Mechanics in embryogenesis and embryonics: prime mover or epiphenomenon?

RICHARD GORDON*

Departments of Radiology, Computer Science and Electrical & Computer Engineering, University of Manitoba, Health Sciences Centre, Winnipeg, Canada

ABSTRACT **Mechanics is shown to be an important, perhaps central component to the differentiation and development of embryos. Mechanics of the nucleus may also be involved in determining which genes are expressed in a given cell. There are two major approaches at present to the mechanics of differentiation in embryos: morphomechanics and differentiation waves. These are compared in detail, to provide a starting point for future experimental work to bring them into one conceptual framework. This may rationalize the present cookbookery of stem cell production by placing it in the context of differentiation waves and the differentiation code. Embryonics, the realization of concepts from embryology in computer hardware and software, might be considerably enhanced by incorporating mechanical concepts of embryogenesis. Segmented robots, modular robotics, cellular microrobotics, flexible electronics, wearable computers, diatom nanotechnology and waves in active media point to a synthesis that we could call embryonic robotics.**

KEY WORDS: *embryo physics, differentiation wave, morphodynamics, differentiation code, artificial life*

Introduction

The ascendancy of molecular biology over the past half century has left untraveled and abandoned roads in biological research. One of them began in earnest with the efforts of Basel born Wilhelm His to explain neural tube closure by analogy to the mechanical buckling of laminates (His, 1874). The idea was that forces pushing from the flanks of the embryo towards the midline caused the buckling. Unfortunately, reality interceded when Wilhelm Roux slit the sides of a frog embryo and the neural plate buckled and formed a neural tube anyway (Roux, 1888). The solution to this impasse can be seen in the three dimensional model of Jacques Loeb (Figure 1), in which the lateral forces of buckling are generated by stretching in the perpendicular direction (a prediction later shown to be correct, with stretching provided by the notochord and/or notoplate (Jacobson and Gordon, 1976; Gordon and Jacobson, 1978; Keller, 1984). Loeb said:

"If we take a thin, flat plate of elastic rubber and lay it on a drawing-board, we can imitate the stronger growth in the center by sticking two tacks into the middle of the rubber, a short distance apart and then pulling them in opposite directions. In this way we may imitate unequal growth, the center growing faster than the periphery. If we then fix the tacks in the drawing-board, so that the rubber in the middle remains stretched, we get the same system

of folds as that shown by the embryo of a chick. I mention this way of demonstrating the effects of unequal growth as the ideas of His are still doubted by some morphologists" (Loeb, 1912).

Indeed, except for Loeb, who generally avoided discussing internal mechanisms (Pauly, 1987) and a few others (Glaser, 1914a,b; 1916), His' mechanical approach to embryos almost vanished from the scientific literature. His was also vehemently opposed by Ernst Haeckel, which didn't help (Oppenheimer, 1967).

The biggest foray last century into the mechanics of development, which unfortunately has little impact in embryology, perhaps because it eschewed genetics (Keller, 2000), is that of D'Arcy Thompson in his book *On Growth and Form* (Thompson, 1917, 1942). Thompson's transformations have proved useful in tracking shape change (Kavanagh and Richards, 1942; Richards and Kavanagh, 1943, 1945; Burnside and Jacobson, 1968; Jacobson and Gordon, 1976a; Gordon and Jacobson, 1978; Bookstein, 1978; Bookstein *et al.*, 1985; Bookstein, 1991), but not, so far, in uncovering underlying mechanisms. For example, given that the mitotic apparatus appears to swing in the direction of elongation of elongated gourds, such as the snake gourd, but is random in round gourds (Sinnott, 1960), one would expect that directed cell division would be responsible for plant shape. However, this has been shown to be false for leaf shape (Smith *et al.*,

Address correspondence to: Dr. Richard Gordon. Departments of Radiology, Computer Science and Electrical & Computer Engineering, University of Manitoba, Health Sciences Centre, 820 Sherbrook Street, Winnipeg, MB R3A 1R9 Canada. Fax: +1-204-787-2080. e-mail: GordonR@ms.UManitoba.ca

1996). Whole leaf mechanical approaches haven't solved the problem (Hay *et al.*, 2000). Similar questioning is needed for oriented cell division in neuroepithelium (Sausedo *et al.*, 1997).

