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LONG ARTICLE

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Abstract In this article, two issues regarding mechanisms are discussed. The first concerns the relationships between "mechanism description" and "mechanism explanation." It is proposed that it is rather plausible to think of them as two distinct epistemic acts. The second deals with the different molecular biology explanatory contexts, and it is shown that some of them require physics and its laws.

Keywords Description · Explanation · Mechanisms · Molecular biology · Physical explanation

Over the last ten years in the field of the philosophy of biology, one branch, called "the new mechanistic philosophy" (Skipper and Millstein 2005), has gained increasing popularity and the notion of "mechanism" has reached the center of a still lively debate. I wish to enter it by discussing two aspects that might allow us a different angle from which the matter could be seen.

The first one concerns the relation between mechanism descriptions and mechanism explanations. It is often assumed that the two are equivalent but I would raise some doubts. In particular, I suspect that we are in the presence of two distinct epistemic acts, and I will try to demonstrate why.

The second issue regards the contexts of physical explanation, which I will discuss without any reductionist ambition. In particular, I will show that a request of mechanistic explanation is always contextual and that there are contexts requiring physics and its laws. This does not mean at all that physics has a necessary role in molecular biology, but that it will be necessary if we decide on a particular explanatory context.[1] I will illustrate this point using a case study dealing with the protein p53 and with one of the many mechanisms in which it is involved.

Mechanism Description and Mechanism Explanation

Although there is already a huge literature on mechanisms, the debate is not yet concluded and different authors have proposed sometimes slightly, sometimes less slightly different definitions of the term at stake. For example,

(1) Mechanisms are entities and activities organized such that they are productive of regular changes from start or set-up to finish or termination conditions (Machamer et al. 2000).
(2) A mechanism for a behavior is a complex system that produces that behavior by the interaction of a number of parts, where the interactions between parts can be characterized by direct, invariant, change-relating generalizations (Glennan 2002, p. S344).
(3) A mechanism is a structure performing a function in virtue of its component parts, component operations, and their organization. The orchestrated functioning of the mechanism is responsible for one or more phenomena (Bechtel and Abrahamsen 2005, p. 423).

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[1] A similar position is shared by Morange (2011). An entire journal issue (*Studies in History and Philosophy of Biological and Biomedical Sciences* 42(2), 2011) has recently been devoted to the relationships between physics and biology.

These three "definitions"[2] show one of the problems that the debate on mechanism is encountering, for in their *definientia* there are terms such as "entity," "activity," "complex system," or "structure" whose vagueness and ambiguity render the *definiens* vague and ambiguous as well.[3] Leaving aside such a problem, in the above three claims there is the shared idea that a mechanism is a (more or less complex) system whose components (whatever they may be) interact to produce an outcome, i.e., a system implementing a process and producing a phenomenon.

Moreover, there appears to be widespread agreement on the fact that "a mechanism is sought to explain how a phenomenon is produced (Machamer et al. 2000) or how some task is carried out (Bechtel and Richardson 1993) or how the mechanism as a whole behaves (Glennan 1996)" (Darden 2008, p. 959). The reasoning behind this statement lies in the claim that "*to give a description of a mechanism for a phenomenon is to explain that phenomenon*, i.e., to explain how it was produced" (Machamer et al. 2000, p. 3; my italics). That is, as Craver (2006, p. 367) affirms: "Models are explanatory when they describe mechanisms."

Actually not all of us would be content with the equivalence (or intersection) of the meaning of "description" and "explanation." For example Reese (1999), in a paper eloquently titled "Explanation is Not Description," highlights that in the recent history of philosophy there have been those who have supported a difference between the two, such as James (1907), Bergmann (1957), and Toulmin (1953), even if, of course, there have been those that have supported the equivalence, such as Mach (1886), Skinner (1931), and Kantor (1953). To argue for his view, Reese emphasizes the fact that while descriptions detail what there is, explanations tell us the reasons why what occurs, occurs.

Even if I would agree with the "divisionists," I suspect that much of the matter depends on the (often latent) definitions that different authors propose for "description" and "explanation." Depending on how the latter are constructed we could claim that the two terms are, or are not, equivalent or overlapping.

However, there are two arguments that could disentangle the quandary and that would spur me to accept the divisionist party rather than the non-divisionist party. One has to do with etymology, the other with epistemology. Let us consider the first.

"Describe" derives from the Latin "*de-scribere*," where "*scribere*" means "write" and "*de*" indicates both the act of "*scribere*" and the fulfillment of the act. Thus the term "*describere*" was originally intended both as the act of representing and as the representation itself of an object, an event, a process by means of writing, that is, by means of a language. Differently, "explain" derives from "*ex-plan-are*," i.e., to make level, make something plain, unfolding, and, by extension, make something clear, especially by indicating the reasons for its occurring.

I am perfectly aware that we cannot solve philosophical disputes by resorting to the etymons, but they could indicate the right way. In particular, in this case they tell us that we have two different terms designating two different epistemic acts.

