

The Naturalization of the Concept of Disease

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Abstract Science starts by using terms such as ‘temperature’ or ‘fish’ or ‘gene’ to preliminarily delimitate the extension of a phenomenon, and concludes by giving most of them a technical meaning based on an explanatory model. This transformation of the meaning of the term is an essential part of its *naturalization*. Debating on the definition of ‘disease’, what most philosophers of medicine have examined is the pre-naturalized meaning of the term: for that reason they have focused on the task of delimiting disease and non-disease (health), mainly used conceptual analysis as a method of choice, and considered the nosological level of ‘disease judgments’ rather than the pathophysiological or psychopathological level of disease mechanisms, thus making them impervious to most scientific discoveries. By focusing instead on the naturalized concept of disease and following some suggestions by philosophers of biology and scientists in cutting-edge fields of biomedical research, they could garner results from a comparison of the mechanisms of diseases. This would ultimately result in a general theory of disease linked with our most general theories on living beings, among them, systems biology and network medicine. Before undertaking such a task, preliminary questions arise: is it likely that there are biological features common to different types of disease? Is it a philosopher’s job to determine what they consist in? What use would such a general theoretical definition of disease be?

Introduction

A definition of ‘disease’ is often considered the foremost question in philosophy of medicine. Most philosophers of medicine who have attempted to capture the meaning of ‘disease’ in medical science (Boorse 1977; Wakefield 1992) have tried to draw it from so-called “disease judgments” (Boorse 1997) rather than from what

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could be called “disease explanations”. A “disease judgment” is a judgment that some condition *is* or *is not* a disease, ideally grounded on some explicit, uncontroversial nosography. A disease explanation, on the other hand, could be defined a causal model of what is happening in a specific pathological condition, and it belongs to pathophysiology. To date, philosophers have considered their main question to concern the *concept* of disease, which would fulfill the role of a primary criterion of what should count as a disease, belong to nosography and, possibly but not necessarily, have a clear pathological explanation. I suggest that this is a misleading methodology. If one is to search for a definition of ‘disease’ *in science*, one should consider what concept, if any, is at work in disease *explanations*, for that is the place where medicine rightfully claims to be a science.

The question is therefore not, “in what sense do we call all those conditions the same, i.e., ‘diseases’”, but rather, “are there natural properties that mechanisms, or the series of events behind most so-called ‘diseases’, have in common?” Instead of drawing conceptual or trivial features from armchair philosophy, such as: “they involve suffering” or “they involve the failure of a statistically normal part-function”, the quest is for natural properties drawn from the lab, or at least from scientific theoretical hypotheses, that hopefully sketch what a non-trivial definition of disease would look like, if such sketch is possible.

Before fleshing out this basic proposal, I ought to point out that I consider it to be compelling in its first two, mostly critical parts, but tentative in its third, constructive part. ‘Tentative’ here means that *in medicine*, it relies on hypothesis or even speculation, and that *in philosophy*, it faces many objections that largely explain why philosophers have sought for a definition in judgments rather than in explanatory theories. I will try to answer them in the course of this chapter.

My criticism of the traditional approaches in philosophy of medicine is based on a single distinction between pre-naturalized terms, i.e., terms that only refer to phenomena, and naturalized terms, i.e., terms that also explain how these phenomena occur. I consider the current debate on the definition of disease to be focusing on a notion of ‘disease’ as a pre-naturalized term, without considering the possibility that it might be naturalized. In the first part of this chapter, I introduce this distinction, and in the second part, I show how it enlightens the debates on the definition of ‘disease’. Turning to the alternate proposal, I try to garner some results from science and from philosophy of biology in order to sketch out a search for a naturalized definition of ‘disease’.

The Naturalization of Scientific Language

I begin with a distinction between ‘pre-naturalized’ and ‘naturalized’ terms, and the consequent definition of the process of ‘naturalization’. Along with ‘naturalism’, these terms have been endowed with various meanings in various areas of philosophy. In the philosophy of medicine, ‘naturalism’ is widely used, not ‘naturalization’. I stand as a naturalist, siding with Boorse and others in giving priority to a

conception of disease as a natural fact rather than a normative one. Yet my argument comes up against a method used by naturalists and normativists alike: conceptual analysis of ‘disease judgments’. For that reason I must clarify in what sense the position I am advocating is one of naturalism.

It is naturalism in a sense very similar to Quine’s; an influential standpoint in the philosophy of science at large, yet strangely ignored in the philosophy of medicine. Its basic tenet is that

it is within science itself, and not in some prior philosophy, that reality is to be identified and described. (Quine 1981, 21)

There is nothing here that naturalists in the philosophy of medicine would not accept, given that to them, “some prior philosophy” would then mean exactly the sort of things normativists are engaged in. My point is that naturalists too are committed to “some prior philosophy” in supposing, if implicitly, that the way reality is to be *identified* mostly does not change according to what is being *described*. In that, they seem to admit of a genuinely independent philosophical stance that they, apparently modestly, do not conceive of as prescribing standards to science, but claim is nothing but descriptive. The kind of naturalism I am defending here does not admit any independent philosophical stance on the notion of disease. What we, as philosophers, should be trying to do is exactly what scientists would try to do, were they to consider the search for a general definition of disease worthy of their time. Gathering their results on specific diseases and types of disease, and reformulating them into the simplified form of a theory, is exactly what naturalistic philosophy of medicine should attempt to achieve. This is not ‘describing’ science, which supposes some external point of view, but trying to do some science, with very low likelihood of any useful outcome.

Many, including Boorse himself, have considered that the term ‘naturalism’ in the philosophy of medicine is rather unfortunate, and should be replaced by ‘descriptivism’ (Boorse 1997, 102). The problem is that in a sense, normativists too are descriptivists. What I suggest then is to distinguish a naturalist notion of disease from a *naturalized* notion of disease. In other words, in naming phenomena ‘diseases’, we surely have some preliminary, if vague, notion of what we are referring to (the notion of disease in general). But in collecting facts about these phenomena, we end up with a resulting, albeit evolving, knowledge of how these phenomena work, and possibly, with a revised notion of what we had called ‘disease’ in the first place. Naturalization implies focusing on the resulting notion rather than on the preliminary notion. Focusing on the preliminary notion of things is exactly what earlier contributions to the philosophy of biology once did, elaborating what laymen and biologists alike first think of when they hear terms such as ‘life’, ‘organism’, or ‘function’. Philosophy of medicine appears to do just the same. A naturalist in the philosophy of medicine trying to define ‘disease’ should not gather terms from a common understanding of disease and try to refine the meaning – defining what ‘function’, ‘organism’, ‘species’, or ‘normal’ mean for instance. Instead, she should investigate biomedical research on diseases and look for more general facts and theories that possibly define disease in general.

