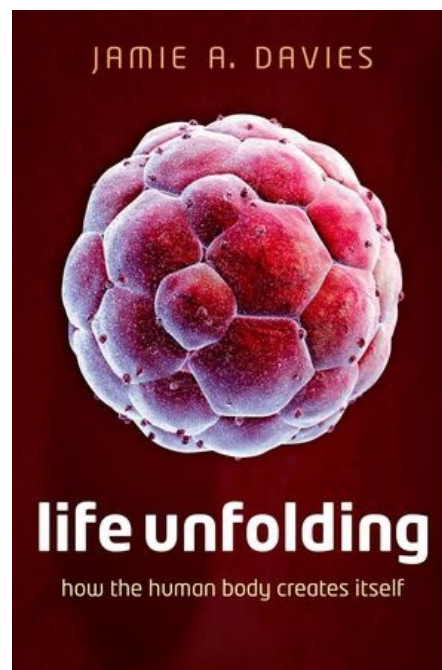




Life Unfolding: How the Human Body Creates Itself

Jamie A Davies

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Where did I come from? Why do I have two arms but just one head? How is my left leg the same size as my right one? Why are the fingerprints of identical twins not identical? How did my brain learn to learn? Why must I die?

Questions like these remain biology's deepest and most ancient challenges. They force us to confront a fundamental biological problem: how can something as large and complex as a human body organize itself from the simplicity of a fertilized egg? A convergence of ideas from embryology, genetics, physics, networks, and control theory has begun to provide real answers. Based on the central principle of 'adaptive self-organization,' it explains how the interactions of many cells, and of the tiny molecular machines that run them, can organize tissue structures vastly larger than themselves, correcting errors as they go along and creating new layers of complexity where there were none before.

Life Unfolding tells the story of human development from egg to adult, from this perspective, showing how our whole understanding of how we come to be has been transformed in recent years. Highlighting how embryological knowledge is being used to understand why bodies age and fail, Jamie A. Davies explores the profound and fascinating impacts of our newfound knowledge.

Life Unfolding: How the Human Body Creates Itself Details

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From Reader Review Life Unfolding: How the Human Body Creates Itself for online ebook

Michael Dubakov says

Great book in general that provides overview picture about organism creation, based on adaptive cell communication. To me it was interesting to dig into some patterns that can be applicable to systems design, but here author provided just rough strokes, without many details, thus 4.5/5.

Nikki says

Well, now I feel silly that I didn't read this before my human biology exam! It describes, in very careful detail, how the human body builds itself, beginning at the point an egg is fertilised. It explains processes like cell division and gastrulation, and generally manages to make the whole complex process comprehensible. Davies doesn't get hung up on quantum biology or how consciousness is generated, but instead focuses on the physical processes by which the human body grows.

You may not find this entirely satisfying, because Davies very much relies on the fact that small events — a chemical gradient, a lack of symmetry in a cell — seem to prompt massive changes. If you feel (like this reviewer) that it's quite impossible for all this to happen just by a number of useful proteins happening to bump into each other in a sea of proteins which won't interact at all, you'll find this unsatisfying. There seems to be no room for a guiding ghost in the machine. But that is the best understanding we have, I'm afraid — and as a biologist, it makes sense to me. Which is not to say that it's all perfectly understood: it isn't. Sometimes, we can't do the experiments in a human context for ethical reasons. Sometimes, the data is just too difficult to obtain. But the fact remains that we do have a reasonable understanding of embryology, and that is described in this book.

I found it an easy and fascinating read, and would definitely recommend it if you have an interest. It doesn't get too technical as far as I'm concerned (but take that with a pinch of salt, since I have admittedly studied human biology). At a couple of points I found it useful to look up relevant Khan Academy videos to get a differently-worded explanation of the same events, taken step by step, but that's as much down to individual learning and teaching styles as anything.

Reviewed for The Bibliophibian.

K-dizzle says

This is a book full of wonder for anyone who is into high level cellular and molecular biochemistry. Others will find it a tough read and fail to appreciate the amazing way we develop from a tiny fertilized egg cell. I especially liked the variety of sources and simple (for anyone with a half-decent Biology background) models Dr Davies used to illustrate the various stages of development we go through. He is very clear in establishing the limitations posed on our understanding due to limited work with human embryos but still manages to explain embryonic development and beyond very well.