Description could be seen as the epistemic act "played out" by realizing a representation of objects, events, and processes of the world. Differently, the explanation could be intended as the epistemic act "played out" working by means of, and on, statements belonging to a representation. We explain statements regarding objects, events, and processes by means of statements. Yet we do not explain objects, events, and processes per se. These could be described. Clearly here we also have the difference between the level of the referent (the ontological level "inhabited" by objects, events, processes) and the level of the representations (the epistemological level "inhabited" by descriptions and where explanations take place).

It should be noted that, within the debate on mechanisms, this difference has already been pointed out by Bechtel and Abrahamsen (2005), when they emphasize that whenever we explain something, in whatever manner this might be done, we—the knowing subjects—perform an epistemic task that very indirectly has to do with the ontological level.

Let us stay with description and ask ourselves: when do we have an exhaustive description of a mechanism? We could try to offer an answer reminding ourselves that this is exactly the same question posed to the writers of the technical booklets that accompany most of the objects we buy. For they have to provide a description of the object that is as complete as possible, of course taking into consideration the competence level of the average potential buyer. From this perspective, it seems that we could arrive at formulating a series of questions that the writers should answer satisfactorily. That is,

(1) "What is the spatial configuration of the mechanism as a whole?"
(2) "What is the spatial configuration of its components?"
(3) "What is its outcome (function/task/aim/behavior)?"
(4) "What is the outcome (function/task/aim/behavior) of its components?"
(5) "How good is it?" or "What is its efficacy in the fulfillment of its function/task/aim/behavior?"

[2] Actually, Machamer et al. (2000, p. 2) claim that they are not exactly providing a definition. This is, however, not that relevant to what I want to point out.

[3] This aspect is one of the topics discussed by many mechanism scholars; see, e.g., Darden (2006, Chap. 4), Machamer (2004), Tabery (2004), Bogen (2008), Torres (2009).

(6) "Which are the states of the implemented process?" or "Which are the states through which its function/task/behavior is fulfilled?"
(7) "Who or what switches the mechanism on?"
(8) "What is its energy source?"
(9) "Who or what controls its functioning?"
(10) "Who or what has realized it?"

Very likely, this is not an exhaustive list.[4] Moreover, it should be clear that in no molecular biology paper dealing with mechanisms do we find an answer to all of these questions. Actually, we find answers only for those that are relevant for the authors of the paper and for the issue discussed.

Note that, in the list above, questions 9 and 10 have a particular "flavor," especially at the molecular level. Question 9 regards the mechanism control. This aspect is of fundamental biological relevance. For no molecular mechanism can work without another mechanism that has been designed (very frequently by natural selection) to control the former. There are molecular mechanisms whose control usually involves other independent mechanisms, as is the case of mechanisms controlling DNA transcription or duplication. However, there are also molecular mechanisms whose control is in themselves, as happens with (negative or positive) feedback loops (see Vilar et al. 2003), or with feedforward loops (see Mangan et al. 2003; Mangan and Alon 2003). Instead, question 10 allows the introduction of evolutionary issues, since we could intend molecular mechanisms as an evolutionary outcome. Therefore they could also be studied from the point of view of "molecular evolution" (see Páll et al. 2006). Nevertheless, we should not forget mechanisms that could not be thought of as the result of an evolutionary process, but, for example, as the consequences of somatic mutations occurring during carcinogenesis.

Among the various questions, I wish to focus on the 6th since it concerns processes, viz., one of the characterizing features of mechanisms. In particular, it deals with the request of detailing the states $S^0, \ldots, S^n$ through which a mechanism (a system) achieves its scope. It follows, thus, that we can describe a process instantiated in a mechanism (in a system) by indicating the sequence of states S^j leading the system from the initial to the final state.

Nevertheless, as soon as we have described the sequence of the states of the mechanisms, we might be "curious" to know something more. That is, we could be spurred to ask:

(6bis): "Why (or how) does the system move from the initial state S^0 to the final state S^n, in particular from the state S^{j-1} to the state S^j?"

In this way, we move from a description of the (states of the) mechanisms to a request for explanation (a why-question) concerning its functioning.

[4] Comparable lists of questions can be found on the web by searching for "how to write a technical booklet" and for similar entries.

Thus we have two different epistemic acts: (1) *the description*, by means of which we represent a state (or a sequence of states) of a system; (2) *the explanation*, by means of which we try to point out both the reasons why the system is in a state and the reasons why the system passes from a state to another one.

We know a lot about explanation, since philosophers of science have extensively discussed this topic over the last 60 years (see the classic Salmon 1989–1990). We know, in particular, that a why-question admits many possible because-answers, depending on the context within which it has been formulated. Let me dwell upon this point. In van Fraassen's (1980) pragmatic account and its generalization (Boniolo 2005), the formulation of the demand for explanation—i.e., the why-question—and the reply—i.e., the because-answer—depend both on who formulates them and on the context in which they are formulated. From this point of view, the logical structure of the explanation is no longer the pivotal issue, even if it remains necessary. Instead the communicative conditions that motivate and support it turn out to be the focus of the matter. This involves realizing that (1) certain why-questions linked to a given context cannot be posed in a different context; (2) in different contexts the same why-question does not necessarily refer to the same problem and therefore does not require the same because-answer. In the end, we can claim that a question is identifiable by the context in which it is formulated and its answer is located.