We are now exiting a long era of genetic determinism, the idea that *somehow* (His' quite valid "To think that heredity will build organic beings without mechanical means is a piece of unscientific mysticism", His, 1888) "genes control development" (Probst *et al.*, 1992). This awakening from a long sleep of reason is occurring in fits and starts. My intention here is to give the reader a sampling of research demonstrating roles of mechanics in embryology and then try to consolidate the two superficially different approaches in my research (differentiation waves) and that of Lev V. Beloussov (morphomechanics). These mechanical approaches have the curious consequence of reopening the question of whether development is an interaction between cells, or a phenomenon involving the whole organism. I resurrected this old challenge to the cell theory (Gordon, 1999) and it is the central theme of a new book (Pivar, 2004; Gordon, 2006). I will end by considering possible implications of all of this for rationalization of the production of tissues from stem cells and for embryonics, the idea that we should create computers that build themselves by analogy to the self-construction of embryos.

Atoms versus form

Any time-lapse movie of a developing organism shows the lie that it is all chemistry. Embryo-scale mechanical effects are blatant, if unexplored and thus unexplained. While at the level of macromolecules, motor molecules abound (Schliwa, 2002) and may be the points at which ATP and GTP provide the ultimate chemical source of energy for the generation of mechanical forces, the spatial and mechanical organization within cells and between cells may govern what happens. This intellectual tension between the ancient Greek idea that all that counts is the motion of atoms, versus higher order structure, has been explored nicely for single cells by Franklin Harold (Harold, 2001b), who moves the problem all the way back to the origin of life.

Is there a way to resolve this tension? Physics, at least until recently, told us that there is "nothing but" the interaction of matter and fields (electromagnetic, gravitational, etc.). While we're not so sure about this, with the discovery that the material of the universe is only 4.4% baryons (Bennett *et al.*, 2003) and acceptance of quantum entanglement as a real phenomenon (cf. Gordon *et al.*, 2005b), it would seem that the interaction model might be sufficient to explain living phenomena. On that basis, classical statistical mechanics provides an example of what I call a "linking discipline" (Proposition 194 in Gordon, 1999), in which the hard intellectual work of linking one level of explanation to another, is done. I would contend that for embryology, this work has hardly begun.

For example, in terms of genetics, we have not yet solved the "simplest" morphogenetic problems:

"We are… exceedingly well informed about bacterial biochemistry, metabolism and genetics. One might expect, therefore, that how bacteria grow and shape themselves would be quite well understood. That is not the case and for a significant reason: even in bacteria, form is the result of multiple coordinated processes, regulated in time and localized in space, that are but indirectly related to what is spelled in the genes" (Harold, 2002).

"I hold the mildly heretical view… that the genetic paradigm as it stands is insufficient, incomplete and fundamentally misleading. Briefly, biological organization is made up of multiple layers, which span the range from molecules to cells [to embryos, adults, populations, ecologies and biospheres]. Genes do, of course, specify order at the level of molecules and supramolecular complexes that arise by self-assembly, such as ribosomes. But molecular structures do not suffice to specify cellular structure, for cells do not arise by self-assembly of their molecular constituents" (Harold, 2001a).

A similar challenge, now of practical importance for "growing nanotechnology" (Gordon *et al.*, 2005a), lies in bridging the intellectual gap between genome sequencing and morphogenesis of diatom shells (Drum and Gordon, 2003; Gordon and Parkinson, 2005). We can be quite certain that the currently popular network approaches, attempting to simulate the gene products of the whole genome (Tyson *et al.*, 2001; de Jong, 2002), will not solve the problem of form of bacteria, let alone form of multicellular organisms, despite the enthusiasm for this approach:

"One of the foremost challenges of 21st century biological research will be to decipher the complex genetic regulatory networks responsible for embryonic development" (Halfon and Michelson, 2002).

