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REVIEW ARTICLE

Can physics help to explain embryonic development? An overview

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Summary Recent technical advances including digital imaging and particle image velocimetry can be used to extract the full range of embryonic movements that constitute the instantaneous 'morphogenetic fields' of a developing animal. The final shape of the animal results from the sum over time (integral) of the movements that make up the velocity fields of all the tissue constituents. In vivo microscopy can be used to capture the details of vertebrate development at the earliest embryonic stages. The movements thus observed can be quantitatively compared to physical models that provide velocity fields based on simple hypotheses about the nature of living matter (a visco-elastic gel). This approach has cast new light on the interpretation of embryonic movement, folding, and organisation. It has established that several major discontinuities in development are simple physical changes in boundary conditions. In other words, with no change in biology, the physical consequences of collisions between folds largely explain the morphogenesis of the major structures (such as the head). Other discontinuities result from changes in physical conditions, such as bifurcations (changes in physical behaviour beyond specific yield points). For instance, beyond a certain level of stress, a tissue folds, without any new gene being involved. An understanding of the physical features of movement provides insights into the levers that drive evolution; the origin of animals is seen more clearly when viewed under the light of the fundamental physical laws (Newton's principle, action-reaction law, changes in symmetry breaking scale). This article describes the genesis of a vertebrate embryo from the shapeless stage (round mass of tissue) to the development of a small, elongated, bilaterally symmetric structure containing vertebral precursors, hip and shoulder enlarges, and a head.

Introduction

Our understanding of developmental biology is undergoing a radical change. Leaps in knowledge have been achieved since the introduction of new techniques for imaging living

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organisms and monitoring embryonic movements over time, often three-dimensionally [1] and sometimes with single-cell resolution [2]. The development of animals has been found to be nearly continuous, akin to the flow of a visco-elastic material such as a gel or foam. However, although tissue flow is continuous, discontinuities occur as a result of the laws of physics. Thus, the source of current progress in knowledge is the physical interpretation of developmental movements, most notably regarding their discontinuities.

Physical methods that have been introduced into the field of biology provide an understanding of movement fields (which are vectors) and deformation fields (tensors). These methods can be used to explain the movements that occur during embryogenesis, including the long-range correlations that link the various parts of the embryo. Due to the laws of physics, forces exerted at one end of the embryo have an impact at the other end (and even on the entire embryo), particularly as embryonic movements start very early, when the tissue mass is still tiny. Thus, many movements previously thought to be locally induced via the expression of morphogenesis molecules (known as morphogens) are only passive consequences of forces exerted elsewhere. This fact constitutes a radical change in concepts about the construction of animals, mandating a reappraisal of all past interpretations and considerably simplifying the problem. As the embryo is tiny when morphogenesis starts (about 4 mm in diameter), movements of a few cells at one end have an impact on the other end, and embryogenesis can only be explained by considering the global movement pattern [3], in a manner akin to the physical analysis of other phenomena such as atmospheric movements.

Another point of physical interpretation relates to the initial conditions. A first consideration is the existence of symmetry breakings, which are polarities induced in the embryo at the initiation of the developmental phenomenon, before any movement starts; examples include the anisotropy of cell division and the entry point of the sperm cell (which defines the antero-posterior axis). These symmetry breakings limit the typology of embryonic movements: for instance, the movements have Left-Right symmetry (producing a bilaterally symmetric organisation). Embryos also have rostral-caudal symmetry, as discussed below. Second, embryonic movements are also governed by geometric boundary conditions. Vertebrate embryos are nearly round at first, but their contours change little by little under the effect of the movements. As the geometric field undergoes deformation, the velocities also change, without any specific gene being involved: it is the geometric boundaries that change. Finally, a profound and subtle physical feature is the existence of scaling laws of phenomena. There is often a tendency in biology to assume that complex laws require complex explanations, whereas in reality simple physical laws such as the laws of conservation impose scaling laws on phenomena, which usually cannot be grasped intuitively: for instance, diffusion propagates as $t^{1/2}$ (where t denotes time), oil layers flow over water as $t^{4/5}$, and cold air currents flow down doors as $t^{1/3}$.

Embryonic development is clearly a biological phenomenon of stunning complexity [4], at least in appearance. However, the underlying causes are not necessarily complex. In physics, simple causes often produce complex effects. In particular, simple force fields can induce spatial deformation and spatio-temporal velocity changes that may seem extremely complex: for instance, a simple sudden push applied to smoke creates vortex rings that leapfrog into one another while expanding, flaring, and slowing down. Thus, simple laws of physics such as the laws of hydrodynamics, with simple starting conditions, generate phenomena that exhibit highly complex spatio-temporal features.

Current knowledge on embryonic development indicates that the morphogenesis of a vertebrate is actually very simple, in terms of its underlying principles [5].

Biochemistry has identified a host of crucially important chemical properties or parameters. Nevertheless, the main features of bilaterally symmetric vertebrates, such as lumps at the shoulders and thighs (terrestrial vertebrates) with a narrowing in the middle, are inherent in the physical process. Certain facial traits, the caudal bud, and even the development of a chorio-amniotic sac can be satisfactorily explained by physical laws, at the quantitative level.

Below is an explanation of the principles underlying the formation of an amniote. These principles were elucidated using a specific imaging technique to film the development of chicken embryos (Fig. 1) [6]. Filming a zebrafish or Xenopus is not easy, as these organisms are three-dimensional even at very early stages [7]. Although stunning fluorescence films can be obtained, the movements are extremely difficult to interpret because the cells cross the reference planes in all directions. With chickens the situation is simpler, as the blastula has a flat discoid shape similar to that of the human blastula. For about 1 day, the developmental movements occur in two dimensions. The velocity field is nearly two-dimensional and easy to interpret. In addition, confocal microscopy (laser microscopy with collimated light), which is often used to reconstruct three-dimensional movements, can have noxious effects on tissues. As temporal resolution must be very high (about one image/10 s), low-intensity white light is a better choice. Chick embryos are therefore preferable, as the two-dimensional velocity field facilitates reconstruction and decreases the amount of detail needed, thereby allowing the use of lower light intensities. Thus, the temporal and spatial resolutions of the data acquired on chick embryos are sufficient for the extraction of movement dynamics. Finally, after about 10 hours of revolving movements, simple folds appear on the flat surface. These features make the chick embryo the easiest to study. In addition, the chicken is an amniote and is closer to humans than are fish or frogs.