Answering a why-question we offer the reasons why in the particular context that object exists, or that event or process occurs and, therefore, we have indicated both the conditions under which that system exists or behaves in that way and the conditions under which it could not exist or behave in that way. That is, we have a particular epistemic act supporting a counterfactual reasoning, or, in other words, we could think of our why-question in terms of what Woodward (2003) calls "what-if-things-had-been-different" questions.

Thus, I am suggesting that it is not so implausible to advance the idea that there is a philosophical difference between a scientific description, detailing the parts and the states of a mechanism, and a scientific explanation, telling us the reasons either of the parts or of the succession of the states.

It does not seem that this difference is only a matter of definition or etymon, even if both definitions and etymons are relevant in philosophy. Instead, it seems to be more a question of two different epistemic acts.

Contexts of Physical Explanations: The p53 Case Study

After having spent some time on the attempt to show the plausibility of differentiating description and explanation, I will move on to the second issue. It concerns the fact that

different molecular biology contexts allow us to formulate different why-questions and different because-answers and that there are contexts requiring physical explanations.

To better illustrate the point, I want to discuss a molecular mechanism that is particularly apt for the purpose—the protein p53 degradation mechanism.

p53 is a tumor suppressor, discovered in 1979, encoded by the *P53* gene located on the short arm of human 17 chromosome (I focus here on human p53). This protein is a central node in a complex signaling pathway that evolved to detect a variety of cytotoxic and genotoxic stresses which could compromise genomic stability and promote neoplastic transformation. Once activated by a stress signal such as DNA damage, hypoxia, unscheduled oncogene expression, viral infection, or ribonucleotide depletion, p53 exerts its role of "guardian of the genome" and mediates a series of cellular outcomes that can vary from cell cycle arrest to DNA-repair, senescence, and apoptosis, depending on the cellular context. The p53 pathway is altered to some degree in all human cancers.

Despite the huge body of knowledge available on p53 and its pathways, many aspects about its functions and regulation remain unresolved. For example, which stimuli lead to activation of p53 tumor suppressive activity? Which modifications and interactions are essential for p53 functions? What are the mechanisms that permit p53 to regulate one particular subset of target genes over another, leading to distinct cellular outcomes? (See Gostissa et al. 2003; Hofseth et al. 2004; Hainaut and Wiman 2005; http://p53.free.fr.)

Let us consider two cartoons representing the p53 degradation mechanism (Fig. 1a, from Moll and Petrenko 2003 and Fig. 1b, from Hardcastle 2007).

Here p53 is represented by ellipsoid spots (and the same for the protein MDM2 and for the others). Such descriptions are clearly extremely simplified fictional representations of p53, and consequently of its degradation mechanism, but they are enough for a molecular oncologist working on this mechanism. If we want a more sophisticated description of p53, we need to change perspective and move to a more detailed level.

We might be interested in the amino acid structure and in this case we will resort to a different description, as in Fig. 2 (from http://p53.free.fr) where the primary structure of p53 is represented. Here we can see that the sequence can be divided into five domains, each corresponding to a specific function: (1) the amino-terminus part, which contains the acidic transactivation domain and the MDM2 protein binding site; (2) the proline rich domain, which is conserved in p53 from different species and which contains a second transactivation domain; (3) the central region, containing the DNA binding domain (90 % of p53 mutations found in human cancers occur in this region); (4) the