The reason for impending failure is that network models do not include the physics of the organism. For example, some bacteria have an internal pressure of about one atmosphere (Arnoldi *et al.*, 2000) and amphibian embryos reach 7 atmospheres (Beloussov, 1998), suggesting that physics may be quite important for both.

Fig. 1. Stretching of a sheet of rubber *(dental dam) leads to neural tube formation by lateral compression, even though there is no external force pushing the sheet laterally (Loeb, 1912).*

Physics can have a global effect on a cell or organism. The relevant physics might include:

1. Volume effects, 2. Electrical effects, 3. Optical effects, 4. Magnetic effects and 5. Mechanical effects. I'll give just brief examples of the first four:

1. The ratio of the volume of cytoplasm to the volume of the nucleus has an effect on the cell division time and has been modeled in sea urchin embryos (Ciliberto *et al.*, 1999). Basal metabolism, dependent on this ratio, affects ecology and evolution (Martin and Gordon, 1995).

2. There is an elegant model for the formation of polarity in the spherically symmetrical algal (single-celled) egg of the seaweed *Fucus*, in terms of current generating ion channels that move together in the cell membrane (Jaffe *et al.*, 1974; Robinson and Jaffe, 1975). Electric (ionic) current passes out of the neural plate in chicks (Jaffe and Stern, 1979) and regenerating limbs (Borgens *et al.*, 1977).

3. Cells can apparently "see" and move in a directed fashion in response to infrared light (Albrecht-Buehler, 1992).

4. Fruit fly embryos develop abnormal segmentation patterns when briefly exposed to weak, static magnetic fields at a critical period (Ho *et al.*, 1992; Ho, 1998).

These phenomena have not been consolidated into explanations of how embryos form or organisms regenerate and tend to be ignored.

Mechanical control of genes

The best antidote to the oft repeated expression that "genes control… X" is to read the literature about X controlling genes. The evidence for mechanical control of gene expression starts with the work of Avri Ben-Ze'ev, who investigated changes in gene expression in cultured cells that depended on whether they were attached to a substrate or suspended free in a gel, otherwise being in the same medium (Ben-Ze'ev *et al.*, 1980; Ben-Ze'ev, 1983; Farmer *et al.*, 1983; Ben-Ze'ev, 1984a,b, 1985). He concluded that "the cytoskeleton may regulate gene expression" (Ben-Ze'ev, 1991). Donald Ingber and his colleagues have placed cells on substrate spots or squares, surrounded by hydrophobic substrate to which they do not adhere and found that cells differentiate at a specific spot size (Ingber and Folkman, 1989; Mooney *et al.*, 1992; Chen *et al.*, 1997, 1998; Dike *et al.*, 1999; Huang and Ingber, 2001). Ingber concludes: "Thus, mechanical restructuring of the cell and cytoskeleton apparently tells the cell what to do" (Ingber, 1998).

Reciprocity between the genome and mechanics

There is much discourse on the emergence of "higher order" properties from the interaction of lower order "units" (Emmeche, 1994; Holland, 1998; Ronald *et al.*, 1999; Johnson, 2001; Gordon, 2000), some of it reaching religious conclusions (Morowitz, 2002). However, most seem to miss what I regard as the essence of the problem: higher order, so-called emergent phenomena can feed back on the lower order phenomena and alter them. Let's take the extreme of our own conscious behavior. While we cannot alter the basic laws of physics, by changing boundary conditions, we can alter what physics happens (Martin and Gordon, 2001).