I will now describe the movements that occur during the development of the chick embryo, starting at the initial configuration as observed when the egg is laid (i.e., after 1—2 days of embryonic development, when the embryo contains several thousand cells). We will simply follow the physical principles that underlie the process, which involves a series of flows and foldings. Once the physical nature of the flow is recognised, the description merely follows the path of the flow. However, a unique feature of the flow is that it moves both forwards and backwards, as discussed below: it must therefore be borne in mind that the same movement includes a flow towards the (future) tail and a flow towards the (future) head. (It is worth pointing out here that even

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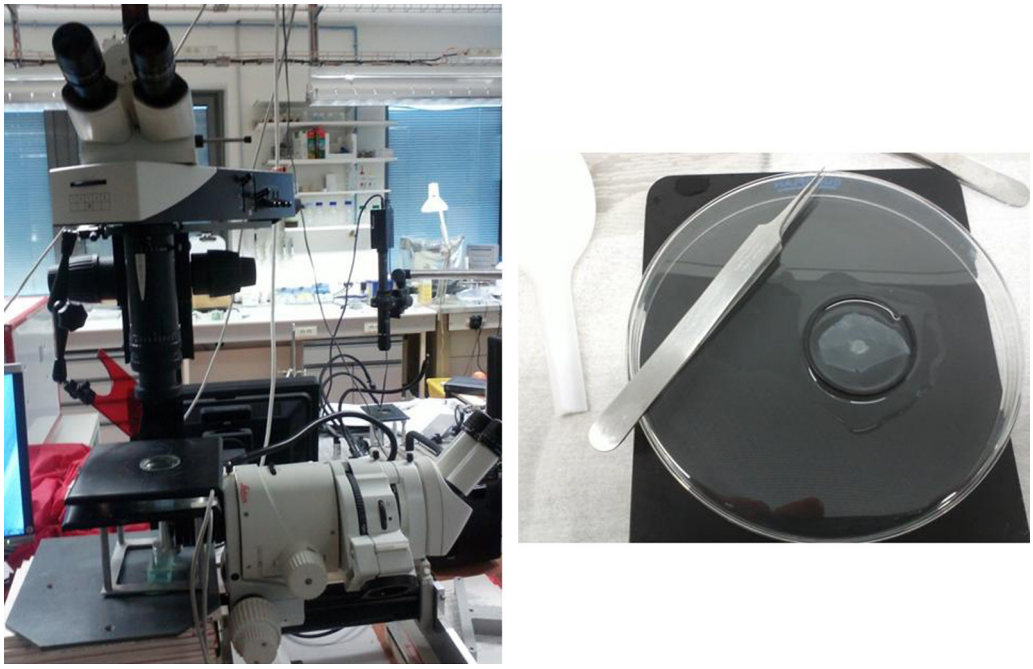

Figure 1 The experimental set-up consists of two microscopes, one conventional and the other inverted (Leica MacroFluo and Leica MZ FLIII, respectively; Leica, Wetzlar, Germany), and of two Minitüb HT300 incubators (Minitüb, Tiefenbach, Germany). The embryo is extracted from the egg and rinsed to ensure that the yolk does not blur the images.

humans have a very small tail in utero, which is very rarely still present at birth).

Initial state or 'reference configuration'

To understand development, one must first agree on the definition of a 'shapeless' animal, i.e., of what is known in physics as the 'reference configuration'. This is the configuration of the chick embryo at arrival of the egg in the incubator. The reference configuration is the simplest possible shape for a vertebrate: it is round – spherical for amphibians and fish and discoid for humans and chickens. I will therefore explain the development of vertebrates starting with a disc. The films to which I refer are available on the university website http://www.msc.univ-paris-diderot.fr/~vfleury.

In reality, the initial disc is not uniform, as cell-size distribution within the disc is not homogeneous: the largest cells are located at the (future) posterior pole. The conventional concepts of polarity and symmetry breakings, which are rather general and vague, become operational in the embryo precisely because cell distribution is inhomogeneous, although the round contours of the cell mass at the blastula stage suggest revolution symmetry.

This point has been well established for many years [5]. Early cell divisions (after the very first division) are asymmetrical, which produces radial and orthoradial cell-size gradients, with the largest cells at the edges, and these largest cells being larger at the posterior pole (Fig. 2). Starting from this initial configuration, the movements shape the embryo via visco-elastic flow. However, the movement is influenced by the initial static configuration with its inhomogeneous cell-size distribution. In simple terms, when inhomogeneously distributed cells start to move, the movement has a shape (velocity distribution) that depends on the cell distribution shape (spatial geometric distribution). The flow is fairly simple, as the symmetry breaking is not complicated, but it may be difficult to understand if it is not monitored from its outset, since it comprises three phases.

First phase, polonaise dance movements

The cell-size inhomogeneity causes rotation of the embryo. This movement can be recognised technically as a quadrupolar flow [8,9] and is designated as Polonaise movement in conventional embryology [10]. The entire disc spins, with four rotations, two large rotations well inside the blastula and two smaller ones more by the edge closer to the outer contour. This phenomenon is counter-intuitive and cannot be explained by chemotaxis.