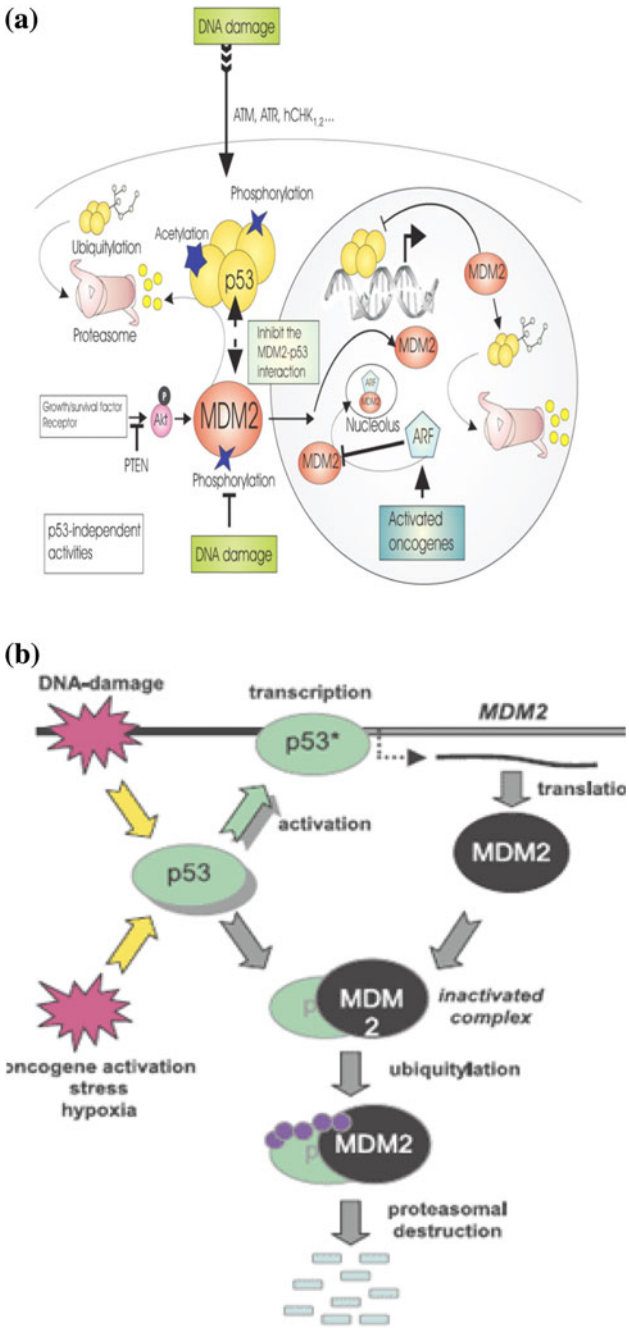

Fig. 1 The p53 degradation mechanism

oligomerization domain (4D), consisting of a beta-strand followed by an alpha-helix (this is necessary for dimerization: p53 binds to DNA as a paired dimer) which contains a nuclear localization signal; (5) the carboxy-terminus, containing three nuclear localization signals and a non-specific DNA binding domain that binds to damaged DNA (this region is also involved in downregulation of DNA binding of the central domain).

Note that up to now we have just descriptions and no explanation is involved.

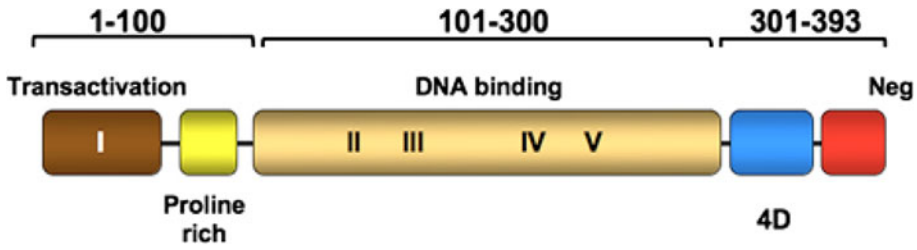

Fig. 2 The primary structure of P53

We might be interested in the three-dimensional structure of the folded p53, as shown in Fig. 3a (from Baumbusch et al. 2006) and Fig. 3b (from Wells et al. 2008). Nor in this case do we have any explanation: at this level we are interested neither in the p53 as a mechanism nor in one of the mechanisms in which it does its job.

Yet if we want to go deeper, we have a very interesting development: *the object-molecule becomes a mechanism-molecule*. For we know that p53 is a macromolecule composed of hundreds of interacting atoms, that atoms are composed of nuclei and orbiting electrons, and that both nuclei and electrons are charged particles. In this case we are interested in a different three-dimensional representation showing the charge distribution, as we see in Fig. 4.

At this point we might be stimulated by the formation and functioning of the p53 mechanism and, thus, we could pose a problem: why and how do the atoms form the p53 molecule? Note that, more or less, the same problem is faced when we try to understand why and how p53 binds to another molecule, as happens, for example, with DNA (Fig. 5a, from Martin et al. 2002) or with the MDM2 protein (Fig. 5b, from http://web.bii.a-star.edu.sg/~madhumalar/).

As we have discussed above, in this way question 6bis, i.e., an explanation request, enters the scene and we should offer a because-answer. The latter could be of various kinds, depending on the context in which it is formulated, and ranging from an extremely generic and not very informative one ("the parts of the type A interact with the parts of the type B") to an extremely sophisticated one, as

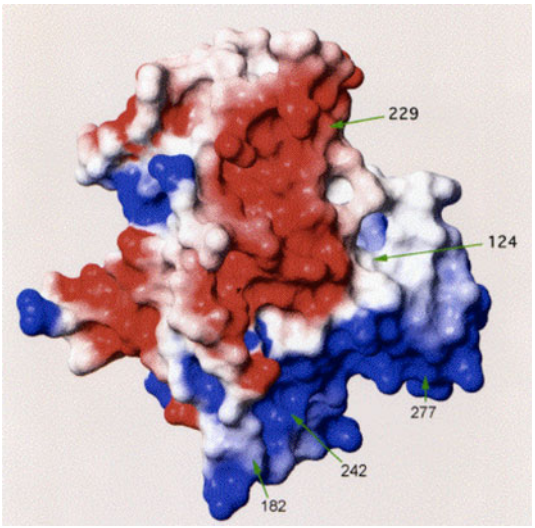

Fig. 4 The p53 charge distribution. *Different colors* represent atoms with different electron density. The *arrows* point to positions of the surface exposed sulfur atoms of the cysteine residues on the surface in this orientation (Wu et al. 1999)

