefronts all bunched together. Naturally if Hensen's node is transplanted, then the tertiary wave will duly follow its programme, and form a complete embryonic axis in the host. Usually Hensen's node is called an "organiser", which can be a dangerous euphemism, because it may lead to a fruitless search for non-existent morphogens that diffuse and "organise". For example [1,p.112] reports the conclusions of Grabowski and Tsung et.al. that "Hensen's node is initially a head organiser, but that as it retreats it becomes successively a trunk and then a tail organiser". We suggest that the concept of a bunch of distorted pre-programmed wavefronts may provide a better conceptual framework for testing experimentally.

REFERENCES

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