It is easily explained by the physical laws of fluid mechanics. The cells (exhibiting the above-described symmetry breaking) exert traction forces along a boundary (separating the larger from the smaller cells), thereby spontaneously generating the rotational movements via viscous friction (Fig. 3). A similar phenomenon can be produced by stirring a cup of coffee with two spoons oriented head-on. This phenomenon is an emergent behaviour: it is not encoded as such step by step; instead, pulling on an edge is sufficient to generate it. A simple cause, i.e., pulling along an edge, produces a 'complex' result, i.e., quadrupolar rotational flow. The parameters that are encoded genetically are the annular edge (produced by successive cell divisions) and the pulling forces exerted by cells on their neighbours (traction dynamics of cell membranes, which bear adhesion molecules).

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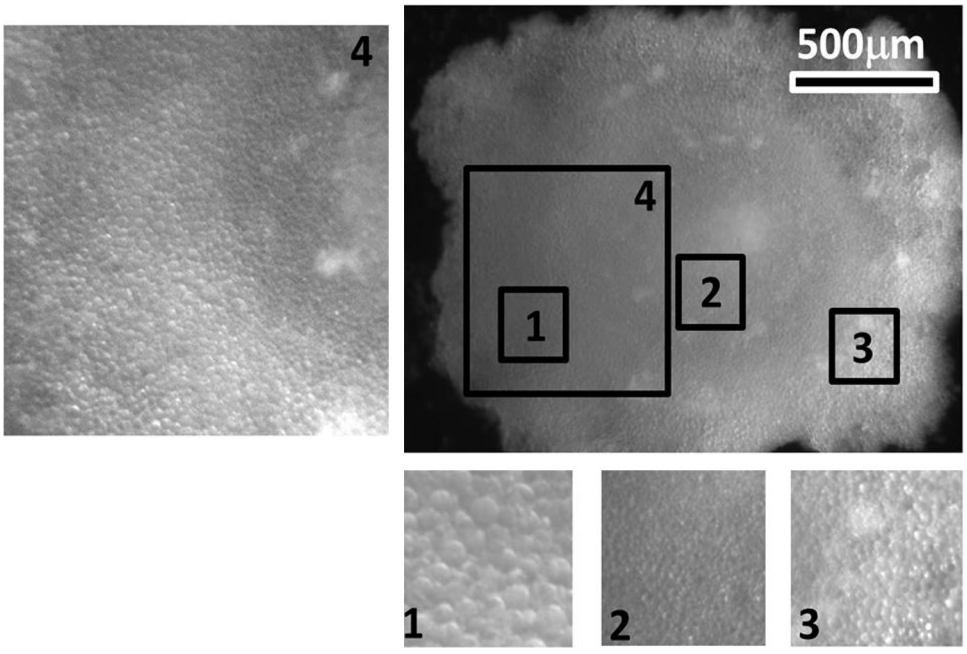

Figure 2 Cell distribution is not uniform in the chick blastula: the cells located along the outer ring are larger and those located within the inner disc are smaller. In addition, the larger outer cells exhibit an orthoradial size gradient, with the cells being larger at the posterior pole of the embryo (on the left) than at the anterior pole (on the right). This non-uniform distribution (symmetry break) develops step-by-step as a result of the early cell divisions, of which only the very first is symmetrical.

This movement begins to change the shape of the blastula, which elongates slightly toward the posterior pole. Thus, an initial symmetry breaking, i.e., a static phenomenon, translates into a morphogenetic movement: the velocities are inhomogeneous, and this inhomogeneity in turn affects the shape of the structure (the disc), which gradually becomes less rounded (leading little by little to the development of the animal shapes, as described below).

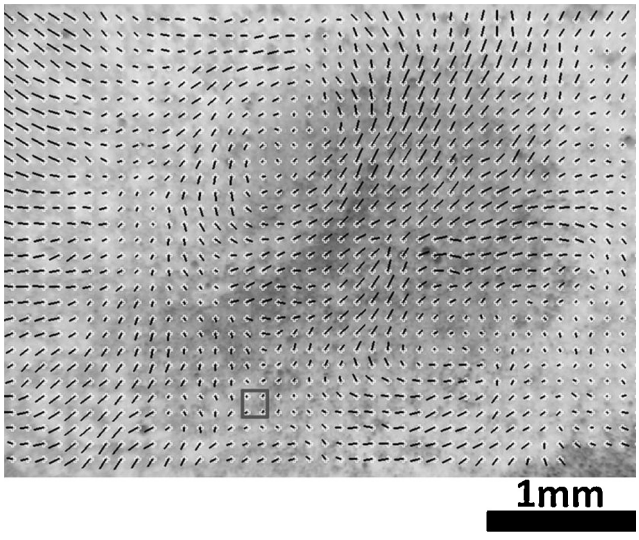

Figure 3 Surprisingly, the first flow of cells is organised into large counter-rotating vortices with a stagnation point (bottleneck). Velocity is greatest at the edge, i.e., at the boundary between the larger and smaller cells (where the ectoderm detaches from the endoderm).

This movement can be likened to a vast collision between the right and left halves of the embryo. There is a high-pressure point, known as the stagnation point. At this point, the cells undergo differentiation (acquiring a migration phenotype) and invagination. This invagination results in the second phase of embryogenesis.

At the stage when cell invagination starts, the flow movements have produced an ampulla-like shape elongated towards the 'bottom'. This shape is not encoded by any specific genetic factors; it is due only to movement dynamics with its underlying laws (law of conservation of matter, law of movement). The only factors needed are a constant traction force applied to inhomogeneously distributed cells (larger cells at the edges, and greater size of these large cells towards the bottom).