Pre-naturalized and Naturalized Terms in Science

There are probably many properties of naturalized terms in science: mathematization, reference to natural kinds,¹ etc. What is needed here to make the important point is only one of them: the fact that they refer to an explanatory model, as opposed to pre-naturalized terms referring to observed phenomena as such.

As a matter of fact, some terms are accepted into the scientific language because they refer to a class of phenomena considered to be of interest to a particular scientific discipline. In present-day chemistry for instance, ‘gold’, ‘copper’, ‘iron’, and ‘oxygen’ are such terms, not ‘orichalcum’ or ‘phlogiston’. ‘Magnetism’ now refers only to a subclass of the alleged phenomena it used to refer to in the eighteenth century, excluding what was then called ‘animal magnetism’. ‘Transmutation’ has today an altogether different sense than it had in alchemy. To denote a class of presumably interesting phenomena is one function of all these terms.

Another function of a scientific term is to link the understanding of this class of phenomena with reference to a theory or to an explanatory model. For instance, whenever the term ‘homology’ is used in evolutionary biology, the phenomena thus referred to are considered to be the result of common lineage in a Darwinian framework. An explanation is supposed – evolution by natural selection – and one must know this explanation in order to understand the term correctly. The term that fulfills that function belongs to the “theoretical vocabulary” (Hempel 1977; Suppe 1977) of a science. The actual word is not necessarily forged anew for that purpose: the same word can fulfill both functions.

However, the meaning of a term endowed with the first function only, i.e., to refer to a class of phenomena, changes when it becomes endowed with the second function too, i.e., to refer to an explanatory model. For instance, ‘temperature’ first referred to a class of observable properties (being more or less cold, warm or hot). The class may not change, but the meaning certainly does, when ‘temperature’ is defined theoretically in the kinetic theory of gas and in thermodynamics, at least in that a new, more relevant meaning is attributed to the term.

As a matter of fact, when a scientific, technical definition is given to a term such as ‘temperature’, the class of phenomena thus referred to sometimes changes. Sometimes it becomes an empty set, as in the case of ‘phlogiston’ (Enç 1976). Sometimes its unity is questioned: ‘fish’ is now a paraphyletic group of various taxa, and its extension does not correspond anymore to everything that lives and perhaps swims in the sea (including whales and dolphins for instance) – cladists even consider that ‘fish’ does not refer to any real group. Sometimes the extension of the term is just modified: in that case, the new sense of the term being considered the true one, we generally refer to older uses (i.e. before the theory became available)

¹ Although the examples given here are very similar to those given in all the discussions about natural kinds, it would require a great deal of discussion to use this very polysemic phrase here. While it is obviously possible to define ‘natural kinds’ in a way that serves the purpose of this chapter, I doubt it is the most straightforward way to achieve its goal.

as gross forms of the newer use, if not erroneous forms (Putnam 1975, 310–2). Sometimes, no extensional change follows, as in the example of ‘temperature’.

Naturalization

Given the preceding distinction, the phenomenon of naturalization comes into focus. Again, there are many properties attached to it. For instance, in the philosophy of medicine, we have an intuitive grasp of what it means in phrases such as ‘the naturalization of mental disorders’, i.e. their transformation into biological entities, and ‘the naturalization of diagnostic reasoning’, i.e. its transformation into a natural object to be investigated by cognitive science. Hippocrates naturalized epilepsy a long time ago by defining it as an ailment of the brain, not as possession by some god. Infectious diseases were naturalized with, or maybe before, the emergence of the germ theory, and so on. There are probably many aspects of naturalization in medicine, but we are interested here in only one of them. In naturalization, a referential term is transformed into an explanatory term with reference to a causal model or a theory. It is not necessary, but it is possible, that a naturalized term comes from common language first, and that its extension changes in the process. However, with the function of the term, its meaning invariably changes. Note that this model refers not only to causes, but to natural causes – as opposed, for instance, to the will of the gods or to the hopes and fears of human-kind. Note also that naturalization does not require knowing the right cause, whatever this may mean, but only to refer the term to natural causes that explain the phenomenon it designates.

Pre-naturalized terms are not exactly pre-scientific terms: they rather belong to what Hempel calls the “pretheoretical vocabulary (...) relative to the theory in question” (Hempel 1977), oftentimes, terms from previous theories. Further, their function is strategic: they reflect a choice by scientists to consider a class of objects to be natural, important or fruitful, before even knowing whether the generalizations based on this class of objects can support further theorization. Ultimately, the definition of pre-naturalized terms is bound to be imprecise. As a matter of fact, what matters most is the fact that we still call ‘x’ what we always have, not that ‘x’ is given sharp criteria of delimitation: hence the resort to complicated sets of necessary and sufficient conditions when we try to define *things*. Achinstein described the general features of such definitions under the label of definition “of physical objects or stuff” (Achinstein 1968, 2).

Naturalized terms in turn are entrenched in explanatory models. They still refer (more or less) to the same class of object, no longer grouped by their manifest features, but rather by their structure or inner working (Thompson 2011). Besides their explanatory function, naturalized terms still delimitate the class of objects. Nevertheless, the kind of definition is not the same anymore: theoretical criteria are precisely determined through necessary and sufficient conditions, for what they focus on is not the natural class of observed objects anymore, but the model these objects are supposed to be similar too (Achinstein 1968, 2).

Lingering on a Pre-naturalized Definition

Again, naturalization consists of manifold processes, among which only one has been defined here. This is because this one suffices to make my main critical point against the traditional debates over the definition of disease. This point is that the traditional debate is only concerned with reference, not explanation, i.e. it lingers on a pre-naturalized notion of disease in general instead of looking for a naturalized one (section “[The debate over the definition of ‘disease’ is about a pre-naturalized term](#)”). What is at stake is not the naturalization of various diseases, but the naturalization of the very notion of disease, if this is possible. At first sight, it seems that the naturalism-normativism debate in the philosophy of medicine is about whether ‘disease’ is a naturalized or a pre-naturalized term. As a matter of fact, this is not really the case: on the contrary, it is about the pre-naturalized term ‘disease’ (section “[The opposition of ‘naturalism’ and ‘normativism’ about disease is about a pre-naturalized term](#)”). This leads to a paradoxical standpoint for so-called ‘naturalism’ in the philosophy of medicine, mainly, its ignorance of contemporary knowledge about diseases in particular and also possibly, disease in general, assuming somehow that the latter is perennial despite scientific progress (section “[The consequences for naturalism of focusing on the definition of a pre-naturalized term](#)”).