A more mundane example is the "higher order" phenomenon

of surface tension (§ 1.10 in Gordon, 1999). The adhesion of embryo cells of the same and different kinds behaves quite similarly to mixed oil and water: like separates with like "due to" the interfacial tension (Townes and Holtfreter, 1955; Steinberg, 1963; Phillips and Steinberg, 1969; Phillips *et al.*, 1972; Gordon *et al.*, 1975; Phillips *et al.*, 1977; Phillips and Steinberg, 1978; Edelman, 1988; Steinberg, 1996). Of course, in this case we have developed the statistical mechanics of interfacial tension to the point where we are quite comfortable in switching between the molecular and macroscopic levels without worrying about philosophical consequences. In this sense, the emergence seems trivial, the awe is gone and the problem seems solved in essentially reductionist terms. The initial boundary conditions are either the arrangement of cells in an embryo when adhesion phenomena are "turned on" (via synthesis of certain membrane bound molecules, Edelman and Jones, 1998), or the configuration in which we place such cells in experiments.

I suspect, if we work at it long and hard enough, we will achieve the same degree of reductionism and understanding of boundary conditions for all of embryological development. The agenda was set out for us by His, but no one is yet doing the sustained work required of us:

"The ways of determining the forms and volumes of germs and embryos are somewhat longer and more tiresome than the simple inspection of stained sections; but the general scientific methods of measuring, of weighing, or of determining volumes cannot be neglected in embryological work, if it is to have a solid foundation of facts, for morphologists have not the privilege of walking in easier or more direct paths than workers in other branches of natural science" (His, 1888).

In the synthesis of adhesion molecules, the role of the genome is to turn on their synthesis at the right time and place. The cells would then begin to move in the embryo due to their interfacial tensions and the nonequilibrium configuration in which they started. But what happens next?

The clue comes from our prediction (Gordon and Brodland, 1987) and discovery (Brodland *et al.*, 1994; Gordon *et al.*, 1994) of waves of contraction and expansion of the surfaces of epithelial cells in urodele amphibian embryos. Our best guess is that each wave in which a cell participates sends a one bit signal to its nucleus. If the wave is a contraction wave, the nucleus exposes one new subset of its genes (compared to the subset currently exposed), while if it is an expansion wave, it exposes an alternate subset of its genes (Björklund and Gordon, 1993b). Genes that are "exposed" are those available to be turned on or off, i.e., available for transcription. Sequestered genes are tucked away, so that they cannot be transcribed.

These "differentiation waves" have a mechanical component, which makes them simple to observe (Gordon and Björklund, 1996). Thus we hypothesize that the mechanics of the waves "controls" the genes. Of course, the genes then alter the boundary conditions, for instance, by synthesizing adhesion molecules, which then changes the shape, tissue configuration and mechanics of the embryo and probably thereby set up the conditions for launching the next waves. We thus see that the reality may be that there is a reciprocal relationship between the mechanics of an embryo and its genome, rather than either "controlling" the other. The "genetic program" is actually a "genome <--> physics" program.

Switching within networks or between networks?

What is occurring inside the nucleus of a cell when the cell changes from one kind to another? Most models assume that the nucleus is an unorganized bag of chemicals (including the genes) arranged in a network of interactions. Such networks have "basins of attraction" that are presumed, somehow, to correspond to the states of differentiation of a cell (Delbrück, 1949; Kauffman, 1993; Huang and Ingber, 2000).

An alternative model starts from the observation that the nucleus has quite a bit of structure, with chromosomes in specific places (Miller *et al.*, 1963a,b; Nagele *et al.*, 1995, 1998) and orientations (Francis-Lang *et al.*, 1996), with mechanical connections between them (Maniotis *et al.*, 1997a), to the nuclear membrane and via the nuclear membrane all the way to the cell membrane (Maniotis *et al.*, 1997b). We then take as a working model that the nucleus has a discrete physical structure, different for each cell type, and that its configuration changes when the cell changes from one type to another (§ 10.13 in Gordon, 1999). In each configuration, some genes are exposed, while others are sequestered. Thus, each configuration corresponds to a different network. The mechanical switching between nuclear configurations would, then, "control" which genes are expressed (Carroll *et al.*, 1995).