Gail says

Davies does a great job telling the events of human development as the story of how bodies build themselves. The structure of the book is to go each chapter through an important stage of development or a particular part of the body, in chronological order. You really get a sense of how "a striking feature of developmental mechanisms is the way they are nested," building on each other as the body builds itself. Partway through the book, I would have given it 3 stars, since some of the middle chapters started to drag - perhaps inevitable when you want to explain a particular organ but know it involves some complicated processes and pathways. However, I felt that it picked up at the end, answering bigger-scale questions like "why are your arms the same length?" that were really fascinating. This book is written for a general readership and I agree that it was very readable (often excellent science writing, sometimes laugh-out-loud funny) although I think you would have to enjoy science to enjoy it at all. That being said, even non-science readers who spot this on a shelf ought to read the last chapter, "Perspectives", to understand why a communication-centered view of development is fuller than a simply gene-centered view, why "nature versus nurture" isn't a good question to ask, and why this matters for understanding disease and treatments. An enjoyable read.

Erik Surewaard says

This is not an easy read. It covers a lot of biological development processes. Starting from a fertilized human egg cell, it covers the growth in the first few months of pregnancy. The discussion stops BEFORE the moment that the main organs are formed.

This book was first of all a great refresher if my high-school level biology. Further, I was also able to pick up quite some new insights on what actually occurs during the first phases of embryo development. Topics like e.g. how cells migrate and develop / specialize into functional cells (e.g. nerves, bone, gut, ...).

I enjoyed reading the book. I however had to spread it over several days. This to digest some of the pretty sophisticated concepts.

This book easily deserves a four star rating.

Atila Iamarino says

Uma ótima revisão de embriogênese. Leve, sem muitos nomes complicados, bem integrativa. O autor entende demais do assunto e sempre explica os fenômenos através de princípios, em que contexto acontecem e com consequências. Quando fala por exemplo sobre sistema circulatório, explica como os vasos se formam, a que sinal respondem, como entendem que parte do corpo precisa de mais sangue e depois como tumores conseguem recrutar isso. Excelente balanço entre profundidade no assunto e leveza de escrita.

Ellen Mobley says

Reading this as a 17 year old it was ambitious and challenging, nevertheless I still thoroughly enjoyed it and would recommend to people interested in human biology since the concepts can be applied to many areas. A tough read but I learnt so many new things and hoping to study this area of embryonic development later in life.

Wing says

This account of how we came into this world will certainly suspend the interested reader in deep awe. The first major breaking of symmetry using simple mechanical mechanism is truly breathtaking. Symmetry has to be broken in order for cells to differentiate and specialize. Then, through an unfathomably complicated network of signaling and feedback loops, complex structures develop. This decentralized system is robust, can adapt to the milieu, and can intrinsically rectify errors. Life is surely a miracle and surely there is a Creator!

Ushan says

In 1948 Hungarian-American mathematician and polymath John von Neumann wondered how biology with reproducing organisms is possible. He devised a mathematical concept called a cellular automaton: a grid consisting of cells, each in one of a fixed number of discrete states, capable of going to a new state depending on its previous state and those of each neighbors, and described a self-reproducing automaton. In real life, the adult human body has about 200 types of cells organized in tissues and organs, which all grow from a single fertilized egg, and with another human body are capable of creating another fertilized egg, completing the cycle of life. How does it all work?

The basic outline of human embryonic development has been known for over a century, but the last couple of decades saw many discoveries at the molecular level; the endnotes of this book have over 300 scientific papers mostly from the 2000s and the 2010s. I think that it is wonderful that von Neumann's model is mostly true: an embryonic cell changes its type according to what its neighbors are: other cells or fluid; we know many of the proteins cells use for signaling each other. At the interface of two cell types, cells of one of the types can change their type to a third one, and now there are two interfaces, and so on; or they can die if they have no place in the adult organism. One thing that the cellular automaton model doesn't cover is cells migrating from one place to another, like lymphocytes do in an adult organism, which happens many times during embryonic development. Another is cells multiplying in response to mechanical stress: for example, as the bones of arms and legs grow, so do the nerves, the skin, the muscles.

On the one hand, developmental biology is indeed, as Davies puts it, "alien technology", so much unlike human technology. On the other hand, its mechanisms: chemical gradients, chemical signaling, feedback loops etc. are not that mysterious. One example from the book: animals are segmented, something easier to see in an earthworm or a millipede than in a human, but the human spine is obviously segmented. The formation of segments is driven by an oscillating chemical reaction. Snakes have hundreds of vertebrae versus the human 33, and this reaction oscillates faster in snakes than in humans.