The Debate Over the Definition of ‘Disease’ Is About a Pre-naturalized Term

In the philosophy of medicine, one of the most heated debates has been around the definitions of ‘health’ and ‘disease’. I will consider here ‘disease’ only, so as to simplify the matter. Many philosophers have proposed and discussed definitions (Boorse 2011), while others have discussed either the possibility (Sadegh-Zadeh 2000) or the usefulness of such a definition (Hesslow 1993). In this section, I present my reasons for thinking that these debates were focused on pre-naturalized terms, and the consequences of this. From the view I propose, this focus follows from two widely shared premises in the field:

- A conceptual examination of ‘disease’ by a philosopher should limit itself to the meaning of the term as it is;
- There is no general theory of disease in medicine, and therefore no naturalized concept of disease (at least, not yet).

To put it differently, conceptual analysis cannot be achieved on a naturalized concept of disease that does not yet or will never exist. On the other hand, there is a pre-naturalized concept of disease, which mostly fulfills the function of determining what is pathological and what is not. It is only this that it is a philosopher’s task to describe.²

²Nordenfelt distinguishes a *conceptual definition* and an *empirical theory* of disease (Nordenfelt 1995, 9). According to him, whereas a definition characterizes a concept, an empirical theory characterizes “the phenomenon represented by the concept”. From an analytic point of view,

I take the second premise to be obvious, at least in the sense that in medicine, there is no science of disease *in general*. As previously stated, specific diseases such as diabetes, epilepsy, cancer, and asthma, have been naturalized successfully: their inner workings are accounted for, fully or partially, by causal, mechanistic models explaining (some of) their various presentations. But there is no corresponding general model or theory accounting for disease in general, and maybe none is possible (or even useful) because of the diversity of specific diseases.

It is the first premise that I question here. Such a descriptive stance on the meaning of ‘disease’ as it is, generally implying the kind of examination that is called ‘conceptual analysis’, I have already analyzed at length in two papers (Lemoine 2013, [forthcoming](#)). As an important result of this premise, the criterion of a proper feature for defining ‘disease’ is its presence in everything (consensually) called a disease, and absence in consensual non-diseases. For instance, ‘pain’ (as such) is not a good feature both because there are many painless pathological conditions such as being paralyzed and because there are painful non-pathological conditions, such as giving birth or teething. Plain statistical abnormality is not a proper defining feature for disease either, both because diseases can be widespread and non-diseases rare, etc.

Taken as such, this is a very narrow interpretation of what could reasonably be called ‘conceptual analysis’ in philosophy, one that seems to equate it with ‘meaning analysis’ (employing a very specific and debatable method) and to eliminate, for instance, the explication of the conceptual relations between terms or the tentative reformulation of vague notions into more precise concepts. Yet it is obviously what philosophers of medicine call ‘conceptual analysis’ (Lemoine 2013), and it is rather consistent with what Hempel said about it (Hempel 1952). It is also very similar to what opposed Millikan and Neander in the philosophy of biology about the definition of ‘function’ (Millikan 1989; Neander 1991).

Thus, the focus of the traditional debate is obviously on the first function of a definition in science, that of referring to, and delimiting, a class of objects. Two associated indications of that are: first, that conceptual analysis seems the most natural method for delimiting diseases from non-diseases, a goal many philosophers of medicine would consider to be theirs; second, that the naturalized knowledge about these particular diseases is generally not relevant to answer the question why they are diseases as these philosophers understand it. For instance, Wakefield questions whether some states labeled ‘major depressive episodes’ by the *Diagnostic and Statistical Manual of Mental Disorders*, are really pathological (Horwitz and Wakefield 2007). Yet almost nothing known or hypothesized about the workings of depression, mental or biological, is thoroughly examined for itself, but the general idea that a pathological condition is the absence of a trait that has been selected for, and for the criterion of the clinically assessed relevance of the reaction to the context. The same goes for Boorse’s analyses of various diseases. It apparently

philosophers engage (or should engage) in definitions, not theories. To some extent, the distinction implies certain independence between both accounts, so that at least two persons may very well have distinct empirical theories about the phenomena of health and disease, and still share the same concept.

suffices to know that some sub-function somewhere, the ins and outs of which do not matter, is impaired and thereby fosters the organism's ability either to survive or to reproduce, and so much for the pathophysiological details. The kind of analysis both Wakefield and Boorse are engaged in does not require much knowledge of physiological, psychological or pathological mechanisms, notwithstanding their declared naturalism (and their own knowledge of these questions). As Murphy puts it,

the approach (...) tries to give the meanings of terms without investigating what in the world those terms actually refer to. (Murphy 2006, 52)

The reason for this is that these philosophers consider nosology, i.e., a list of conditions that should be classified as diseases, not pathophysiology or psychopathology, the natural science of the inner workings of actual dysfunctions in the human body or mind, to be the test criterion of a good definition. They need that list to provide examples, and all they need to know about these conditions is whether their proposed definition can or cannot be applied to them. A first problem with this position is that it provides little help in considering major issues that nosology actually encounters, which is not whether a particular condition is a disease, but rather how diseases form classes or types such as: infectious, genetic, mental, neurological, and so on, and according to which criteria – etiological, anatomical, and so on.³ The second and most important problem here is that the features these philosophers propose to define 'disease' are very general, and so is the level of knowledge on particular diseases required. This sounds paradoxical for naturalists. As a matter of fact, if they ventured to advance more specific features of diseases, say for instance, that *in every one of them* there is a determined enzymatic phenomenon defined as..., then there would be much more to know about particular diseases to test this hypothetical definition.

The Opposition of 'Naturalism' and 'Normativism' About Disease Is About a Pre-naturalized Term

'Conceptual analysis', or 'meaning analysis', is often understood as capturing 'what people have in mind' when using a given word. What I previously called the term's function remains implicit from this point of view. The main opposition in the debate on disease, normativism versus naturalism, is about the meaning of the term as a means to delimit the class of diseases. According to normativists, the conditions referred to in this class are heterogeneous from a biological point of view, and uniform only from the point of view of their specific consequences for human existence (harm, disability, and so on). To naturalists on the other hand, the class is homogeneous when considered as a group of subtypes of biological phenomena implying dysfunction.