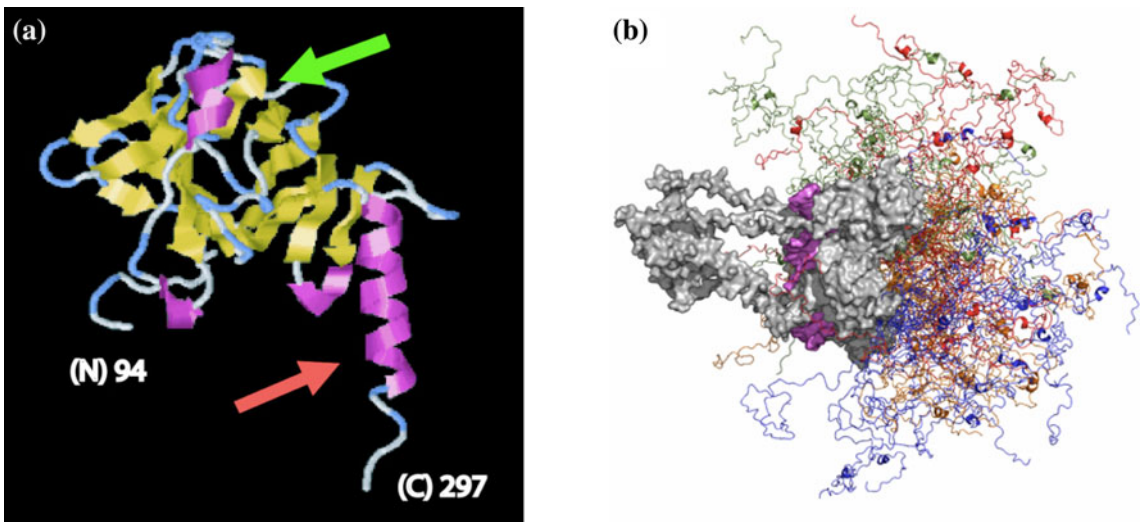

Fig. 3 The p53 three-dimensional structure

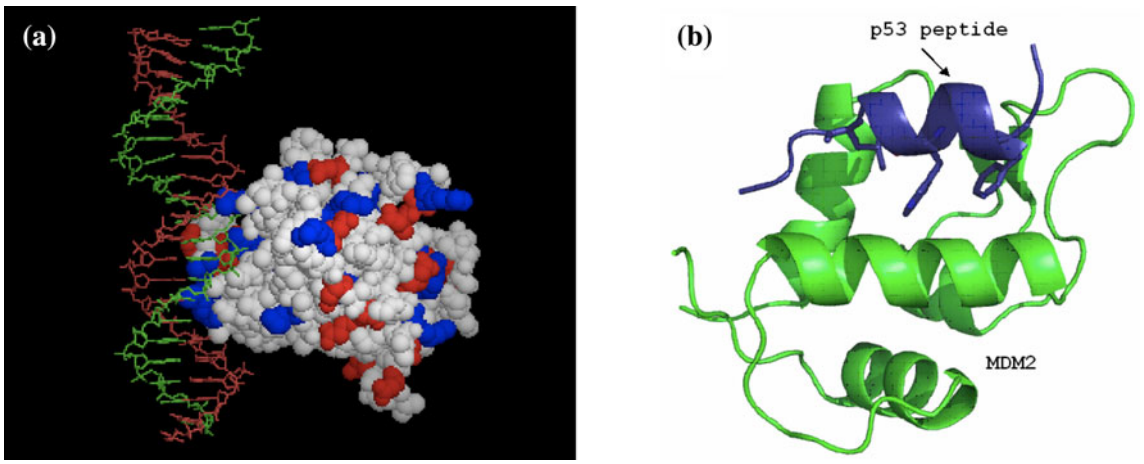

Fig. 5 The p53-DNA bond and of p53-MDM2 bond

it could be by resorting to quantum mechanics. Let us dwell upon this one, also to see the role of physics in molecular biology.

Since the spatial configuration of the atoms composing the two binding molecules is known, it is possible to represent this interaction more precisely using quantum mechanics and its laws. This means that we can begin addressing question 6bis within a new context in which physical explanations are necessary.

Let us come back to the p53 degradation mechanism. In this case, we should try to address question 6: "Which are the states of the p53 degradation mechanism?" To provide a response, we can use at least three different tools: (1) natural language *plus* some technical terms referring to the molecules involved; (2) iconic language; and (3) formal language.