David says

Goes into some of the serious details of embryonic development without getting lost in the thickets and

without needing to resort to the mysto hand waving that is so common in popular science these days.
Probably not a good first book on the subject.

Kerem Bozdas says

Great book. I was a little bummed but not surprised when I realized one-third of it consists of glossary and references.

Dana Slaughter says

Development presented in an interesting and understandable way! This was a topic I never studied in school, but I found it fascinating.

Gendou says

This book is great. It's about embryology. The reader will learn in great detail about the genes which govern cell growth in different animals. Like other aspects of biology much of the knowledge comes from what we learn when diseases cause development to go wrong. There's also a lot to learn from modern genetics though we're still in the middle of this particular scientific revolution. Cataloging the genes is only the first step towards understanding how the human body creates itself.

Pete Welter says

Human life is not a miracle. A system of such complexity that we don't yet understand it does not mean that system is miraculous. It's just really complex.

We live in a time where we are starting to understand complex systems. We have the computing tools, the intellectual frameworks (from information and complexity sciences), and in this case the biological tools to start making sense of these intricate systems we can't understand fully.

"Life Unfolding" presents a communications-centered view of human development. This doesn't mean it supplants genetic explanations - in fact they are two sides of the same ideas - but it does mean that many of the explanations here center on how proteins, cells and organs communicate enough information to create a human body without a grand plan.

The picture of the developing human here is one of emergent behavior and complex and intricate information flows. The vocabulary here includes "signaling" and "gradients" and "feedback loops." Because of the constraints of evolution (far easier to add on to an existing process than change it), and development (stuff has to work all the while it's being created and changing form), the form that these take can sometimes be bafflingly and - at least at first blush - needlessly intricate. However, because of this, the ability of this system to develop, function and repair in the face of varying environmental conditions, mutations, and errors far exceeds what humans have been able to thus far create.

As a computer scientist, this is a view of biology that I could deeply understand: not just a big list of cell types and organs and functions, but a picture of the simple mechanisms (albeit combined in incredibly complex ways) underlying their creation and their function.

This isn't a biology textbook - it's meant for a popular audience. So you won't find exhaustive coverage of every aspect of development or precise names of genes and proteins. However, he curates examples of various mechanisms and subsystems so that he covers them in enough depth to communicate the concept, and then moves on to the next topic.

As a software/systems person with an interest in emergent phenomena, this book fit where my brain is right now. So, for me, this was the most enlightening book on human biology that I've ever read. My copy of the book is underlined and dog-eared and annotated on every page. Depending on your background, you may not find it as compelling.

At the very least though, it is a great book to give yourself a view on human development that you may not have been exposed to before, in a very readable and enjoyable form. Highly recommended.

The one wish I had while reading it was for some interactive simulations of the concepts. Sometimes, it takes many words to describe something that an interactive, dynamic, visual representation would communicate more clearly and in greater depth. It would be awesome if this book had an accompanying web site or app with such simulations.

Alex Telfar says

I got interested in embryology/development as I heard a computer scientist talk about how crazy it is that a ~725 MB program (our genome) can produce such complexity (us...). Our engineering skills are just nowhere near this level, the ability to construct fabulously complex systems from simple generating patterns.

Thoughts on the book : Interesting read, could have been written better. Otherwise, here are just a collection of thoughts and notes from the book.

Jamie seems to beg the question: "How does the fertilized egg, something symmetric, with low information/structure become asymmetric and highly structured?" I don't think this question makes sense, as there is plenty of structure in the DNA of the zygote. Information is not necessarily create but rather decoded/translated from genes to cellular structure. It does remind me of a puzzle I have come across before: how do neural networks generate an image from a single vector (through the conv transposes).

I like how Jamie pointed out that in our construction of requirement is that the fetus/baby must be a viable/functioning life form while it is still developing. This is a really nice contrast to most of the systems that we build.

Sequence of development is approximately the same as the sequence of evolution. Why!?! bc natural selection finds it easier to adapt existing mechanisms to new uses (want to collect some more examples of this). Adding a modification to something that already works is far easier. I would love to see some formulation of this as an optimisation problem. We are in state S, what are the minimal set of changes/steps we can take to minimise our loss. Given this strategy, how does it effect our regret? How can this number of steps be traded off for other goals/measures of efficiency? Fundamentally there is a computational problem, too much memory/energy/luck is required to explore more diverse solutions?