The opposition of naturalism and normativism is not the opposition between defining a naturalized term and defining a pre-naturalized term or concept of disease.

³Thanks to Marie Darrason for drawing my attention to this point.

Both positions are in fact focused on the pre-naturalized concept of disease. The bone of contention is about the kind of features that actually describe the class of diseases: do the correct features sound scientific, biological, physiological, or do they refer to human condition, praxis, hindrances to aspirations and achievements? This could be phrased more precisely in the following manner: are the defining features of 'disease' *likely to be naturalized*, as expressed by terms such as 'dysfunction', 'adaptation', 'fitness', 'evolution', 'statistical', and so on, or are they not, as expressed by terms like 'inability', 'evil', 'happiness', 'harm', and so on?

As a matter of fact, as long as there is no general theory of disease, it is possible to think that there can be no consistent grouping of diseases after naturalizable features, no concept of disease as a natural fact, no single natural definition of disease. Indeed, normativism seems to require this state of affairs. For, if the concept of disease was naturalized, it would become hard for a normativist to make a case. One could still gather imaginary cases (in the 'thought experiment' style) where we would readily think that something not fulfilling the naturalized conditions for being a disease is a disease, or the contrary. One could still assume that the concept of disease was initially formed as a normative means for classification. Eventually, one could melt one's position down into a general constructivist stance, claiming that we were looking precisely for a class of phenomena we disvalued in the first place, and so on. Nevertheless, as there would be this robust theory of a whole class of phenomena, the scientific notion of disease would now stand on its own feet. The situation would be the same as it has been for the acceptance of the consequences of evolutionary theory: some, despite accepting the evidence that humans and other animals share a common ascent dating from some remote time in the past, would still assume that this cannot be what we understand when we are talking about 'ascent', and that somehow, human ascent is very special. They would make their case, for instance, by positing beings of another ascent that we would still call humans, etc. It is conceptually defensible, but what is the point? 'Ascent' is nevertheless a conceptually consistent scientific notion. If 'disease' was thus successfully naturalized, it would similarly be a non-starter to claim that there is no consistent scientific concept of disease. Yet, of course, this remains an open question.

The Consequences for Naturalism of Focusing on the Definition of a Pre-naturalized Term

It is strange enough for naturalists not to bother about more details of what is known of the processes at work in various diseases than their own proposed definition requires. What is more embarrassing still is the consequence that major discoveries on how diseases work would not have any effect on their proposed definition, as long as the class of diseases remained the same. The discourse on 'function' and 'dysfunction' seems to be so general that no empirical discovery could impinge on it, and that on the contrary every new result is somehow bound to fit with that very general conceptual framework. Whatever is discovered, say for instance that in

microbiology it was shown that *every* disease actually implies a microbial signature specific to diseases (e.g. unbalance in the various microbial population inhabiting the human body), which would provide a powerful naturalized definition of disease, we could probably still think of disease as a part-dysfunction.⁴ To be sure, this captures one traditional way of thinking about disease in medicine, but the fact that it is not at odds with other ways of thinking about disease does not mean that it is all that physicians have in mind when they use the term.

It would probably be exaggerated to worry about the power of conceptual analysis to hinder scientific progress by imposing some kind of conceptual straightjacket on the term ‘disease’. At least in Boorse’s case, possibly in Wakefield’s too, one cannot assume that this conceptual straightjacket is the commonsense notion of disease:

Wakefield is analyzing a concept that plays a role in commonsense thought and arguing that the task of science is to identify the natural processes that accord with that commonsense concept. We argue that this represents an attempt to use conceptual analysis to legislate what should be acceptable science. (Murphy and Woolfolk 2000, 271)

Although they might resist the introduction of new conditions or their exclusion in the name of their definitions, all naturalists do not claim to impose on further developments of the notion of disease itself. For the time being, Boorse says, the definition is adequate, and when it will not be anymore, it will be changed (Boorse 1997, 53). How are we to know that a previously correct analysis is not anymore, and that the problem is not with new conditions hitherto wrongly considered to be diseases? Boorse’s answer would probably be that scientists will decide and that philosophers should follow. What would philosophers do if some naturalized definition such as that of an unbalance of microbial populations in the human body came to redefine disease, and was at odds with the received, conceptual analytic view on disease? Most probably, Boorse would admit in the same way that his conceptual analysis is not correct anymore. Wakefield’s position would probably be more delicate, for he seems to conceive of conceptual analysis as a way to resist abusive medicalization.

Now, what would conceptual analysts do if a naturalized definition of disease emerged which would *not* be at odds with their conceptual definition? Most probably they would stick to the latter and admit the former. This is precisely what is wrong with naturalism as it is: any possible definition goes, provided that it is successful in conceptual analysis and phrased in terms of natural science, however vague. This is the case because naturalists focus on the prenatalized, existing notion of disease – ‘disease’ as a term with no reference to any general explanatory model. For this reason, conceptual analysis can be a conceptual straightjacket, but my concern is rather that it is a loose shirt.

⁴The notion of disease is currently considered to be multiply realizable. In the microbiome *Gedankenexperiment*, it would still be. Yet instead of being just a concept, disease would refer to a specific fact in nature. The multiple realizability of one specific disease is another, similar question.

A Sketch of What a Naturalized Definition Would Look Like

The search for a naturalized concept of disease is obviously more sympathetic to naturalism than to normativism, but it does not share its reliance on conceptual analysis. I advocate the search for a naturalized, theoretical definition of disease rather than the pursuit of the conceptual analysis of the term. Much of what can be offered to that end here is just lifting some objections that stand in the way of such an enterprise. This begins with questioning the idea that a definition of disease in general can result from the analysis of linguistic use only, not from a general theory of disease (section “[Questioning the implicit science-philosophy division of domains](#)”). As a matter of fact, a naturalistic stance is not necessarily restrained within the boundaries of conceptual analysis, but can extend to the theoretical use of natural features of disease as proposed by science, an approach I call ‘inductive’, of which I provide a short example (section “[Inductive approach to the empirical properties of disease](#)”). Such an inductive approach necessarily leads to a second question: whether explanatory models of dysfunction endow them with specific features never to be encountered in models of normal functioning (section “[Are there features specific to disease in explanatory models?](#)”). A third question is that of the link between two general properties: being a living organism, and being subject to diseases. Here again, I would advocate a naturalized approach to what ‘living organism’ means, but not reject theoretical consideration such as what theoretical biology has to say about a general theory of disease (section “[Is disease definable at the level of theoretical biology?](#)”). Finally, I briefly consider a possible shift in the notion of a function and its possible consequences for that of a dysfunction: can it renew the traditional theoretical template of medical science (section “[A new disease template for disease sciences?](#)”)?