Consolidating differentiation waves with morphomechanics

Roughly in parallel with our efforts on differentiation waves (Gordon and Brodland, 1987, 1989; Björklund and Gordon, 1993a,b; Brodland *et al.*, 1994; Gordon *et al.*, 1994) Lev V. Beloussov and his colleagues have worked out a mechanical approach to embryogenesis they call morphomechanics. The basic idea of "contact cell polarization" is that an epithelium with an internal pressure (perhaps 7 atm in amphibians; see p. 90 in Beloussov, 1998) can undergo a transition in which some cells contract their apical surfaces and the rest do not. Beloussov (Beloussov, 1998) attributes the theory explaining his observations to the late Boris Belintsev (Belintsev *et al.*, 1985; Belintsev *et al.*, 1987; Belintsev, 1991). There is no need for positional information: "…the model shows a way for a really *delocalized* regulation of morphogenetic processes, without each cell 'knowing' its exact position…." (Beloussov, 1998; cf. (Beloussov *et al.*, 1994).

Positioning of the boundary between contracted and (passively) expanded cells in the ectoderm is provided by its nonuniform strain state, which can be altered by relieving the strain over the whole surface (Beloussov *et al.*, 1990), at the lateral margins (Yermakov and Beloussov, 1998), or at the dorsal lip of the blastopore (Beloussov and Snetkova, 1994; cf. Beloussov, 1988). I have similarly postulated that the strain state of the ectoderm determines the trajectory of the ectoderm contraction wave (§ 9.25 in Gordon, 1999). Slitting experiments in the neural plate reveal anisotropic tissue tensions (Jacobson and Gordon, 1976) that could affect differentiation waves that may be involved in segmentation of the neuroepithelium (Gordon *et al.*, 1994). Convergence-extension movements in *Xenopus* also involve anisotropic strains (Davidson and Keller, 1999). Thus we can see that my redefinition of the genetic program as a branching alternation of physics and gene expression (Proposition 14 in Gordon, 1999), can be extended to include the physics of morphomechanics:

1. one of a pair of differentiation waves produces:
2. change in gene expression in the cells propagating that wave, leading to:
3. change in strain state and other physical effects (electrical, etc.?), which result in:
4. launching of a pair of differentiation waves, etc. (i.e., go to #1 for each wave).

All of these are subsumed in a single node of a differentiation tree (§ 4.02 in Gordon, 1999). To take into account the hypothesized mechanical events in the nucleus, the full, branching "cycle" becomes:

1. one of a pair of differentiation waves generate a:
2. one bit signal to the nucleus, which produces:
3. change in the structure of the nucleus, resulting in:
4. change in gene expression in the cells propagating that wave, creating:
5. change in strain state and other physical effects (electrical, etc.?), which result in:
6. launching of a pair of differentiation waves, etc. (go to #1 for both waves).

This model reconciles the either genetics/or physics approaches (Beloussov *et al.*, 1997) by incorporating both. Contact cell polarization, then, may be seen as setting up anisotropies that shape the trajectories of differentiation waves and perhaps create the mechanical conditions for their launching (Gordon and Brodland, 1987; though electrical phenomena may also be involved: § 9.27 in Gordon, 1999). Morphomechanics may, further, explain the suggested mechanical dependence of the launching of one wave on the completion of another (a wave-wave interaction and relay mechanism), which could then explain the temperature independence of the sequence of developmental events in poikilothermic organisms (Proposition 82 in Gordon, 1999).

A number of observations suggest similarities and differences between contact cell polarization and differentiation waves:

1. The height programs in neurulation stage urodele embryos (Jacobson and Gordon, 1976; Gordon and Jacobson, 1978) may correspond to the maps of contact cell polarization in gastrulation stage anurans (Figure 2.26 in Beloussov, 1998). The rate of propagation of the latter phenomenon is 2 to 8 µm/min (Beloussov and Petrov, 1983; Petrov and Beloussov, 1984), comparable to the speed of the ectoderm contraction wave in axolotls of 3 µm/min (Brodland *et al.*, 1994) (expected to be slower because of the longer duration of gastrulation in axolotls compared to *Xenopus*).