Second phase: gastrulation

While the cells change their phenotype and undergo invagination at the flow stagnation point, a remarkable 'explosive' phenomenon occurs. I use the term 'explosive' to mean non-linear and accelerating. The cells acquire a migrating phenotype, but the cells that go through the stagnation point then use the undifferentiated cells for traction support. To migrate away from the stagnation point, they pull on the disc, moving it towards the centre by virtue of the action-reaction law (Fig. 4). Thus, greater centrifugal migration of the differentiated cells translates into greater centripetal migration of the ectoderm. These movements draw an increasing number of cells to the stagnation point, where differentiation occurs, resulting in a snowball effect with non-linear acceleration of the invagination, which is called actually gastrulation in classical embryology. An increasing

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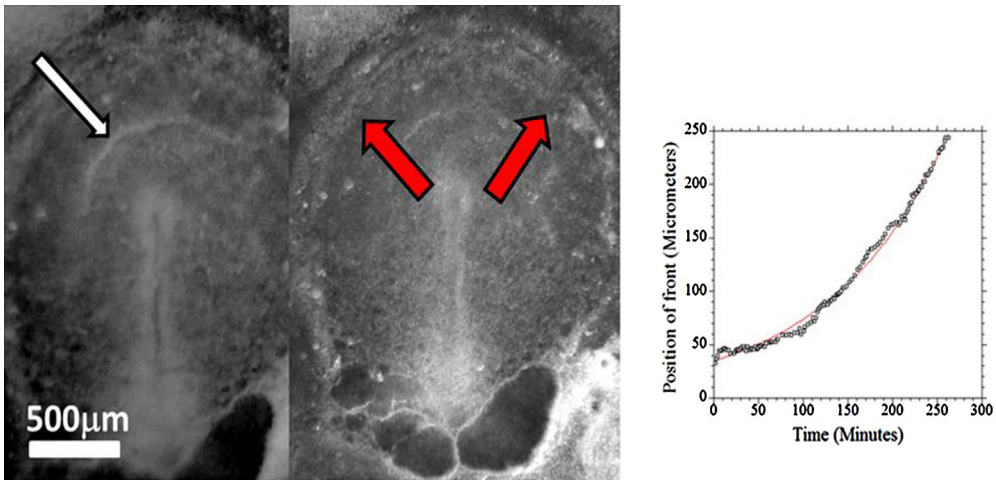

Figure 4 Cells pass under the blastula through the flow stagnation point (arrow on the left) and form a wave of differentiated cells that flow from the stagnation point, i.e., centrifugally (two diverging arrows). The wave front advances non-linearly: the movement accelerates (as shown clearly on the graph on the right).

number of cells travel under the disc (i.e., undergo ingression), 'wetting' it, to use a term from wetting physics [5]. The term 'wetting' designates the flow of a fluid over a surface, for instance of a drop of water on glass. Mesenchymal cells, such as fibroblasts, have the unique property of predominantly wetting epithelial cells, such as those of the ectoderm. Technically, this property leads the mesenchymal cells to spread over the ectoderm like jam, covering it as much as possible; whereas the ectoderm behaves more like a row of books neatly arranged on a shelf. Physically, interaction forces exist between the mesoderm and ectoderm and promote mesenchymal cell spreading over the ectoderm surface. Wetting physics is of considerable importance in many fields of biology, for instance at the surfaces of feathers and plant leaves, as well as in the manufacture of products ranging from paints to car windshields. Similar wetting phenomena have been reported during cancer cell migration [11].

Wetting is a very rapid process that allows the migrating mesodermal cells to promptly colonise the undersurface of the ectoderm all the way to its edges. When they reach the edges, they begin to pull on the inner disc (simply because there is a stiffer surrounding ring). The result is the formation of the neural folds, called neurulation.

Neurulation

When they reach the edges of the ectoderm, the mesenchymal cells continue to apply a traction force. However, this force then pulls on the entire inner ectoderm, in all directions but predominantly posteriorly, since the invagination process started in the posterior area. At this site, the cells are nearest to the edges and are oriented along the initial hole through which ingression occurred [5,9,10]. The result is a massive traction on the surface, which folds along the antero-posterior axis, generating the first suggestion of the body shape, with the first out-of-plane dorsal structures.

At this stage, a small bilateral three-dimensional animal with dorsal folds is recognisable. Simply pulling on a malleable surface produces elongated folds between the traction points. This effect can be easily demonstrated using a sweater or a piece of rubber. Thus, a small two-dimensional sheet of live tissue, when subjected to traction forces, produces two elongated folds that almost form a tube. This phenomenon underlies the vertebrate pattern characterised by bilateral symmetry (side-to-side symmetry and central body axis extending from the head to the tail). The tiny animal at this stage resembles a cephalochordate [12]. Remarkably, the folds spontaneously roll towards each other, in a manner similar to tank treads, until the two halves of the gastrula come into contact, producing folds in each (Figs. 5—7). This tank-tread movement (involution) pushes the tissues in the forwards and backwards directions when the rolls make contact, simply by virtue of the law of visco-elastic conservation of matter [3]. As a result, the neural folds are pushed upwards above the plane of the blastula/gastrula and form the gut pocket.

Formation of the gut

In accordance with the law of mass conservation, the two dorsal halves of the embryo collide and are pushed forwards and backwards, as clay is pushed out from under the thumb when flattened on a surface, except that here the left and right sides push against each other. Discontinuous changes in velocity, of huge magnitude (200%!), have been shown to result solely from the collision between the two halves of the embryo (Fig. 7) [13]. Importantly, before collision occurs, the situation corresponds mathematically to a free boundary problem: the folds advance without encountering any obstacle; after contact between the two halves, however, the situation is a reflection boundary problem (axial symmetry along the antero-posterior axis). Thus, the mathematics of the problem change radically. The true cause of the tissue recirculation in the forwards and backwards directions are physico-mathematical (flow conservation, with or without a 'wall' along the midline axis). There is no genetic cause to