Questioning the Implicit Science-Philosophy Division of Domains

Usual definitions of ‘disease’ come in three different forms, as definitions of disease x (i.e. diabetes, cancer, flu, ...), as definitions of types of disease (i.e. infectious, metabolic, mental, ... disease) or as definitions of disease in general. I take for a fact that there is as yet no general scientific theory of disease. The consequence is that no unified naturalized concept of what disease in general consists in is currently available in medical science. This is good enough reason for philosophers to have focused on a pre-naturalized concept of disease instead, provided that all there is to philosophy of science is conceptual or meaning analysis.

Another, related claim is that scientists actually display no interest whatsoever in a general theory of disease, and that they focus instead on particular theories of diseases (Thagard 2006). This correctly reflects what is considered to be known for facts so far in medicine, but omits the many hypotheses research generates about diseases.

From these two claims, one can draw the following received view:

- Definitions of *particular* diseases and types of diseases rely on theories or models and belong indeed to scientific thinking exclusively;
- Definition of disease in *general* relies on conceptual analysis and belongs to philosophical thinking exclusively.

I can see three main reasons why this divide is questionable. First, philosophers could try conceptual analysis on specific diseases or types of disease as they do with ‘mental disorders’. Most philosophers probably deem a conceptual analysis of particular disorders such as diabetes pointless. Some might not agree though (Engelhardt Jr. 1975; Severinsen 2001; Horwitz and Wakefield 2007). The same goes for the concept of disease in general: most consider that a concept of disease must exist if we are not to gather particular diseases randomly under the same label, and some defend the view that it relies on a *petitio principii* (Sadegh-Zadeh 2000).

Second, I suggest that there is no a priori reason to think that it is impossible to apply both methods, i.e. naturalization and conceptual analysis, to the definition of either particular diseases, types of disease or disease in general. It can be the case that a formulation of such a definition does not rest upon lexical analysis alone, but is based on a general theory of disease as a particular natural phenomenon.

Third, the fact that such a theory does not exist yet is not an obstacle if philosophers do not consider their task to be *describing* science, but rather *contributing* to science, by formulating as tentative theories whatever generalization the science of diseases produces. Description is conservative and there is no point in trying to do it in a constantly changing domain. This is why philosophers of science tend to rely upon parts of medicine that do not seem to change much, typically, semiology instead of pathophysiology. Let us consider, for instance, that a philosopher of science is engaged in defining a particular disease, type 1 diabetes. If she tried conceptual analysis, the main features she would rely on are clinical, because those do not readily change. Research, on the other hand, shows the entrenchment of mechanisms diabetes consists in: it can be considered either an auto-immune disease, or a metabolic disease, or a genetic disease, and who knows what else. Another example is the investigation of the links between vascular diseases, Alzheimer’s disease and late onset depression. Although there are interesting hypotheses about the nature of these links, a traditional approach still prevails in therapeutics, where they are respectively considered, say, as a dysfunction of the arterial system, a degenerating process and a problem with monoamine levels. A philosopher looking for a naturalized definition of a particular disease would try to encompass all we know about the inner mechanisms of this disease in order to define it, rather than analyze orthodox usage of the term as it is defined in semiology. This is very likely to be premature and to result in failure, but it is also very likely to contribute to science in a way scientists do not often contribute themselves. It is all the more true for the search of a type of disease or disease in general. As a matter of fact, research, not its application, should be where philosophers of medicine start if they conceive of themselves as philosophers of science.

Inductive Approach to the Empirical Properties of Disease

The latter result implies that naturalists using conceptual analysis of a pre-naturalized term have worked *deductively*. Instead of looking for what medical science has actually discovered about disease, they have more or less checked whether their assumptions hold or looked for features general or vague enough to hold whatever science discovers in the near future, such as: ‘dysfunction’, or ‘impairment to normal functioning as designed by evolution’. On the contrary, working on the naturalization of disease implies to work *inductively*, that is, take into account as many details as are available about diseases, select the right ones, and look for what science itself suggests might be unified properties of disease in general. These properties are not trivially conceptual, but they are theoretical in the sense of scientific theories of nature. By trivial or conceptual properties, I mean such predicates as ‘survives’ or ‘reproduces’, as defining features of living beings in general. Theoretical properties are either empirical properties such as ‘contains DNA or RNA’, or explanatory properties such as ‘evolves’ in a Darwinian sense, in the case of a living being.

Yet considering the whole field of alleged pathological conditions, “a congenital clubfoot, a sexual inversion, a diabetic, a schizophrenic”, as Canguilhem once put it (Canguilhem 1991), one hardly deems it possible to gather empirical features common to all. One part of the solution is: not trying to subject natural facts to lexical constraints. When science discovers interesting common mechanisms in various phenomena, it sometimes contradicts the previous use of a term to denote them. The same goes for a naturalized theory of disease: were it not to include congenital clubfoot and hypertension or schizophrenia, but diabetes, cancer, neurological, infectious, metabolic and auto-immune diseases, plus a few other categories, including what is now considered ‘normal aging’ for instance, it could stand for a general theory of disease anyway.

Another objection is that there have been many attempts at general, non-trivial natural theories of disease: Hippocrates’ theory of the unbalance of humors, the iatromechanists’ theory of mechanic disruption, Broussais’ theory of irritation, Groddeck’s psychosomatic theory. All were failures. On the other hand, the view that medicine started progressing precisely when physicians stopped searching for a general theory accounting for all diseases and focused instead on the explanation of each particular disease has a very strong rationale. As a matter of fact, what made these attempts failures is probably not generality, but prematurity. How would we know before trying whether it is the case nowadays? Moreover, the search for generalization is not incompatible with the search for specific explanations: although it apparently makes it more difficult because of the great diversity of what is known about particular diseases, it alone also provides the means to make correct or powerful generalizations. This is the case for instance each time a new mechanism is discovered in one disease and unexpectedly also happens to be of importance to other diseases.