Jamie claims that development uses "No global coordination. Local rules. No hierarchy." Which is true in space, but not time? Consider the tree of cells as they divide, each passing on instructions, this is a hierarchy...

Gosh... some of the experiments we have done... Cut off and graft extra limbs of chicken fetuses so we can count the number of motor neurons produced. Grow disabled rabbits, one leg is lame, by inhibiting growth hormone locally, to see how organs are proportioned...

I love how hacky evolution is, we are just such a cluster-fuck of patches to side-effects of patches... A few strategies; augment something that already exists, allow the existing thing to grow and then delete it, (the kidney(s) ...) (want to collect more examples!)

The overpopulate and cull strategy (the trophic hypothesis) is interesting. It effectively gives the developing embryo the ability to auto-scale/size many features of our neural, muscular, ? systems to ...? at the cost of extra energy. Also has benefits for evolution making it easier to change one thing and have all the other systems auto-fit themselves given this change. Thus it is easier to make adaptations.

The HOX genes and the development of the somites was kind cool. The HOX genes are effectively a sequential program using counters to iterate through the various hox genes.

We deal with error correction in a seemingly successful manner. There seem to be a couple of strategies; keep a master copy (somewhere that is less likely to get damages) - stem cells grown in marrow. Or peer replication, just replace with neighbor. Relatedly, programmed cell death is also quite interesting, would like to look into this more. Obviously we are not perfect at this as an error in error correction normally leads to cancer.

Other things to think about

- Worm segments each contain their own kidneys, lungs, ...
- Bootstrapping a cell and bootstrapping a compiler.

Per Kraulis says

A brilliant book. It manages to explain a very complicated process of development of the embryo by focusing on the fundamental mechanisms. In particular it makes clear the fact that all forces working during development are in a certain sense local, that is, there is no overarching direction or plan. Every cell is doing what is natural for it at that specific place given its internal and external context.

A most important point that the book brings across is that the phrase "gene X is responsible for feature Y" is extremely misleading. It is a short-hand for the scientific statement that when one alters gene X, for example makes it non-functional, then feature Y of the embryo or the mature organism is in some way changed or dysfunctional. This does not mean that gene X contains all information required to produce Y. The genome is **not** a blueprint of the organism, it is more like a recipe for how to produce the organism given a suitable environment, a recipe where many genes are involved in creating each feature of the organism.

Giles says

A delightfully written book that caters to a wide unspecialised audience - you can skip some geeky bits without losing the whole sense of the work - who wants to learn a little more about the multidisciplinary science approach to the understanding of life: how it begins and how it continues to grow and specialise while it is ALREADY functioning.

The general theme is about the "how" in self-adaptive systems. There are plenty and honestly open questions, but this makes its reading all the more pleasurable.

Steven says

In depth narrative on how we grow from a single fertilized cell to a new-born baby ... Great if you want a crash course in Embryology.

Tristan Sherwin says

Jamie A. Davies has done an excellent job in explaining some of the mysteries of how a human life forms and develops through the gestation period and even beyond birth. An unfolding journey that begins as a single cell dividing itself over and over, with each layer of replication adding enough complexity and difference to define and guide the following stages. Cells, through variances in location to one another, the strength of signalling proteins and mechanical forces, and the influences of the environment around it, adapt and change via switching off/on particular genes to become the varying diverse biological components of a living being – all without having to have some kind of “blue-print” of “fore-knowledge” of the final structure that they are forming. As Davies puts it, at the end of an early stage in an embryo’s development,

“It has pulled itself up by its own bootstraps, first using simple geometrical tricks to create differences where there were none, and then using these new differences between cell types as a source of information to create yet more differences, more information, and more organisation. All of this was accomplished by relatively simple mechanisms that obey simple, local rules” (p.64, Hardback edition)

How a body builds itself, as explained by Davies in the introduction and throughout, is not analogous to how we construct a car or a bridge. There is no foreman or workers following a design. The body builds itself via the “simple” responses of individual cells to their environment with no comprehension of the “grand scheme of things” beyond their decisions.