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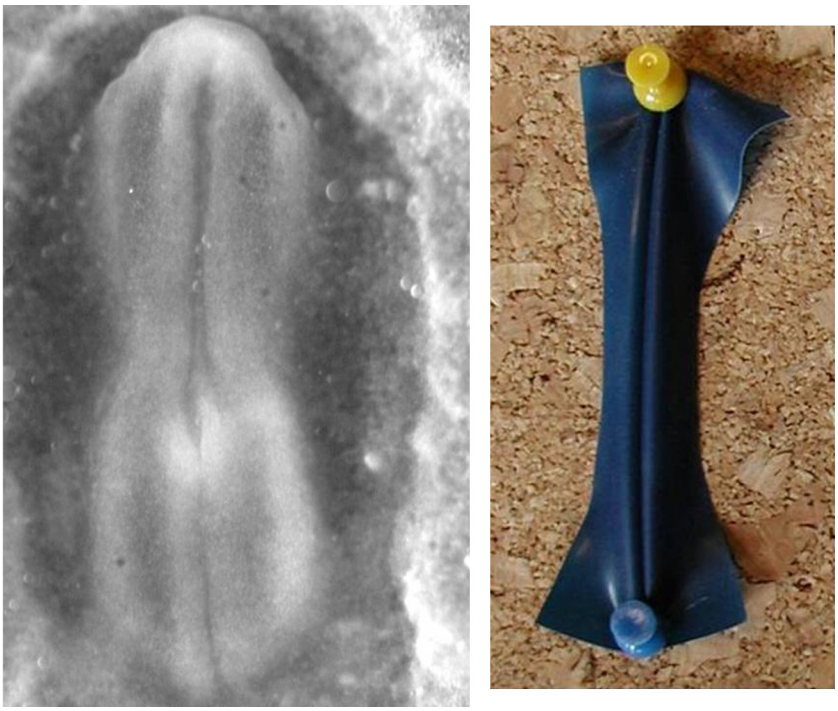

Figure 5 When the mesodermal cells reach the edge, they elongate the blastula, which starts to form two large folds (on the left, where anterior is at the top and posterior at the bottom). These folds resemble simple folds in a sheet of rubber that is held taut (buckling).

the change in velocity direction, despite the 200% magnitude of this change (with the velocities even changing their sign at some sites), and the highly complex spatial changes are ascribable to simple laws of physics.

The collision between the right and left halves produces three effects. One effect is gradual closure of the neural crest in a zipper-like manner. Closure advances both forwards and backwards (morphogenesis is not

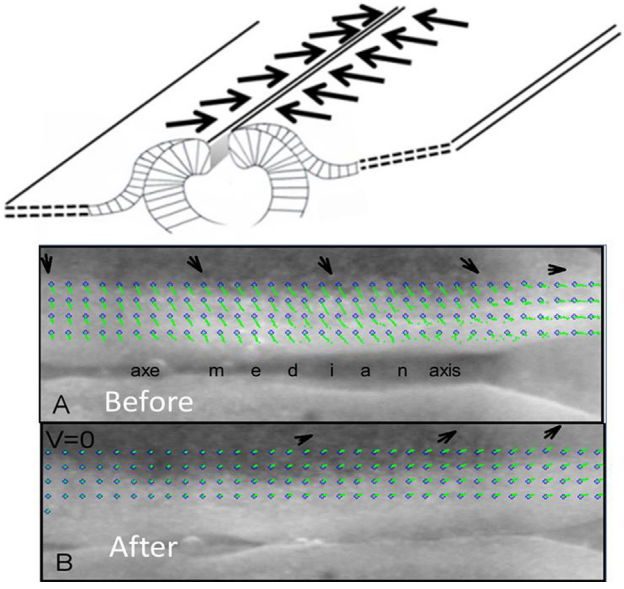

Figure 6 A detailed velocity analysis shows that the folds advance in a tank-tread pattern in the region where the fold rolls on itself (top). The folds advance towards each other until they collide. Quantitative analysis shows a huge change in velocities at the time of contact (bottom: velocities just before and just after the collision between the two folds).

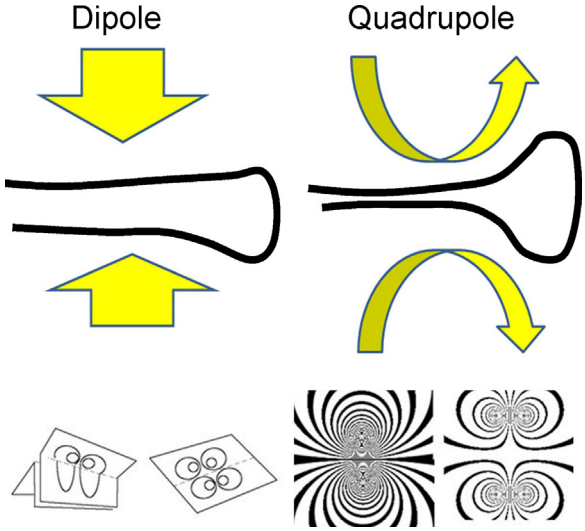

Figure 7 The considerable change in velocity is ascribable to the transition from dipolar flow to quadrupolar flow (top). This transition occurs when the tank-tread folds collide with each other, and it induces a change from two independent rotatory movements to four adjacent vortices (bottom). Mathematically, this change is a modification in the boundary conditions of flow along the midline, from the free boundary condition to the reflection boundary condition.