An example of such a descriptive, inductive work on empirical properties of disease would be to incorporate the contribution of network medicine to the

naturalization of disease.⁵ *Network medicine* consists in the study of biological networks implied in diseases (Barabási et al. 2011). One kind of biological network is the interactome: the gigantic interaction of protein-coding genes, RNA, proteins and metabolites, of which sub-networks are gene networks, protein networks, and so on. Within the interactome, ‘modules’ consist in clusters of components with relatively more interactions between them. Disease phenotypes are associated with some of these modules, called ‘disease modules’. Another kind of biological network in network medicine is the diseasome, that is, the graph of the links between all genetic diseases and disease genes (Goh et al. 2007).

What is to be said from the perspective of a naturalization of the concept of disease? First, this approach takes a definite step away from the regionalization of explanatory models of distinct diseases (‘short-range definitions’), towards some form of generalization, in that it tries to link many diseases previously thought not to have anything causal in common, but only to have the conceptual property of being ‘genetic diseases’ in the broadest sense. Jimenez-Sanchez et al. consider that

the functional classification of disease genes and their products will reveal general principles of human disease. (Jimenez-Sanchez et al. 2001)

Darrason also suggests that network medicine provides a “genetic theory of Disease” (Darrason 2013). According to her, it is a theory of *Disease* and not a theory of *diseases* insofar as it should be instantiated in each particular disease whatever its type, i.e., it does not necessarily reflect the classification of diseases currently received, but possibly classifies diseases according to various kinds of genetic mechanisms. It is a *genetic* theory of Disease in that it geneticizes diseases without genocentrism, i.e., without claiming that genetic mechanisms are the main causal processes involved in the explanation of diseases. Thereby it includes all diseases with a genetic component, that is, probably nearly all pathological conditions, injuries or intoxications excluded. In short, it contains a theory of the role of genes in the global biological phenomenon called ‘disease’.

Second, network medicine exemplifies what kind of naturalized property of diseases science can discover. For instance, it draws on the distinction of ‘essential genes’, i.e. genes whose homologous recombination leads to death in utero, and ‘non-essential genes’ (Jeong et al. 2001). There are disease genes in both groups, in the proportion of approximately 1 ‘essential’ for 3 ‘non-essential’. These non-essential genes in turn are more likely not to encode for ‘hub’ proteins, i.e., highly combinable and therefore ubiquitous proteins. In the end, such non-essential, non-hub proteins are much more likely not to be housekeeping proteins, that is, to be peripheral and not central from a functional point of view. This result, although highly speculative, is also theoretically important: it tends to prove that genetic diseases affect more peripheral functions than central functions in the self-maintenance machinery of the living being, and to quantify how much more. This is

⁵Another example would be microbiome medicine: the importance of the microbiome in the human organism is very likely to change our conceptions of at least some diseases, and possibly disease in general (Dupré 2011).

a naturalized property of genetic diseases as a whole, although it is not specific. The same kind of approach has since been applied to pleiotropic human disease genes (Chavali et al. 2010) and comorbidity (Park et al. 2009).

Third, network medicine shows how disease entities could be grouped in entirely new types. For instance, Jimenez-Sanchez shows that four functional categories of gene products, namely, transcription factors, enzymes, receptors and modifiers of protein functions, are significantly more involved in four kinds of diseases with different typical onset: in utero, 1 year old, till puberty, early adulthood (Jimenez-Sanchez et al. 2001). A more general framework for such a reorganization of nosology according to the results of ‘-omics’ has been sketched in various papers (Loscalzo et al. 2007; Loscalzo and Barabasi 2011). From a philosophical perspective, Darrason examines the case of the classification of infectious diseases in the same perspective (Darrason 2013).⁶ A renewed classification of types of diseases is likely to provide insights into a potential deep unity of disease, as it would be based on a single principle rather than on several heterogeneous principles.

Such properties of disease are not trivial, but empirical: they do not obtain by explicating what we usually mean by ‘disease’, but rather by observing what the properties of the phenomena themselves are. A philosopher does not contribute either as a direct observer of nature, or as an analyst of linguistic use, but as someone emphasizing and combining interestingly universal properties that could contribute to a general theory of disease.

Are There Features Specific to Disease in Explanatory Models?

After having considered whether some empirical properties of various diseases may provide a basis for a general theory of disease, I now turn to the question: are there theoretical features of disease such as a theoretical definition of ‘dysfunction’ that could be relevant to the task of naturalizing this concept?

In biomedical science, normal and pathological mechanisms respectively pertain to related, but distinct sciences. For the knowledge of normal, psychological/physiological facts does not by itself contain the knowledge of abnormal, pathological facts. In the philosophical debate over biological functions, it has often been overlooked that most potential ways in which a system might conceivably fail to do what it is supposed to are never observed nor can even be the case. For instance, there are many different structures for functional hemoglobin, many different structures for dysfunctional hemoglobin, but many more conceivable structures of dysfunctional hemoglobin than could ever be observed. It follows from that as well as from other arguments that the science of biological dysfunctions is not just

⁶Many more contributions could illustrate what naturalized predicates of a definition of disease could look like. Among them are ecological views on the involvement of the microbiome in health as in many diseases, sometimes unexpected (as is the case for the so-called “mind-body-microbial continuum”), but also Darwinian medicine (Nesse 2001) and its critiques (Germain 2012).

deducible from the science of biological functions. Although this is not the place to delve deeper into that question, overlooking that discards most of what has been said about functions in the philosophy of biology, as non-applicable to pathophysiology. Dysfunction is not just a reflection of function but a different kind of phenomenon, a fact of its own. I have discussed elsewhere what the opposition of the healthy and the pathological could mean logically (Lemoine 2009), and analyzed Canguilhem's, Boorse's and Nordenfelt's position on the question. In the end, trying to naturalize health could lead to an entirely different result than trying to naturalize disease.

A related question is whether the knowledge of the pathological nature of a fact comes from the knowledge of a set of normal facts that the former deviates from. It is true that we classify a condition as a disease in the first place because we disvalue it, not because we observe specific biological properties. Yet it is also true that we do not classify this condition as a disease only because it is harmful or unpleasant, but because we also suppose it implies dysfunction of some sort, before even knowing it. It is true again that in so doing we may wander for a long time – maybe there is nothing biologically dysfunctional in most cases of depression for instance. My question is: is there some notion of a pathological dysfunction that scientists have discovered or are discovering, after which it would be possible to check whether what we considered *in the first place* to be dysfunctional because it is harmful in some way, *really is* dysfunctional?

