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Active Matter, Then and Now

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Abstract

Historically, living was divided from dead, inert matter by its autonomous activity. Today, a number of materials not themselves alive are characterized as having inherent activity, and this activity has become the subject of a hot new field of physics, "Active Matter", or "Soft matter become alive." For active matter scientists, the relation of physics to biology is guaranteed in one direction by the assertion that the cell is a material, and hence its study can be considered a branch of material science, and in the other direction, by the claim that the physical dynamics of this material IS what brings the cell to life, and therefore its study is a proper branch of biology. I will examine these claims in relation to the concerns of 19th century scientists on the one hand, and on the other, in relation to future prospects of the division between animate and inanimate.

For Cartesian mechanists, matter was inert, passive, and conserved;¹ according to OED (def. 21), matter is what “has mass and occupies space; physical substance as distinct from spirit, mind, qualities, actions, etc.” Certainly, by itself, such a notion of matter could not be expected to explain very much. As Locke put it, “Matter, then, by its own Strength, cannot produce in it self so much as Motion” (Locke, 1690, p.314). Indeed, the intrinsic inactivity of matter was for many mandated by deep theological concerns.² For Robert Boyle, e.g., the “vulgar notion of nature”, its personification as ‘she’ or as a goddess and hence as capable of generating activity, was to “detract from the honour of the great author and governor of the world” (Boyle, (1686) 1744, IV, 361). More generally, to grant activity to nature was to “detract from the profound reverence

¹ Fox example, see Descartes, *Principles of philosophy*, II, 4: “That the nature of body consists not in weight hardness, color and the like, but in extension alone”.

² See, e.g., Keller, 1990. The focus of this earlier paper is less on the location and analysis of activity *in* the natural world and more on the relationship between natural scientists and their subject that was then being articulated. More specifically, it was on the role of gender metaphors in these developments.

we owe the divine majesty since it seems to make the Creator differ too little from a created (not to mention an imaginary) Being” (Boyle, (1686) 1744, IV, 366).

In much the same spirit, Newton too was committed to the view that all motion and all life derived from without, from “active Principles” associated not with material nature, but with God. As he wrote in 1781 (*Opticks*, p. 260), “And if it were not for these Principles, the Bodies of the Earth, Planets, Comets, Sun, and all things in them would grow cold and freeze, and become inactive Masses; and all Putrefaction, Generation, Vegetation and Life would cease...” (quoted in Henry, 1986, p. 337).

However, the denial of activity to matter deprived Cartesian Materialism of much of its explanatory power and thus continued to be a major source of philosophical and scientific discontent. It is often held by historians of science — largely under the influence of Westfall — that it was Newton’s reliance on secret principles of motion, his belief that “Nature contains *foci* of activity, agents whose spontaneous working produces results that cannot be accounted for by the mechanical philosophy’s only category of explanation: particles in motion.” (quoted in Henry, 1986) that in fact saved mechanical philosophy. Whether these “*foci* of activity” were an inherent property of matter or external to matter remained a matter of contention, but Newton himself insisted they were external. For him as for most of his followers, the activity of matter was not intrinsic to matter but induced by principles that remained external, even while their subtle spirit might be everywhere infused. Gravity, for example, can be understood in this framework.

The introduction of such “active principles” made an enormous difference. Above all, it made possible an explanation of the generation of motion — that crucial property that earlier accounts of matter had not been able to explain. As Newton wrote in his “Vegetation of metals”³ in the early 1670s, “the immediate seat of ... operations is not the whole bulk of the matter but rather an exceeding subtle in imaginably small portion of matter diffused throughout the mass, which, if it were separated, there would remain but a dead and inactive earth” (quoted in Henry, 1986, p.343).

It is worth pausing at the association between life and activity that Newton (at least tacitly) invokes, however *en passant*, for this association was almost surely foremost in every mind. A world without activity was a cold, non-generative, and dead world; an object that cannot move itself is inanimate. Not alive. Indeed, the first definition for the term ‘animate’ given by the OED,

³ In Burndy MS 16, with the *incipit* « Of Natures obvious laws and process in vegetation », the quotation is from f.5r.

dating from 1398, is: “Endowed with life, living, alive; ... alive and having the power of movement.”