Let us start with the first possibility. In this case we could state that the function/task/behavior of the p53 degradation mechanism consists of regulating the quantity of p53. This is realized by the ubiquitin ligase MDM2, a protein encoded by the gene *MDM2*, which binds the N-terminal trans-activation domain of p53, thus inhibiting its transcriptional activity and stimulating its ubiquitination and consequent proteasome-dependent degradation. Ubiquitination is the process that causes a protein, in this case p53, to be labeled by the protein ubiquitin. This "labeling" step marks p53 for destruction by proteasomes, very large protein complexes within the cell. Moreover, we have a paradigmatic exemplification of a regulatory loop/mechanism. Indeed, one of the genes that is actively transcribed as a consequence of p53 activation is *MDM2*, ultimately resulting in production of the MDM2 protein and in increased *MDM2* activity. Therefore, p53 regulates the activation of a protein (MDM2) that is itself a regulator of p53 (see Moll and Petrenko 2003). This means that by describing the states of the p53 degradation mechanism, we are also answering question 9 ("What controls its functioning?"). On the other hand, we have answered question 3, as well: "What does the p53 degradation mechanism do?"

Of course, we could also choose to describe the process occurring in this mechanism via a formal language, be it that of the theory of differential equations (see, e.g., Barenco et al. 2006; Brewer 2006; Wee et al. 2009), or be it that of logic (see, e.g., Boniolo et al. 2010).

Let us focus on the p53-MDM2 interaction, i.e., on a part of the degradation mechanism. We know that there are two many-atom systems involved, or rather two many-nuclei-plus-many-electron systems: one system involves p53, while the other involves the MDM2 protein. But whenever we meet systems like this, quantum mechanics and its laws enter the scene, that is, physics. More precisely, working with quantum mechanics means working with the time-independent Schrödinger equation:

$$H\psi = E\psi$$

where H is the Hamiltonian of the system, E is the energy, and ψ is the wave function.

In many-atom systems, such the one we are analyzing, the Hamiltonian, in a semiclassical approximation, is made up of the kinetic energy of the electrons and of the interaction energy of each electron with the nuclei and with other electrons. If E is known for a given nuclear configuration, we can find the corresponding potential energy for the nuclei. However, the difficulty lies in finding out the expression of the electronic wave function ψ, since this depends on the spatial coordinates of the n electrons in question.

This is the hurdle that must be overcome in order to give a physical account of how two molecules (in our case, p53 and MDM2) interact. The last four decades have seen many efforts dedicated to solving this many-body problem. A many-body problem can neither be tackled via analytic and deterministic tools (we cannot deal with more than two bodies), nor via statistical tools (there are an insufficient

number of bodies). An alternative successful approach has been based on numeric solutions. Thanks to progress in algorithm theories and to increased computing power, we are now able to represent what happens at the binding sites of molecules, and thus to construct quite precise descriptions of the stereospecific complementarity, based on quantum mechanics.[5]

It is totally outside our present sphere of interest to write down the Hamiltonian of the time-independent Schrödinger equation concerning the bond between p53 and MDM2, and to solve it (but it could be done, even if not so easily; see, e.g., Zhong and Carlson 2005; Ding et al. 2008; Wang et al. 2011). Actually, what is really interesting for us is that now we can comprehend even more in which sense the why-question and the because-answer depend on the contexts in which we want to work. In particular, at one extreme we could content ourselves with the intuitive and commonsensical explanation based on the claim that there is an interaction between the two molecules; instead at the other extreme we could use physics. Here, of course, there is no invocation of any form of hierarchical relevance or of reduction of molecular biology to physics. I am only stressing that we use the knowledge pertaining to the context in which we are working and that there is a context in which we are compelled to use physics. It is not a problem of hierarchies or reductions; it is a problem of contexts and perspectives (see Callebaut 2012). Nothing more.

At this point, it is worth noting that I am speaking of something different from the *explanatory heteronomy* defended by Weber (2005, 2008). He suggests that often "experimental biologists must apply theories from physics and chemistry in order to provide explanation for biological phenomena." I would not deny this position, rather I am saying that there are explanatory contexts in which physics is necessary, since in those contexts the biological phenomenon needs to be analyzed from a physical perspective. This does not mean that physics is explanatory heteronomous. On the contrary, we are in the presence of a totally autonomous molecular biology explanation that, in that context, requires physical laws.

The p53 Network and Why a Molecular Mechanism Works

Let us suppose we want to know the reasons why the p53 degradation mechanism works. For this purpose it is worth recalling that p53 is a hub-protein at the center of an intricate network. Fortunately the p53 interactome (the network of proteins interacting with p53) has been identified and it can be represented in different manners (Fig. 6).

Actually the p53 interactome is one of thousands of interactomes present within a cell, which implies that each element of the p53 interactome can potentially interact with each element of any other interactome.

Let us recall that the original force of all movements within the cell is given by thermal energy, which is the total kinetic energy of motion of all the particles (i.e., the molecules) that make up the cell. Of course increasing/decreasing the temperature of a cell has the consequence of increasing/decreasing the average kinetic energy of the particles of that system. More precisely, each molecule has an associated kinetic energy (along each axis) $E_K = ½\ kT$.[6] This is valid for Brownian motion, i.e., for random motion of particles suspended in a fluid, as is the case for molecules suspended in the aqueous medium inside a cell.[7]

Since biological molecules are not found in a vacuum, but in an aqueous medium full of other molecules, this means that they bump into both surrounding water molecules and other molecules within the cell. In so doing, they wander around executing a random walk.