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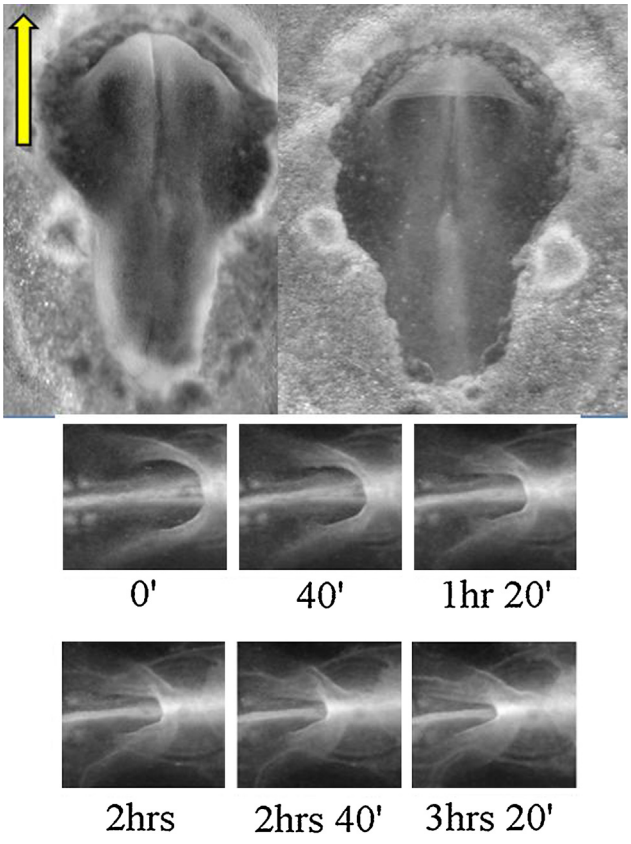

Figure 8 As the folds advance, they slip above the plane of the blastula (top). The result is a sigmoid-shaped fold, which forms an empty hood-shaped cavity. This cavity is the gut pocket that will develop into the thoraco-abdominal cavity. Contraction of the edge of the 'hood' forms part of the heart (bottom).

particularly directed posteriorly but instead occurs in both directions). Second, the cephalic fold applies shear forces to the blastula/gastrula, slipping above the plane like the finger of a glove and forming an empty cavity known as the gut pocket. The gut pocket resembles a hood that contracts and becomes increasingly hollow and vast (it will develop into the thoraco-abdominal cavity) (Fig. 8). This phenomenon is very counter-intuitive and is difficult to understand if not monitored dynamically, as can be done with current technologies. The films (http://www.msc.univ-paris-diderot.fr/~vfleury) show a rapid process that does not correspond to any specific gene but consists in visco-elastic buckling of a malleable sheet. Finally, the third effect is the production of a fold edge (S-shaped in the transverse direction) that contracts and applies complex local torsion forces to the tissue. This process results in the formation of the lower part of the heart (Fig. 8A). The bottom of the fold serves as a mould for the large blood vessels (e.g., the thoracic aorta and brachiocephalic arteries).

Formation of the amnios

At this stage, shown in Fig. 9, new 'traits' that are characteristic of vertebrates develop. The limbs, head, and amniotic sac develop gradually, as part of the morphogenetic movement, starting on the third day of development. In particular, the amniotic sac, which is a crucial characteristic of humans and other amniotes, is simply the fold located in front of the head. This fold also contracts, similar to the drawstring of a bag.

Thus, that amniotes developed after anamniotes during evolution makes perfect sense: to form an amnios, the embryo must push on the blastula/gastrula and apply shear forces to its edge until the fold slips over the embryonic head. Once this fold is formed, it contracts persistently until complete closure is achieved.

A sac is simply a folded round edge that contracts circumferentially, like an iris. Dynamic measurements have established that the heart and amniotic sac contract at constant velocities that are quantitatively very similar for these two structures [12]. The underlying physical principles seem similar in both cases. As indicated previously for gastrulation, no specific gene encodes the relevant shape (here, the amniotic sac or heart). This shape results instead from a continuous movement whose real causes are the physical principles underlying contracting folds.

The limbs

The limbs and head are more complicated than a simple sac. Detailed analyses of the lateral plates (the tissues that fold back on either side of the antero-posterior axis) have established that neural fold elongation pulls on the tissues located on either side, rolling them like a coffee spoon in a cup of coffee or perhaps more accurately in a cup of thick honey or a visco-elastic gel (having a jam-like consistency). As a result, the midline axis elongates posteriorly at constant velocity, although the velocities exhibit a rib-arch profile exactly along the midline, similar to that seen when a paste is pushed through a tube. On the sides, the lateral plates turn like solids (Fig. 10). Fig. 10 also shows the zipper-like closure of the neural crests.

This behaviour is typical of a visco-elastic solid exhibiting bands of shear stress: the solid segregates (a technical term designating the development of two separate domains separated by a boundary; here, there are two domains of uniform tissue separated by a deep furrow) into two domains, thus undergoing spontaneous organisation with a lower-density zone along a singular line. This line is visible between the axis of the back and the future hip; eventually, it will be the boundary between the vertebras and the pelvis. It is as if shear forces were applied to a toothpaste pancake. The vast passive rotation of the lateral plates shapes the hips. In the upper region, the structure is symmetrical, albeit complicated by the proximity of the heart. However, rotation with formation of a hairpin-shaped fold is also visible in this region, at the site of the presumptive elbows.

These rotational movements turn, fold, and twist the lateral plates, whose subsequent unfolding gradually forms the limbs [14]. It is therefore unsurprising that the physiological limbs cannot be replicated exactly using artificial means, as these would not produce a perfect copy of the subtle physical characteristics of the rotational movements [15]. Although the relevant chemical pathways can be triggered, no means are available for replicating all the initial phys-