“Life” was not a special category of existence for Newton -- that came a hundred years later, primarily with the writings of Jean Baptiste Lamarck. Nor did Newton share Lamarck’s preoccupation with the question of what distinguishes a living earth from a living organism. Living beings were natural phenomena for Lamarck, but they were clearly different from “inorganic” beings and he wanted to understand what accounted for that difference. He wrote,

“If we wish to arrive at a real knowledge of what constitutes life, what it consists of, what are the causes and laws which control so wonderful a natural phenomenon, and how life itself can originate those numerous and astonishing phenomena exhibited by living bodies, we must above all pay very close attention to the differences existing between inorganic and living bodies; and for this purpose a comparison must be made between the essential characters of these two kinds of bodies.” (*Philosophie zoologique*, p. 191)

Firmly rejecting any evocation of extra-natural causes, he sought a purely physical account of the “power of life”, of its natural tendency to increased complexity, and of the origin of entities that Kant had described as “self-organizing.” In the *Philosophie Zoologique*, he offered his definition of ‘Life’: “an order and a state of things that permit organic movement there; and these movements, which constitute active life, result from the action of a stimulating cause that excites them” (*Philosophie zoologique*, p. 403).

The stimulating, or excitatory cause of organic movements, which he likened to the spring of a watch, was to be found in subtle, imponderable, and invisible fluids (like caloric and electricity) that came originally from outside, insinuating themselves in the interstices of the soft parts of the body, exciting movement, tension, and increasing organization of that body. Caloric, he saw as the prime source of irritability, electricity of animal motion. The “power of life” resided “principally in the movement of the living body’s own fluids” (*Histoire Naturelle des Animaux sans Vertèbres*, I, 182-3)—movement that gave rise to growth, development, and increasing complexity of animal organization.

Lamarck did not to my knowledge refer directly to Newton, but I see a certain consonance between the subtle spirit of Newton’s forces, and the subtle fluids that Lamarck believed were responsible for exciting organic movement. Where the analogy with Newton’s forces breaks down is between the formation of simple forms of life, in which the excitatory causes of organic movement remained external to the organism, and organisms sufficiently complex to incorporate the “productive form of movement” (and hence, the ‘power of life’) within themselves. Where the simplest forms of life (much like inorganic matter) must rely

directly on their environment for the excitation of internal activity, over time, that internal activity itself gives rise to morphogenesis, i.e., to the formation of differentiated structures, and to ever-greater complexity:

“That the characteristic of the movement of fluids in the supple parts of the living bodies that contain them is to trace out routes and places for deposits and outlets; to create canals and the various organs, to vary these canals and organs according to the diversity of either the movements or nature of the fluids causing them; finally, to enlarge, elongate, divide, and gradually solidify these canals and organs” (*Recherches sur l'organisation des corps vivants*, 1802, p.8).

Perhaps like running water carving out the Grand Canyon. Eventually, or so Lamarck argued, the same kind of fluxes and flows give rise to mechanisms enabling the internal generation of movement directly.

With the help of a microscope, one could almost see such processes unfold under one's eyes. Certainly one could observe the clear jelly-like material extruded from protozoa that Felix Dujardin (1801-1860) suggested was responsible for locomotion. Dujardin called this material sarcode; soon after it became known as protoplasm. By the middle of the 19th c., proponents of protoplasm as the seat of vital activity were everywhere. As Graeme Hunter has written, “Franz Unger in 1852 described protoplasm as 'this marvelous substance, this self-moving wheel'. Ernst Haeckel wrote that protoplasm is 'the active substrate of all vital motions and of all vital activities: nutrition, growth, motion and irritability’” (Hunter, 2000, p. 67). Similarly, Ernst von Brucke questioned the need for anything else, like a nucleus. And he emphasized the unique character of protoplasm as a physical substance — neither simple solid nor liquid, but the special organization of such material into structures which, because of their organization, were capable of manifesting vital phenomena. In short, vital phenomena were not the products of a special form of matter, but rather of ordinary matter organized in a special way (Hunter, 2000, p. 65 sq.).