It would be the case if explanatory models of dysfunctional processes endowed them with specific properties never encountered in normal processes or explanatory models thereof. Focusing on mechanistic explanatory models, Nervi has proposed that pathological mechanisms are causal sequences of biological events with specific properties not displayed by physiological or normal mechanisms. They are not just a sequence of biological events strictly corresponding to the normal sequence except for one step at least, which is absent, impaired or altered. Whereas inductively discovered properties of disease are empirical, these are, or would be, system-related properties of disease.

According to Nervi, some diseases display *outcome variability*, i.e. the fact that their nature is not identified by specific outcomes; while a physiological mechanism has always a favourable outcome in normal conditions, a pathological one may result in outcomes ranging from death to complete recovery. (Nervi 2010)

They also display *no range constraint* of either internal or external conditions of working, whereas normal mechanisms necessitate relative invariability of background conditions. Lastly, they display *ambivalence*, that is, they possess

the potential to work as adaptive or maladaptive in the presence of different regulating factors. (Nervi 2010, 221)

Nervi does not take these properties to be general, conceptual and defining properties of diseases as such, but rather some interesting natural properties of some pathological mechanisms that hitherto went unnoticed. Critiques (Gross 2011; Moghaddam-Taaheri 2011) have focused either on the existence of specific properties of explanatory models of diseases, or on the very properties Nervi proposed. These are distinct points.

Whatever the outcome of this debate, it is worth noting that the perspective is completely different than that proposed by conceptual analysis. For the discussion is about the kinds of features to be encountered in pathophysiological explanations, not just in symptoms or in gross ideas about how a human organism usually survives or reproduces. They also differ from the types of properties previously referred to and likely to be drawn from empirical science such as network medicine, genomics, microbiology, epidemiology and so on. Yet it is expected that both these empirical properties and these theoretical features, if compatible, should combine, but not necessarily result, in a complete theory of disease based on some general theory of organisms.

Is Disease Definable at the Level of Theoretical Biology?

There have been contributions to a theory of disease in theoretical biology, such as a general theory of organism. Only organisms suffer from diseases, and it seems that all organisms can suffer from diseases. Is it a universal fact, i.e., would it be naturally possible that some organisms cannot suffer from disease, or a theoretical necessity, i.e., any organism must be able to suffer from a disease because of what being an organism implies? In the latter case, theoretical biology provides essential ground for a theory of disease, whereas in the former case, it is more likely that diseases are just unrelated empirical facts with no overarching theory thereof.

Systems biology renews traditionally important notions for the definition of a disease, such as that of a function. Moreno, Mossio, and Saborido proposed replacing the concept of a function by an ‘organizational’ concept of function translated into the language of theoretical biology and complex systems theory (Mossio et al. 2009). Among systems, some are characterized by self-maintenance (Mossio and Moreno 2010), such as organisms, hurricanes, autocatalytic networks, and among these, some are also organizationally differentiated, that is, they produce

different and localizable patterns or structures, each making a specific contribution to the conditions of existence of the whole organization. (Mossio et al. 2009, 826)

The baseline idea is that in a self-maintaining, organizationally differentiated system S,

a trait T has a function if and only if:

C1: T contributes to the maintenance of the organization O of S;

C2: T is produced and maintained under some constraints exerted by O;

C3: S is organizationally differentiated. (Mossio et al. 2009, 828)

In systems fulfilling C3, some traits fulfill C2 but not C1. They are *dysfunctional* traits and must be distinguished from *side effects* of traits that do not prevent these traits from fulfilling C1. On the one hand, the usual contribution of those dysfunctional traits is either not indispensable and can be compensated so that the system continues to self-maintain in the same way (that is, belong to the same class of self-maintaining systems), or indispensable, so that a new regime of self-maintenance is

either required or impossible (which leads to destruction). Most non-fatal diseases belong to the second category: they involve a new regime of self-maintenance.⁷ On the other hand, dysfunctional traits resort either to primary or to secondary functions, that is, contributions to either baseline or complex regimes of self-maintenance (such as respectively the heart's functions of 'pumping blood' and 'making diagnostically interesting noises').

Third, systems biology also provides us with some new potential features for a description of disease. Consider the notion of disease as a living process of its own, as opposed to complete breakdown. Gross notes that

(...) only a specific class of perturbations will be able to affect an organism in such a way as to bring about a persisting state of disease. They must overcome the organism's mechanisms of defense and homeostasis, but at the same time not kill it right away. Conversely, it is obvious that states of disease themselves must exhibit a certain degree of robustness since they resist the organism's attempts to restore a healthy equilibrium. (Gross 2011, 481–2)

An organism is a dynamic system with several sets of states, each called a 'basin of attraction', which tends toward one stable state, trajectory or cycle, called its 'point attractor'. Healthy states are such point attractors, and so are diseases. Perturbation factors tend to push the organism out of its healthy 'basin of attraction', and once its resistance is overcome, it falls into another basin of attraction, this one possibly being pathological (Gross 2011, 484–5). Two examples are analyzed from that perspective, metabolic syndrome and cancer: it is interesting to note that this kind of view also pervades some groups of researchers (see Gross for references), not only philosophers of science. Ultimately, it is also noteworthy that this perspective explicates that many perturbation factors may lead to the same basin of attraction, which defines the same disease despite the variety of possible causes for such a transition. The question here is whether this health-disease transition itself is a necessary feature of organisms. It is probably the case that there are different basins of attraction for one organism; but this does not explain why different basins of attraction must be called either disease or health.

A New Disease Template for Disease Sciences?

Boorse's classic view on disease assumes that physiology consists in a functional analysis of health resulting in a description of all the interlocking functions that typically secure survival and reproduction in a reference class of a species (Boorse 1977). In the same paper, Boorse suggested that this conception of health and disease provided an unchanged theoretical template for all new data so far:

In general, there is clearly some plausibility in the claim that the history of medical theory is nothing but a record of progressive investigation of normal functioning on the organismic, organic, histologic, cellular, and biochemical levels of organization, and of the increasingly subtle kinds of pathology this investigation reveals. (Boorse 1977, 560)

⁷This seems to involve the Boorsean notion of a 'reference class'.