2. Our empirical observation that a contraction wave in a given tissue may be followed slightly later by an active, epiboly-like expansion wave (Figure 16 in Gordon *et al.*, 1994), launched at a distance in the same tissue, would seem to fit the Belintsev model (Belintsev *et al.*, 1987). However, contracted ectoderm cells relax back to their previous apical diameters (Brodland *et al.*, 1994), while contact cell polarization appears to persist in an "all-or-none" manner (Belintsev *et al.*, 1987).

3. The theory of contact cell polarization assumes that contraction of a cell is active, while expansion is passive (Belintsev *et al.*, 1987). Differentiation waves appear to be based on a tensegrity cytoskeletal apparatus, the "cell state splitter" (Brodland and Gordon, 1987; Chapter 3 in Gordon, 1999), which actively brings a cell to either an apically contracted or expanded state via

contraction of the apical microfilament ring in a cell or expansion of an apical mat of microtubules oriented parallel to the apical surface (Gordon and Brodland, 1987). An intermediate filament ring provides elasticity and allows for a metastable state of the cell state splitter (Martin and Gordon, 1997), which presumably allows a cell to wait for a wave to impinge upon it.

4. The trajectory of the ectoderm contraction wave (Figure 17 in Gordon *et al.*, 1994) covers the hemisphere of ectoderm that becomes the neural plate, while contact cell polarization appears to have a smaller trajectory (Figure 2.26 in Beloussov, 1998), though some contact cell polarizations do move in the cranial direction (Novoselov and Beloussov, 1990).

5. Beloussov suggests that it is a particular contact cell polarization wave, not all, that leads to cell differentiation (Beloussov, 1982), whereas every differentiation wave observed so far correlates with a step of differentiation (Gordon *et al.*, 1994).

6. Beloussov (Beloussov, 1998) suggests that morphomechanics provides a solution to the problem of generally decreasing symmetry as an embryo develops. However, the same objection that I raised to Turing diffusion/reaction mechanisms (Turing, 1952) applies: there are multiple choices for symmetry breaking at each step (§ 1.09 in Gordon, 1999). (Turing (Turing, 1952) in fact considered a mechanical alternative to his primarily chemical model for symmetry breaking: § 1.15 in Gordon, 1999).

There are enough distinctions between contact cell polarization waves, which are of two distinct types (parallel and perpendicular to an epithelial surface (Beloussov, 1998)) and differentiation waves, to suggest that both (or all three) exist as separate phenomena. For example, the unexplored 50% apical area reduction of the neural plate as it changes from a hemisphere to a flat disk, certainly a massive columnarization (Figure 25 in Jacobson and Gordon, 1976), may be a contact cell polarization wave.

We thus see that the two contemporary approaches to mechanics in cell differentiation in embryos have much in common and need to be brought into one framework. They both show a central role for mechanics in embryogenesis. Thus mechanics in embryogenesis is hardly an irrelevant epiphenomenon.

Stem cells and developmental mechanics

The differentiation tree may be a useful guide to how to produce replacement tissues for our bodies. The egg could be our clone. Instead of using it to produce a whole infant and sacrificing it for parts (a bioethics nightmare), the undifferentiated egg could be proliferated (as in embryonic stem cells) and the cells then forced through a particular sequence of contractions and expansions. Such a "tissue synthesizer", following a specified differentiation code (Björklund and Gordon, 1994) might turn all the cloned cells into the one needed replacement tissue and rationalize the current cookbookery of how to get stem cells to differentiate the way we want them to. Of course, since each mechanical event of contraction or expansion of the apical surface of the cell is actually a mechanochemical event, we may find ways to intervene and accomplish execution of the differentiation code biochemically. The role of mechanics in stem cells is a burgeoning field, suggesting that its role may indeed be more than incidental (Wang *et al.*, 2001; Banting *et al.*, 2005; Kobayashi *et al.*, 2004; Park *et al.*, 2004; Roeder *et al.*, 2005; Yamamoto *et al.*, 2005;