In November of 1868⁴, Thomas Huxley electrified his audience in Edinburgh by proposing a simple solution to the problem of life. Everything vital depends on protoplasm, “the physical basis of life.” What sustains his vital activity in the giving of this talk is the mutton he had had for dinner. That mutton was certainly dead, decomposed from living to non-living protoplasm by cooking, but then, it is subjected to subtle influences in the “inward laboratory” of his body — influences that “will convert the dead protoplasm into living protoplasm and

⁴ Thomas Huxley (1899) “On the physical basis of life”.

transubstantiate sheep into man.” We may not yet understand the nature of these influences, but in principle the problem is no different from many others — think, e.g., of the composition of water. Just as the passage of an electrical spark through a mixture of hydrogen and oxygen produces a compound, water, with different chemical properties from those of its component gases, so too, water can be combined with carbonic acid and ammonia to make something different again, protoplasm. In other words, he invokes the kind of process that we would today put under the category of “emergence”:

“ We do not assume that a something called 'aquosity' entered into and took possession of the oxide of hydrogen as soon as it was formed, and then guided the aqueous particles to their places in the facets of the crystal, or amongst the leaflets of the hoar-frost. On the contrary, we live in the hope and in the faith that, by the advance of molecular physics, we shall by-and-by be able to see our way as clearly from the constituents of water to the properties of water, as we are now able to deduce the operations of a watch from the form of its parts and the manner in which they are put together.

Is the case in any way changed when carbonic acid, water, and ammonia disappear, and in their place, under the influence of pre-existing living protoplasm, an equivalent weight of the matter of life makes its appearance. What justification is there, then, for the assumption of the existence in the living matter of a something which has no representative or correlative in the not living matter which gave rise to it? What better philosophical status has 'vitality' than 'aquosity'?

If the properties of water may be properly said to result from the nature and disposition of its component molecules, I can find no intelligible ground for refusing to say that the properties of protoplasm result from the nature and dispositions of its molecules.”⁵

It might be said that Huxley was here outlining a research program aimed at the explanation of living matter in terms of the physical and chemical properties of its constituent molecules. But this was a program that found little place in the subsequent history of biology. By the last part of the 19th century another way of thinking about the genesis of vital activity in living organisms was beginning to take shape — a way of thinking that, over the course of the 20th c., came to attract an ever larger share of biologists' attention. I refer of course to the program of reducing the explanation of the distinctive properties of living entities not to the physics and chemistry of their constituent molecules, but to the biochemistry .of their constituent

⁵ Huxley (1899), p. 152-153.

genes – i.e., of those units of heredity that biologists came to see as the basis (and even locus) of life. In close conjunction with this supposition came the view, increasingly popular among geneticists, that both the form and function of living beings could best be understood in terms of the activity of the units of inheritance, i.e., in terms of *gene action*. Genes, in this view, were somewhat mystical entities that, by virtue of their inherent (albeit not yet understood) activity, would set in motion the long chains of activity that would transform a fertilized egg into an adult organism.

The research program Huxley was proposing (along with the “physicalist” tradition to which it belonged) was conspicuously different; it sought the genesis of vital form and function not in the action of a discrete collection of themselves quasi-vital entities, namely genes, but in the movement of the purely material constituents of cells and organisms which, through the physical-chemical interactions among them, would generate the organization required to support life. This “physicalist” tradition was clearly alive and well in biological circles well into the second half of the 19th century. But by the time of Huxley’s address, its influence in biology was already beginning to wane⁶; by the beginning of the 20th century, its absence was famously mourned by D’Arcy Wentworth Thompson (1860-1948) in the introduction to the first edition of *On Growth and Form*:

“The zoologist or morphologist has been slow, where the physiologist has long been eager, to invoke the aid of the physical or mathematical sciences; and the reasons for this difference lie deep, and are partly rooted in old tradition and partly in the diverse minds and temperaments of men. To treat the living body as a mechanism was repugnant, and seemed even ludicrous, to Pascal; and Goethe, lover of nature as he was, ruled mathematics out of place in natural history. Even now the zoologist has scarce begun to dream of defining in mathematical language even the simplest organic forms. When he meets with a simple geometrical construction, for instance in the honeycomb, ... he is prone of old habit to believe that after all it is something more than a spiral or a sphere, and that in this 'something more' there lies what neither mathematics nor physics can explain. In short, he is deeply reluctant to compare the living with the dead, or to explain by geometry or by mechanics the things which have their part in the mystery of life.” (D’Arcy Thompson, 1917, p. 2)

⁶ Although clearly not on all disciplines. Especially noteworthy is research in fluid dynamics, where interest in the collective dynamics of simple material systems continued to grow over the next century (consider, e.g., the excitement among fluid dynamicists that was generated by the demonstration of Bénard cells (his “rouleaux de convection”) in 1900 and the subsequent use of this example as a model for pattern formation.