This may seem illogical to us, “how can cells, that know nothing of the final picture, go in to form such a complex working biological marvel?” Davies does a good and persuasive job of putting his case across, using his own experience in the field of cellular and anatomical development, and by citing years of research that has (and continues) to explore this exiting field.

Seeing how cells “pull off” this amazing feat doesn’t in anyway diminish the wonder of “the miracle of birth” – in many ways, after reading this, that wonder has intensified. How life holds itself together, how this community of an organism that I call my body maintains and extends itself is extraordinary. This is the kind of book, that once you’ve read a chapter, you’ll find yourself wondering at the movements of your hand and contemplating your ability to see those movements. Life really is fascinating.

That doesn’t mean that this is an easy book to read. Davies has done a fine job in simplifying all this, and there are many areas that haven’t been touched on and developmental journeys that have been side-tracked for the sake of brevity. But bodies are not simple things, and to grapple with things that are complex will require the

reader being prepared to stretch their thinking. For those who are familiar with this area, then this book will provide a good condensed view of the basic principles (and providing further works/research papers to explore). For those new to all of this – and I still think of myself in this boat – then you might find yourself getting a little bit lost with new terminology, membrane names and protein labels (although Sonic Hedgehog is pretty easy to remember). So for the newbies in this field, be prepared to take your time, and be willing to sometimes read back before reading forward.

Overall, I found this book a fascinating, compelling and well written treatment of how we come to be.

It's not the only book I've read on this topic, and I certainly wouldn't say it's the only book you need to read. So, if you're interested, I'd also recommend the following works: The Epigenetics Revolution by Nessa Carey, The Music of Life by Denis Noble, and, for a more philosophical treatment of human biological and evolutionary development, Aping Mankind by Raymond Tallis.

Greg Nigh says

I continue to be amazed by what science pretends to understand. Outside of mathematics and physics, predictions beyond the trivial are scarce and mere descriptions abound. Materialists say that everything - biology included - boils down to physics and chemistry, but even chemistry is largely descriptive. The physical properties of any new compound - its boiling and crystalization points, for example - can rarely be predicted with any accuracy from its chemical composition. You just heat it and cool it and take notes.

Life scientists have struggled to translate the dynamics of life into an explanation that calls *solely* upon physics and chemistry. If such an explanation were to stick, then there would be no need for a ghost to be resident in the machine. It would be all machine. There would be no *elan vital*, no *deus ex machina*, no force that is vital beyond that exerted by molecules and their motions. And this project has developed into a budding genre unto itself within popular science writing, whereby established experts explain to an educated public how every process is just a set of elaborate mechanisms, all the way down. The field of neuroscience is laden with these tomes. To this, add embryology.

Life Unfolding: How the Human Body Creates Itself is by Jamie Davies. I can't offer a comprehensive review of the book, because I haven't finished it and certainly won't. But I want to use just the first few chapters of the book to illustrate a grand deception, one that is both colossal in scope and virtually ubiquitous throughout this genre of writing, and I hope it explains why I won't finish the book and don't recommend it to others. The deception is to speak of information, a very precise concept and representational presence throughout living systems at every level, as though it just happens.

Davies wants his readers to believe that building a human body only *seems* complicated, but that it is merely the replication of simple and basic components compelled by chemical and engineering principles into ever higher levels of organization. He starts his book by describing the simple components that do complex things. Simple components like genes, like regulatory networks, like centrosomes, and like microtubules. After describing an astoundingly complicated set of interrelated networks, he summarizes thusly:

Seen as a whole, the systems described ... may seem very elaborate and complicated. Seen component-by-component, though, they are very simple. Each component has only to do a very simple task ... The use of simple component parts connected together with rich feedback is

characteristic of life ... systems of 'dumb' biological molecules can be organized to solve problems... (26-27)

One quickly gets the sense that Davies doesn't understand the subjects he is writing about.

I wish I had time to go through the absurdly absurd impossibility of each of these systems he describes as composed of these numbskull molecules, which all interact, for all practical purposes, flawlessly, and have done so for damn near 3 billion years. Davies does his level best to cast these characters as simpletons.

Microtubules (to take one example), he says, are just repeating units that stack like Legos to form filaments that span the cell. But these are hardly mere tubes. The eminent mathematician Roger Penrose attributes nothing less than consciousness itself to the quantum events that unfold within the meticulously precise space of the microtubules, a space that depends completely on its ultrafine structure.