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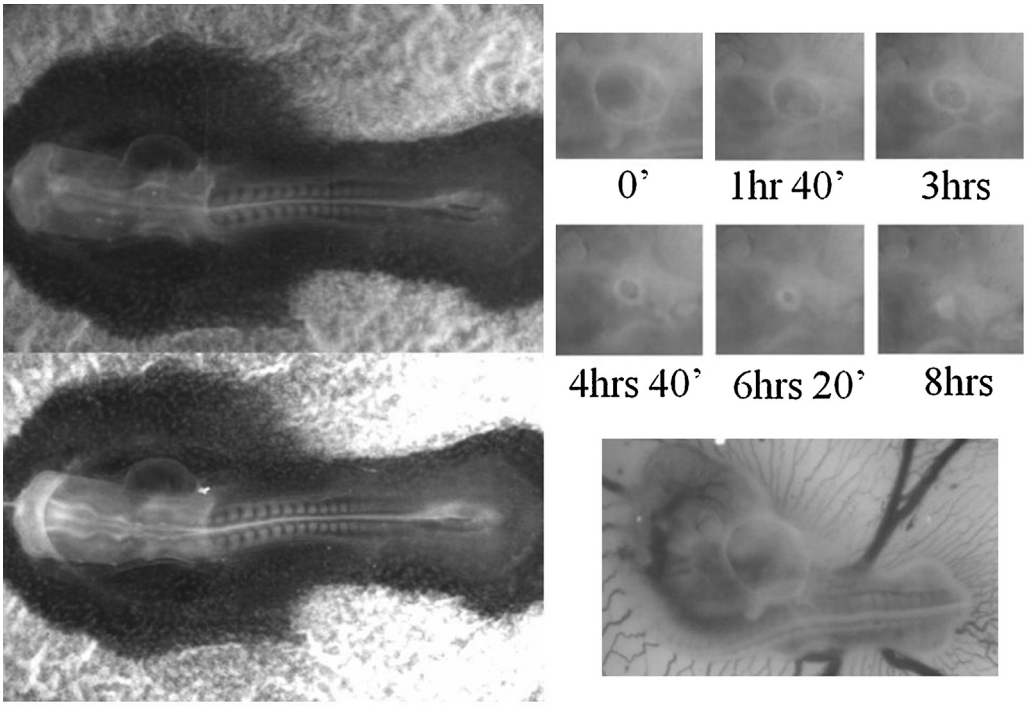

Figure 9 Dual dorso-ventral imaging showing that the amnios is simply a fold in the blastula that forms in front of the head (on the right) and behind the tail (on the left). This fold slips over the head then contracts in a manner akin to a drawstring. This 'drawstring' contracts at constant velocity and collapses centripetally, like a contracting iris.

ical features of the problem, for instance by implanting a bead loaded with growth factors under the ectoderm [15], a method widely used by biologists.

Formation of the head

Several remarkable phenomena occur during formation of the head. First, the collision between the two halves of the embryo pushes the tissue located anteriorly off to the sides. However, the end of the neural groove continues to close until a complete tube is formed. The result is a complex situation in which neural tube closure antagonises the antero-posterior movement, which consequently evaginates laterally. The optical tissue thus spreads out to the sides, similar to clay flattened under the thumb [16]. This phenomenon is directly related to extremely severe birth defects such as holo-prosencephaly [17]. Depending on the force with which the movement flattens the anterior 'clay', the distance along which lateral spread occurs will vary. Normally, this distance is sufficient to produce two separate optical vesicles that are clearly independent, i.e., at a distance from each other [18]. This point explains the phenotypic continuum that ranges from cyclopia to asymptomatic close-set eyes.

Coupling between differentiation and morphogenesis

At the stages described until now, differentiation remains minimal and essentially limited to two phenomena, namely, epithelium-to-mesenchyme differentiation during gastrulation and neural crest cell migration induced or partly induced by the collision between the neural crests. (There is however a radial gradient of epithelial cell sizes). The neural crest cells form the nervous system and regulate numerous other morphogenetic events such as teeth formation [19]. Thus, the embryo can reach a stage that is roughly close to completion (although each component is rudimentary), despite only minimal differentiation: the process consists in the shaping of a mass of gel, almost at constant volume (for some animals at least).

Recent studies suggest coupling of the morphogenetic events to the events involved in differentiation [20,21], as well as links between substrate rigidity and differentiation [22] and between movement and differentiation [23]. Although gastrulation is undoubtedly related to epithelial cell differentiation into fibroblasts (which is better described as a change in cell type), these two phenomena exert feedback on each other. The movement causes the differentiation to occur at the singular sites involved in movement, but the differentiation process then propagates and exerts feedback on the movement itself.

Similar phenomena occur at the eyes: the optic cup and lens develop exactly at the apex of the optic vesicle, when this vesicle flattens against the superficial ectoderm. However, the invaginating tissue expresses genes such as pax6 and shroom3 [24], which are intimately related to vision. Thus, the forces that shape the eye, considered as an object, are closely linked to the biochemical processes that allow vision. The eyes see not only because they have the necessary connections, but also because these connections are established within a cup equipped with a lens whose geometrical features ensure the collection of light beams. The