By this reasoning, we understand the cause of any molecular interaction within a cell: thermal energy. Note, by the way, that in this manner we have also answered questions 7 and 8: "What switches the mechanism on?" and "What is its energy source?" Moreover, thanks to the laws of the Random Walk Theory and the laws of Brownian Motion Theory, we can have an explanation of what occurs (and so we may satisfy question 6bis).

Due to their kinetic energy, two molecules with Brownian motion can interact, although this is not sufficient for them to bind. Thermal motion allows interactions among the molecules, but it also hinders binding, both as a consequence of thermal agitation of molecules and of

[5] Two successful examples of this approach are worth citing here (cf. Car 2002; Carloni et al. 2001). In *Density Functional Theory*, attention is focused on single particle density, rather than directly calculating the expression of the many-electron wave function. This simplifies calculations, since such density depends on only one spatial coordinate (cf. Hohenberg and Kohn 1964; Kohn and Sham 1965). Alternatively, in ab initio *Molecular Dynamics*, only the valence electrons are considered. These are the only ones relevant from the point of view of the biochemical bonds, with the others being considered negligible in terms of their effects on the binding properties and, consequently, irrelevant for the calculi (cf. Car and Parrinello 1985).

[6] T is the absolute temperature and $k = 1.3806504 \times 10^{-23}\ JK^{-1}$ is the Boltmann's constant.

[7] From this, and knowing that $E_K = ½\ mv^2$ (m is the mass of the molecule and v its velocity), we have $<½m\ v^2> = ½\ kT$, where $< >$ denotes an average over time, or over an ensemble of similar molecules. Therefore, $<v^2>^{1/2} = (kT/m)^{1/2}$. This means that, for example, lysozyme at 300 °K (27 °C) (which has a mass of $m = 2.3 \times 10^{-20}$ g) has a $<v^2>^{1/2} = 1.3 \times 10^3$ cm/s. Thus, if there were no obstacles, this protein would travel a distance of 10 m in 1 s (see Berg 1993).

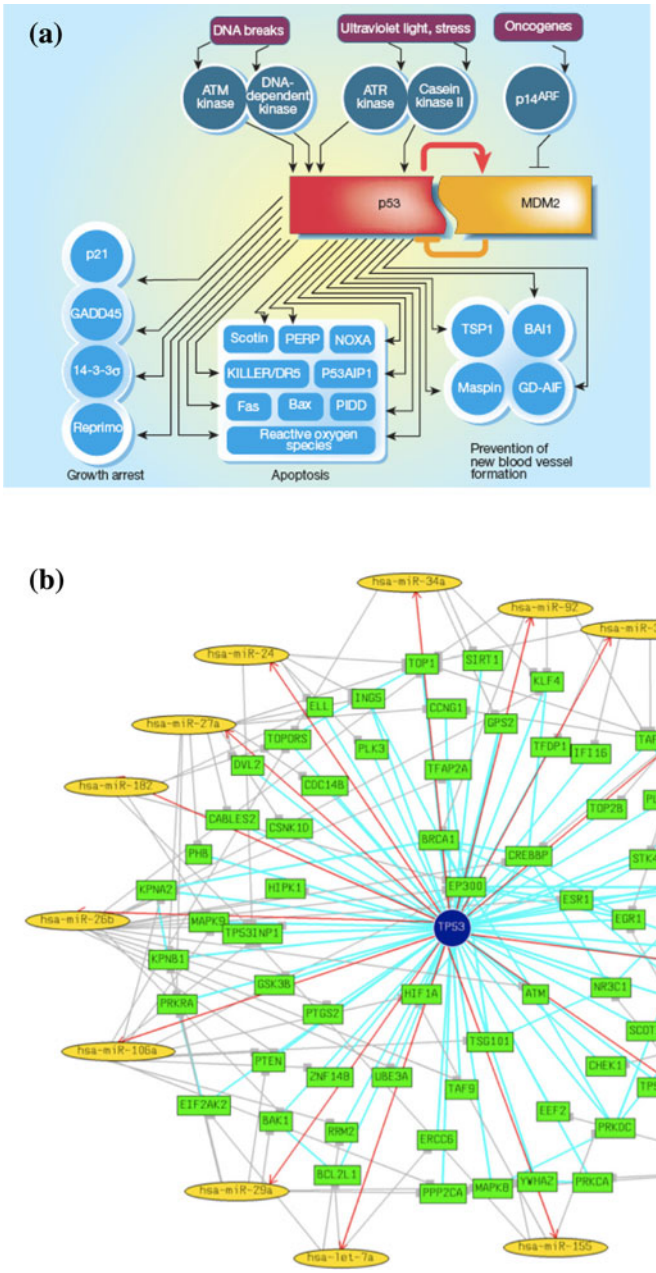

Fig. 6 The p53 interactome. (**a**) is taken from Vogelstein et al. (2000). In (**b**), miRNAs are represented by *ellipses*; target genes are represented by *boxes*. Induction of the miRNAs by p53 is represented by *directed light lines*. Negative regulation of the target genes by miRNAs are represented by *dark lines*. The protein interactions are represented by *undirected light lines* (Sinha et al. 2008)