This suggests that the concept of disease has to date been unchanged, despite progress in medical knowledge. Wakefield would probably not agree, since he advocates the view that the notion of function has itself evolved, but nevertheless he does agree to a form of continuity of the notion as regards medicine, a complementary view he calls ‘black box essentialism’ (Wakefield 1999).

Yet contemporary medicine has undergone a revolution through the landslide of data that follows from going both molecular and epidemiological: ‘-omics’ on the one hand, evidence-based medicine on the other, have provided so much more information on diseases and diseases mechanisms and processes that it is a rightful question whether *any* functional description is still able to enlighten what health and disease consist in.

Observations of the mechanisms of a function or a dysfunction are characterized by a level of ‘resolution’, defined not by the scale of the entities involved, but by how much detail or complexity is resorted to (Richardson and Stephan 2007). At some resolution, functions appear clearly: in diabetes, in metabolic syndrome, the function of insulin, the function of glucose, the function of specific receptors of muscle cells, and so on, are obvious. Boorse’s contention seems to be that in principle, functional analysis can go deeper without changing its form, maybe until it “bottoms out” in physical laws (Machamer et al. 2000). In fact, biology seems to be shifting already from a kind of description where attributing functions is what clarifies phenomena the most, to a kind of description where describing interactions between entities in mechanisms without function attribution is our best approach. The reason is that it is not very enlightening when complex processes are described, appealing to dozens of agents achieving dozens of effects, none of which are either necessary or sufficient, as is the case for metabolic processes. Should we say that the functions of a protein x_1 are to $y_1, y_2, \dots$, and y_n , and that a function of $x_1, x_2, \dots$, and x_n is to y_1 ? It is still possible in principle, but not very useful in fact. As Hartwell et al. put it,

a discrete biological function can only rarely be attributed to an individual molecule, in the sense that the main purpose of haemoglobin is to transport gas molecules in the bloodstream. In contrast, most biological functions arise from interactions among many components. For example, in the signal transduction system in yeast that converts the detection of a pheromone into the act of mating, there is no single protein responsible for amplifying the input signal provided by the pheromone molecule. (Hartwell et al. 1999)

For that reason, this shift, if it is indeed happening, would not be a radical change: mechanistic models are still interpretable as functional models (Piccinini and Craver 2011). The kind of data that ‘-omics’ provide even suggests that functional analysis might not “bottom out” after all, but rather dissolve out in biochemical networks.

This obviously might have important consequences for the notion of disease: if it is not relevant anymore to describe causal roles as functions, what about dysfunctions? Can dysfunctional systems be described without any reference to attributable functions? These are the stakes.

For instance, Gross’ attractor perspective does not resort to the notion of function – but at the same time, it makes no distinction between healthy and pathological

states of a system. In network biology, the cell's activity is considered to consist in a "network of networks" (Barabási and Oltvai 2004). A crucial notion is that of a 'functional module', that is,

a discrete entity whose function is separable from those of other modules. This separation depends on chemical isolation, which can originate from spatial localization or from chemical specificity. (Hartwell et al. 1999)

It is debated though whether such modules are 'real', the alternative being modular organization or a large integrated intracellular network (Ravasz et al. 2002). Even in the modularist view, functions could be read off from subparts of organisms down to the level of modules only, but not further down. On the other hand, it is a fact that entities intervening in one functional module can, and often do, intervene in another one. There are already interesting interpretations of what diseases might consist of in the light of the hypothesis of 'functional modules' (Debret et al. 2011). Down to the level of functional modules, it is possible to talk about dysfunctions. In the case of genetic disorders,

A disorder then represents the perturbation or breakdown of a specific functional module caused by variation in one or more of the components producing recognizable developmental and/or physiological abnormalities. (Goh et al. 2007, 8688)

The result is that either the results of different genetic abnormalities are given the same disease label because they involve the same dysfunction via the involvement of various mechanisms, or they consist in different diseases although the dysfunction is the same. Either way, the notion of a disease as a dysfunction might be considered an approximation, and it is indeed a question, not a principle, that it is and will always be the appropriate framework to define what disease consists in.

This should suffice as a sketch of what awaits philosophical elaboration of the concept of disease beyond conceptual analysis.

Conclusion

The distinction between a pre-naturalized and a naturalized meaning of 'disease' casts some light on the limits of what philosophers of medicine have been focused on, namely conceptual or meaning analysis. It also shows why this traditional and central area of philosophy of medicine seems so unconcerned by important and relevant developments of philosophy of biology about the concept of disease.

Naturalization of the concept of disease in the form of a general theory of disease is a project, not a result. It supposes that philosophers of medicine stop being directly concerned about the boundaries between health and disease. Although the concept of disease is fuzzy, it nevertheless clearly excludes conditions or processes such as pregnancy, menstruation, ageing or being dead. From the point of view of conceptual analysis, it is therefore a mistake to consider one of these to be a disease. It is not necessarily so for a naturalized definition of disease. This is probably why some philosophers have stuck with conceptual analysis as a means against

over-medicalization, thereby defined as undue medical treatment of a problem relative to our traditional concept of disease (plus or minus a few special cases such as birth control). Yet considering that, say, hyperactivity or sadness is indeed a disease does not imply that it should be treated medically, for the fact that there is a treatment is far from involving that the treatment is desirable.

Naturalization also supposes that philosophers of medicine delve deeper into cutting-edge research in biology and biomedicine. Instead of refining the possible meaning of ‘function’ and ‘dysfunction’ by confronting them to elementary examples or even imaginary ones, they would examine the strengths and weaknesses of functional explanations in the latest hypotheses and results of science, and consider which notions of ‘function’ or ‘dysfunction’ are required, and whether they are.

The ultimate goal of such a method is not a social one – that of protecting people against over-medicalization, for instance – but a scientific one.

It has often been pointed out that medical science has made ‘tremendous’ progress without any general theory of disease (Hesslow 1993; Kincaid 2008), maybe not even a consistent theory of one type of disease such as cancer (Kincaid 2008). Yet it does not follow that producing one would be useless. As a matter of fact, much had been achieved in various areas such as astronomy, clock-making or ballistics before Galileo, Huygens and Newton. It did not follow that a general theory of movement was useless. Similarly, the hope is that a general theory of disease would provide the means to understand it even better than we currently do, and provide a much more relevant concept of what disease is.

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Classification, Disease and Evidence

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