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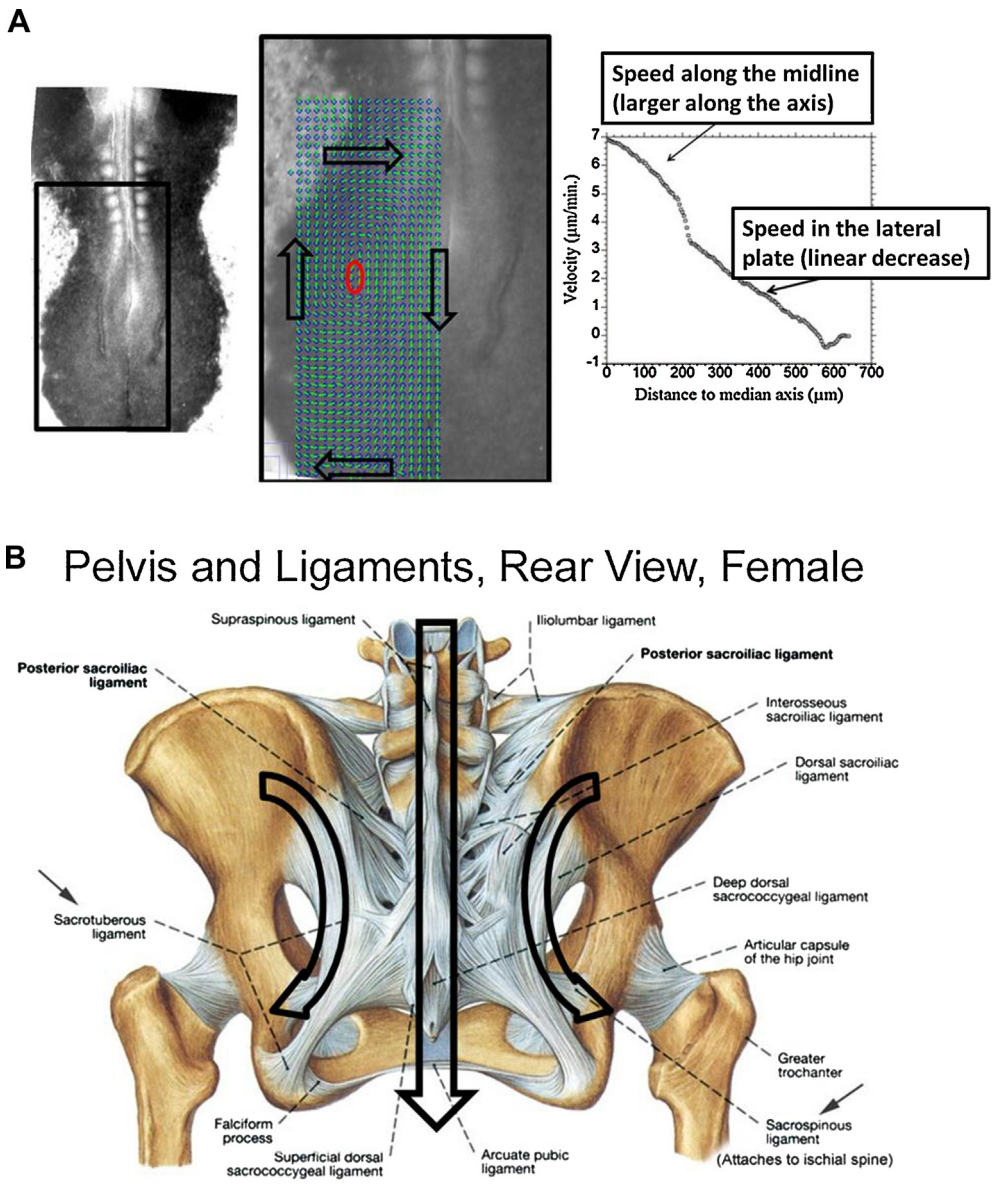

Figure 10 Continuing movement causes vast rotation of the lateral plates according to vortex dynamics (A). These vortices can be measured in vivo. Rotation within the vortices is typical for solid core rotation (it turns like a merry-go-round). Traces left by these movement are recognisable on the adult pelvis (B).

geometrical features of this object are produced by physical morphogenesis. Errors in morphogenesis (faulty physical parameters) induce aberrations such as aniridia, a genetic birth defect in which the eye has either no iris at all or a poorly developed iris [25]. Films produced recently using our techniques show the movements and clearly establish that the folds forming the optic cup develop as a result of mechanical factors. These movements are currently under investigation[2].

Flexion of the spine

The previous paragraphs describe the growing complexity of the animal shape: a disc changes into an elongated ampulla then into two small folds lying in close contact with each other; the folds elongate and rise above the blastula (to form the abdomen), after which winding movements of the elongated portion prepare the development of the limbs, pelvis, and other structures. The shape of the spine is the final result of all these movements, along the back. Segmentation of the back into vertebras adds a layer of complexity, which will not be discussed here. However, independently from the segmentation process, the development of bends in the spine is inherent in the cascade of elongation and growth movements, which is superimposed

[2] Fleury V, Foubet O. Understanding the physics of facial development in the chicken embryo with direct optical time-lapse video-microscopy and PIV tracking [Submitted].

(and precedes) the segmentation process. The bends that develop in the spine during morphogenesis are particularly difficult to observe, as the embryo must be viewed from the side, which requires challenging specimen preparation procedures. Nevertheless, bend formation can be observed in the chick embryo, at least during the first few days of development. Bending of the spine is seen to indicate feedback between growth and flexion of the 'back'. At the stage where the embryo has a gel-like consistency, growth corrects the bending, and bending modifies the intensity of the pushing forces related to growth. The result is the development of the physiological bends in the spine, which originate in dynamic waves that can be understood only via in vivo time-lapse imaging. Birth defects probably result from flaws in the movement pattern due either to absence of one of the parameters controlled indirectly by genetic processes or to idiopathic chronic postural problems that irreversibly alter the morphogenesis of the spine. Investigations into these movements are in their very early stages.

Conclusion

Embryology is being re-built from its foundations based on new knowledge into the deepest origins of the movements that shape the animal body. This new knowledge has been obtained via cross-fertilisation between the fields of biology and physics. Genetics clearly play a crucial role by dictating the visco-elastic parameters of living matter, as well as non-linear feedback mechanisms known as 'differentiations' and characteristic of living systems. For the physicist, differentiation changes the parameters governing the source force terms involved in developmental processes, which should be viewed as a visco-elastic problem.

This visco-elastic problem is characterised by three main factors: a symmetry breaking in the starting condition (e.g., quadrupolar for bilaterally symmetric animals such as vertebrates; and monopolar for radially symmetric organisms such as jellyfish and Hydra); the visco-elastic parameters of the material (viscosity, elastic modulus, etc.); and the source force terms (in general, cell traction and dilation). We are currently witnessing the mathematisation of the early stages of embryogenesis, at the quantitative level, with the entire visco-elastic field being viewed as a whole. Clearly, much work remains to be done, particularly regarding evolution.

Disclosure of interest

The author declares that he has no conflicts of interest concerning this article.

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