Thompson put the blame for ignoring the biological significance of physical forces on the zoologist and morphologist, but as the century unfolded, the growing influence of genetics (a subject Thompson himself had little use for) becomes more and more evident, and more and more relevant. Conversely, to 20th c. experimental biologists, physical dynamics (and the mathematical associated with their analysis) becomes less and less relevant to 20th c. experimental biologists. Thus, e.g., when Nicholas Rashevsky, addressing a meeting of cell biologists at Cold Spring Harbor in 1934, attempted to argue that his analysis of fission in liquid drops might be of some relevance to the problem of cell division, he was laughed out of court. Similarly, when Alan Turing (1952) offered a solution to the embryological dilemma of how the apparently identical cells of a complex organism can differentiate in a regular and controlled way, a solution that depended only on ordinary physical and chemical forces, he was generally ignored by biologists. To be sure, what Turing offered was no more than an “in principle” solution: based on a purely fictional set of chemical reactions, he showed how patterns could be generated, not by how they are generated. Such an approach seemed alien to experimental biologists. Yet even when efforts were made to apply Turing’s reason to known systems (real rather than fictional — e.g., slime mold aggregation), there was little interest. These were simply not the sort of explanations to which researchers in biological culture were accustomed.⁷

I could say more about this (and in fact have said, much more), but here I want to return to my main theme, and simply use these brief remarks as a rationale for skipping over the 20th century (i.e., for skipping over what I have called the “Century of the Gene” (Keller, 2000). I want to pick up the story line that I left off with Huxley’s address in 1868 as it resurfaces at the end of the 20th c. when, I claim, it resurfaces with the emergence of a new field — a branch of soft matter physics — that has come to be called “Active Matter.”

By this time, biology had changed dramatically, and the state of our knowledge incomparably advanced. Yet, despite the extraordinary advances in genetics and in molecular biology more generally, in the development of tools and techniques previously unavailable, even unimagined, some of the most basic puzzles of the life sciences remain unanswered. What is the difference between living and non-living? What is the source of vital activity? How are genes products organized (or how do they organize themselves) to produce the still mysterious dynamics of living beings? How much, if anything, can the physical sciences tell us about these dynamics?

⁷ For further discussion, see Keller (2002), Chap. 3.

Many of the most striking developments over the course of the 20th c. have been in the area of microscopy and graphic representation, and; the result of these developments is an astonishing detailed visual access to the molecular details of vital movement. The vista of protoplasmic activity available to biologists of the 19th century, and that inspired so much of their thinking, pales before the panorama now available to us.⁸ Some of the movement shown is due to passive diffusion, but most of it is not; rather it is both initiated and coordinated by the physical dynamics of the constituent parts (particles) and the medium in which they move. Molecular motors, using the energy released from the conversion of ATP to ADP, generate the motion (see, e.g., <https://www.youtube.com/watch?v=YAva4g3Pk6k>).

The original discovery of protein motors was relatively early (the breakthrough paper often cited is the chemo-osmotic model of Peter Mitchell (1961)). This work did not depend on visual technology, but the subsequent development of our understanding of molecular motors did. Recent use of the green fluorescent protein for tagging organelles, proteins, and RNA has proven of particular importance to the (literal) elucidation of the transport of intracellular cargo. The 2012 Albert Lasker Basic Medical Research Award went to Michael Sheetz, James Spudich, and Ronald Vale for their detailed analyses of the cytoskeletal motor proteins that move cargoes within cells, that contract muscles, and that enable cell movements. Prokaryote motor molecules use cytoskeletal filaments to move stuff around, eucaryotes use the far more stable cytoskeletal structure. More stable, but still dynamic structures — e.g., tubulin -- exist in a non-equilibrium steady state in which the component tubulin molecules turn over with great rapidity.