pushing forces originating from other molecules. To achieve binding, molecules must thus interact correctly, by creating a sufficient number of non-covalent bonds between them to avoid separating. This happens when the two binding sites have an appropriate stereospecific atomic configuration. In other words, the non-covalent bonds between two molecules are sufficient only if the stereo-specificity of the two binding sites is complementary, that is, if they match well. The specificity of the biological recognition between two molecules is a totally contingent evolutionary result, of course within certain chemical constraints (see Knight et al. 1999; Berg 1993; Kirkwood et al. 1986; Karplus and Petsko 1990). Therefore, we have a possible evolutionary answer to question 10, which can be interpreted in this context to mean: "What has realized the complementarity of the two binding surfaces?"[8]

[8] We could also offer a probabilistic description of the formation of the molecular bonds inside a cell, and thus of the p53-MDM2 bond. By means of such a representation we could also have a probabilistic explanation of their formation. Let us start with a generic intracellular molecular interaction (for an animation, www.youtube.com/watch?v=LakZiSC9kSc). Let M be a molecule of a given type and let us suppose that there are m molecules of such a type. Within a cell we have $m_1, \ldots, m_n$ molecules of, respectively, the types $M^1, \ldots, M^n$. In such a case, the probability that a molecule of the type M interacts

What has been said above already suffices to indicate again that if we want to work in given molecular biology contexts the laws of physics, in particular that of molecular dynamics, enter the scene.[9] In short, physics enters the molecular biology scene whenever the context in which we are studying that particular biological phenomenon requires it.

Conclusion

Biologists frequently use the term "mechanism." No one, I think, could deny this evident fact nor that in the world of molecular biology there is something called "mechanism."

In what has been said above, first of all, I have indicated a series of questions which should be answered to have a more complete description of a mechanism. Of course, I have underlined that, in all likelihood, there is no molecular biology paper that offers a description of a mechanism in terms of all of them. Actually, each paper is devoted to answer a different subset of questions, and such subset depends on the authors' interests and on the issue faced.

Among the questions, I have stressed that one regarding the different states of the process characterizing the mechanism at issue. In so doing I have shown that we could be stimulated by introducing a new question, which actually has to be understood as a why-question, that is, as a request for explanation. The difference between the two has been the core of my argument for a plausible distinction between two epistemic acts: the mechanism description and the mechanism explanation.

By discussing the p53 degradation mechanism, I have shown that the why-questions and the because-answers depend on the context in which they are formulated and that there are contexts in which physics and its laws are necessary.

In particular, I have shown, by analyzing the p53 degradation mechanism, in which context physics enters the play and how quantum mechanics or other physical theories (Random Walk Theory, molecular dynamics, and statistical mechanics) could or should be used by molecular biologists. All of this is without any reductionist aim but simply because in that context, physics is required.

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Footnote 8 continued
with an arbitrary molecule of the type M^i is $p^i_{M/M}$. This probability depends strongly on the concentration of the two molecules and on the strength of the thermal motion. For a measure of scale, consider that for the standard concentration of ATP within a cell, each site of any given protein will interact with ATP molecules some 10^6 times per second. For a productive interaction to occur, a bond must be made. For this, the two interacting molecules must have sufficient kinetic energy to overcome the two repulsive potential barriers of their interacting sites. This kinetic energy depends on the strength of the thermal motion, that is, on the temperature T. Let p_T be the probability that such an event will occur. Further, the two molecules which have interacted and whose kinetic energy allows them to overcome the potential barriers, must have complementary binding sites that permit stable binding. Let p_C be the probability that the two interacting molecules have the correct stereospecific configuration. It follows that the probability P_B that a molecule M generates a bond with a certain other molecule M^i is $P_B = p^i_{M/M}\, p_T\, p_C$.

[9] In this explanatory context we can better understand metabolic errors, that is, infringements to biological generalizations that have often been emphasized by those who argue for their inexistence in biology. Such metabolic errors are instead physiological (and graspable by physics), since all the interactions can potentially be realized, including the more energetically disadvantageous ones. Only infinite potential barriers could prevent these errors from occurring, but these are physically impossible. It is this physical impossibility that drives that engine of evolution, which is based on the modification of the primary structure of DNA and which may lead to DNA mutations.

Consider DNA mutations induced by base analogs (compounds that are structurally similar to DNA bases). As a consequence of their incorporation into DNA these compounds can induce changes in base-pairing within the DNA, and thus cause mutations. For example, 5-bromouracil (5-BU), a thymine (T) analog, can insert into DNA at sites normally occupied by thymine.

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