But back to Davies. Once the necessary genes (where did *they* come from?) in the DNA (now a whole encyclopedia of genes?) transcribe the appropriately structured proteins (huh?), and do so with the aid of myriad other regulatory proteins (what the...?), then mere chemicals gradients (from whence came the feedback loop?) and intrinsic properties of the involved biologically useful proteins (aren't those exceedingly rare?) simply crank out processes and structures with the inevitability of Newton's second law.

This scenario is not unlike a curtain rising on a stage. Revealed is a magician holding a top hat and standing next to an elephant. With great bravado he describes how he just got done pulling the elephant from the hat.

Davies seems to equate information with complexity, though he never really defines information. He uses the word at every turn, allowing it the luxury of simply arriving at its destination without the bother of traveling there. At one point he says that proteins contain information, and qualifies things to say that "information here is synonymous with structure." But how did the structure come to hold information? This is no small matter, being the crux of any explanation for how things like bodies construct themselves.

In the landscape of possible proteins - a veritable infinitude of them - fewer than a trifling have biological utility and, as such, have information built into them. Protein structures that are not biologically active may very well be complex, even exceedingly so, but they hold no information. Since physics and chemistry would have no way to intentionally navigate toward an information-bearing protein structure, it has to get there via the old fashioned route of trial and error. But in this regard we don't have to guess how many trials are needed to hit the jackpot of a useful protein. Doug Axe already worked this out, both experimentally and mathematically.

For each biologically useful protein that can be built, there are 10^{77} useless proteins. For perspective, our galaxy, with all its stars and planets and galactic riffraff, has somewhere around 10^{68} *atoms*. The universe has around 10^{80} atoms, give or take. It is from this that Davies needs his reader to divert their eyes during his otherwise convincing sleight of hand. If you didn't know better, you'd think that these information-bearing structures really did just happen to be wandering through and, as in a 1940s musical, all the disparate actors just start stepping the right steps and singing in harmony to churn out a body.

Davies never explains anything about where information-bearing structures come from. Next he has to explain how these structures, without higher-level input, hoist themselves into interactive process that generate higher and yet higher levels of organization. Davies can't get through this impossible mess without the help of a *deus ex machina* of his own, and he brings it on stage with him from the very first chapter: adaptive self-organization.

Each of these events [related to cell division] involves coordinated actions at scales vastly larger than the sizes of the individual molecules that drive them, and each has to take place properly even though the precise prior location of key components, such as chromosomes, will be quite variable. The events therefore rely heavily on adaptive self-organization and provide an excellent example to illustrate this principle (20).

Davies uses this "concept" extensively, quotes here used to recognize that it is a shell without a whit of explanatory guts. It is a veil, a puff of smoke that he brings out to hide a fundamental unknown. More precisely, he uses it to imply that the parts are self-directed. How do we know that direction for their concerted movements comes from within and not without? Well, because, um, they self-organize. Adaptively.

My point is not to eviscerate Davies' book, but to use it as an illustration. Things are indeed complex, but they aren't *just* complex. Complexity is easy. It increases as regularity diminishes, by definition. Once every repeating element has been squeezed out, complexity has been maximized and randomness reigns. When a tornado twists a barn into a heap, the heap is complex, more complex than the barn was, but the **structure** of the barn contains more information than the heap. We *understand* what a barn is.

In order to bear information, as all the structures in Davies' book do, a system of material symbols such as proteins or DNA has to be complex, but it has to be *more than* complex. Complexity is too trivial to bear the weight of information all by itself. A string of random letters is complex, but not every string of random letters conveys information, and in fact none of them do beyond the occasionally brief and trivial. Information rides on the arbitrary arrangement of symbols, an arrangement that is **arranged**, and that begets **understanding**. Complex structures might interact, but informational structures communicate.

Embryology is indeed fabulously complex **and** saturated with information-bearing systems. Embryology was the second subject of study that led me to scratch my head in realization that the mechanistic explanation of things didn't make any sense (botany was the first, a tame prelude to embryology in retrospect). Adaptive self-organization, or any reference to organization that has a material source, carries no scientific weight at all beyond the agreeable nods given it by other scientists who are equally perplexed. They entertain a reading public confident that someone must understand how these mechanisms turn the impossible into the happenstance.

Davies, bless his heart, has given it a good go. How do two cells ratchet themselves up the ladder of organization into snails and wildebeests and even Republicans? He doesn't tell us, but he does a stellar job of describing the events that make it happen.