Molecular motors deployed in intra- and extra-cellular motion are interesting in part because they are so dramatic: Watch these processes unfold and you know you are watching life. But the proteins of which these motors are made do not themselves arise spontaneously: their amino acid sequences are encoded in the DNA; and these are generally assumed to define their structure — i.e., the transformation from linear sequence to working motor is assumed to require no further information. But in fact, intra- and extra-cellular dynamics seem to involve more than genetic information: they seem also to involve many processes crucial to cell division that are induced by the physical and chemical dynamics of all the molecules that make up the cell — processes that break symmetry and form patterns in ways that are not predictable by DNA sequence alone.

⁸ Many videos illustrating such motion are now readily available. Here's one: <https://www.youtube.com/watch?v=wJyUtbn0O5Y>.

The publication of a draft sequence of the human genome in 2000 marked the highpoint and culmination of the century of the gene; it also marked a pivotal turning point in the trajectory of mainstream biological research. Suspicions that the sequence of the genome would not be enough had been growing; now they seemed to be confirmed. To understand the making of an organism, not only is more than sequence required, but it was also becoming clear that traditional modes of analysis were not up to the challenge of unraveling the ever-growing complexities that access to sequence data were now making conspicuous. This challenge was a direct stimulus to the development of interdisciplinary programs in systems biology at universities around the world. A new openness was in the air, especially to approaches that had long been dismissed, and vigorous efforts to recruit scientists with quantitative skills (physicists, mathematicians and engineers) were launched in biology programs everywhere.

A particular telling indication of this shift to the language of physics is provided by the publication in 2000 of a review article by three leading figures in developmental and systems biology (Mark Kirschner, John Gerhard, and Tim Mitchison) under the title, “Molecular ‘Vitalism’”. The scare quotes in the title (as in the article) are important: they are intended to distance the authors from nineteenth century views of biological properties as completely “separate from the inanimate world” while at the same acknowledging the seriousness, and persistence, of the problem these thinkers confronted. Nineteenth (and early twentieth) century vitalism is surely to be rejected, we do not believe that living beings are “completely separate” from the inanimate world, yet how do we explain their distinctive attributes, their special “activities”? Can we, e.g., explain the genesis of protoplasmic activity in physical and chemical terms? As the authors explain,

“In the nineteenth century pattern formation, growth, physiological adaptability, and inheritance were considered properties of living organisms that seemed to separate them completely from the inanimate world. At the turn of the century, we take one last wistful look at vitalism, only to underscore our need ultimately to move beyond the genomic analysis of protein and RNA components of the cell (which will soon become a thing of the past) and to turn to an investigation of the “vitalistic” properties of molecular, cellular, and organismal function. Such an opportunity is now possible because of the great advances in genetics and molecular and cell biology during the past century. As it is now clear that gene products function in multiple pathways and the pathways themselves are interconnected in networks, it is obvious that there are many more possible outcomes than there are genes. The genotype, however deeply we analyze it, cannot be predictive of the actual phenotype, but can only provide knowledge of the universe of possible phenotypes. Biological systems have evolved to restrict these phenotypes,

and in self-organizing systems the phenotype might depend as much on external conditions and random events as the genome-encoded structure of the molecular components... Yet out of such a potentially nondeterministic world, the organism has fashioned a very stable physiology and embryology. It is this robustness that suggested “vital forces”, and it is this robustness that we wish ultimately to understand in terms of chemistry. We will have such an opportunity in this new century.” (Kirschner et al, 2000: 79)

At the same time as the prospect of investigating the molecular basis of “vitalistic” properties were inspiring Kirschner and his colleagues, patterns of intra- and inter-cellular molecular dynamics had also begun to excite interest among physicists still residing in physics departments, especially among those interested in the properties of “soft matter” — i.e., of material made up of large weakly interacting polyatomic structures suspended in a viscous fluid (like, though not restricted to, the protoplasm. Soft matter includes liquids, colloids, polymers, foams, gels, granular materials, all displaying a surprisingly rich repertoire of behaviors. The web page of the Oxford Center for soft and biological matter explains its name, “Biology is soft matter come alive”.