Bakker *et al.*, 2004; Kawanishi and Oikawa, 2004; Schild and Trueb, 2004; Marquez *et al.*, 2004; Cui *et al.*, 2004; Barkhausen *et al.*, 2003; Naka *et al.*, 2004; Berry *et al.*, 2003; Yamamoto *et al.*, 2003; Simmons *et al.*, 2003; Yoshino *et al.*, 2003; Wan *et al.*, 2003; Sambajon *et al.*, 2003; van Griensven *et al.*, 2003; Altman *et al.*, 2002; Pearson, 2003).

Impact on embryonics

Embryonics starts from the laudable goal that computers that grow by processes similar to embryos would be worth having for self-replication and self-repair (Sipper *et al.*, 1997a,b; Mange *et al.*, 1999, 2000; Restrepo *et al.*, 2000; Sipper, 2002). However, the computers envisaged are rather stiff and unlifelike: "…the ultimate goal is to use huge chessboards – with billions of cells…", not at all like the liquid metal T-1000 robot in the movie *Terminator 2: Judgment Day* (1991). This is perhaps because embryonics has been based on one particular, perhaps erroneous model for embryo development: the concept of positional information, which requires a coordinate system for cells, an ability of each cell to determine its coordinates and a means of decoding what it is supposed to do by "looking up" those coordinates in its genome (Proposition 35 in (Gordon, 1999): "positional information does not exist"). Differentiation waves, by contrast, require only that a cell's genome respond to the sequence of contraction and expansion waves that the cell participates in. It need not know where it is at all. Waves in an active medium (Markin *et al.*, 1987; Scott, 1970; Villar *et al.*, 1996), which include differentiation waves, can be simulated on two and three dimensional tessellations (Gerhardt *et al.*, 1990), but this is not essential: they can also propagate through a more flexible, less organized sheet, volume or spatial network of units with the same or better global effect (Markus, 1990, 1999).

It seems to me that an alternate physical model of computers is needed. Two kinds of computers are being developed that, if they were combined with the embryonics approach, might yield a better approximation to a growing, differentiating embryo. Modular robots are made of units that have motors and can configure and reconfigure themselves in many ways (Yim *et al.*, 2002), going beyond simpler segmented robots (Hirose, 1993; Menzel and D'Aluisio, 2000). The other technology that is rapidly being developed is the wearable computer, building circuitry right into clothing (Mann, 2002; Mann and Hall Niedzviecki, 2002), one form of flexible electronics (Dorsch, 2001).

The modular robot units are 5 cm wide, but could be shrunk (Yim *et al.*, 2002). A modular robot rearranges the units it has, but does not build new units from smaller components. Neither do cells. They, rather, double their essential components and then separate the components into two daughter cells. This takes a degree of internal flexibility that goes beyond present flexible electronics.

A new thrust into direct three dimensional growth of nanotechnology starting with single celled algae called diatoms (Gordon and Aguda, 1988; Gordon *et al.*, 2005a) could help unite the field of cellular microrobotics (Fukuda and Ueyama, 1994) with embryonic robotics. An alternative approach would be to incorporate living cells into the electronics (Potter and DeMarse, 2001; Potter, 2001).

Robotics brings mechanics into computing. Embryonics brings

the idea of imitating growth and differentiation into computing. I have shown that mechanics may be an essential component of real life embryos, so perhaps we should reach for embryonic robotics as the next goal, perhaps a little beyond what Wilhelm His imagined:

"But we must go further in our propositions. Embryology and morphology cannot proceed independently of all reference to the general laws of matter, - to the laws of physics and of mechanics. This proposition would, perhaps, seem indisputable to every natural philosopher; but, in morphological schools, there are very few who are disposed to adopt it with all its consequences" (His, 1888).

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