They don’t exactly say what they mean by alive, and in most places with the same interests, the term “active” is used instead, and that term refers to systems “composed of self-driven units, each capable of converting stored or ambient free energy into systematic movement” (like protein motors). “Self-driven” is the crucial qualifier here, but self-driven units are not restricted to protein motors: they can also be structures that arise spontaneously (in cells or in micro-fluidic chambers) — structures that are formed not by inherited “instructions” on the DNA, but solely by the internal dynamics of passive rod-like entities (like tubulin elements) suspended in viscous fluids and, crucially, are maintained far from equilibrium. Like the spindle, these structures are steady state (i.e., non-equilibrium), maintained by the flow of energy through the system.

Active matter is now the name of a hot new subfield of soft matter physics — one that has literally exploded over the last 15 -20 years, with its own journals, its own conferences, its own training programs, its own institutes. Its focus is not restricted to microscopic motions — it encompasses all scales, includes schools of fish, flocks of birds, bacterial suspensions, and herds of elephants. It is also not restricted to living matter: it includes the properties of colloids, liquid gels and crystals, as well as those of synthetic chemical or mechanical constructions that exhibit highly correlated collective motions and mechanical stresses like those seen in living matter.

The field has been growing by leaps and bounds. As it happens, these non-equilibrium self-organizing phenomena have turned out to be of tremendous interest qua physics itself. Physicists have been able to deploy a whole range of tools coming out of recent development in statistical mechanics and fluid dynamics in their analyses. It is not obvious (it least not to me) what relation these tools have to the modes of analysis about which Kirschner et al. were thinking — but this I suppose is a historical question, and as such, of little interest to the physicists themselves.

For active matter scientists, the relation to biology is guaranteed in one direction by the assertion that the cell is a material, and hence its study can be considered a branch of material science, and in the other direction, by the claim that the physical dynamics of this material IS what brings the cell to life, and therefore its study is a proper branch of biology.

Fifteen years ago, the funding agencies of biology sent out an invitation to physicists to join them in their endeavors, and they came. Many devoted years to the effort of overcoming the cultural divide that had been dividing the disciplines for so long, and some succeeded. But that cultural divide has still not completely gone away. The study of “Active matter” initially excited attention because of its promise to unify the physical, chemical, and biological sciences — to explain what it is that makes matter come alive. So far, biology has proven to be a rich source of questions for physicists, and at least some of the efforts of physicists in this field have proven of considerable interest to biologists. Especially noteworthy are the (ongoing) attempts to model and simulate the processes of spindle formation and cell division in ways that permit concrete and experimentally testable predictions.⁹ These efforts are of evident value to both quantitative modelers and experimental biologists. Other efforts, of rather less interest to biologists, seem aimed at extending the explanatory range of recent developments in experimental physics. Still others seem to be aimed at understanding the properties of novel kinds of material (like protoplasm). These too are likely to be of little interest to biologists, but they are unquestionably evocative. At the very least, they make for great videos.¹⁰

⁹ For recent reviews of this literature, see, e.g., Shelly (2016) and Civelekoglu-Scholey and Cimini (2014).

¹⁰ Here are two: <https://www.youtube.com/watch?v=t6AYWAYd-8g>, and https://www.youtube.com/watch?v=YEMm0dcUPo8&list=UUj8RD26B1M_hUvOdobg2uig.

But will they lead to a dissolution of the boundary between living and non-living with which 19th c. scientists were concerned? And will they help Marc Kirschner and his colleagues understand the development of particular phenotypes? Not clear. Indeed, it seems to me that such manifestly more biological goals are in danger of getting lost once again. Part of the problem may be that the physics has turned out to be just too interesting in itself, and the appetites of material science (especially in the age of nanotechnology) too great. Still, I keep an open mind, and choose to wait and see.

Acknowledgements

This essay touches on a wide range of issues, all of which have extensive literatures, and I apologize for the cursory treatment they receive here. My excuse is that my aim here is more meditative than scholarly, less to review or even add to than it is to provoke this literature, to raise novel questions, and to attempt to connect a long and rich history to certain contemporary developments in scientific practice.

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