The Physical Basis of Medicine

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What is medicine? What is physical science? Can one really place limitations on the realm of experimentation or modeling in any particular discipline? A potential answer to some of these questions is actually based on simple molecular physics. Which for the last several years (since the advent of powerful supercomputers) has been a relatively neglected area in biomedical research.

Through the understanding of chemical interactions, many medical discoveries can be approached. For example, if one is trying to find a molecular substance that may potentially suppress a particular type of cancer cell growth from a series of structures, this may easily be done by finding structures with particular electrostatic potential properties. A quantum chemical computational study can be performed, and a structure ready for laboratory studies can be found within a matter of hours (if the structure is modest in size, 100–few hundred atoms).

Other more intriguing investigations can even make use of the chiral properties of certain molecular species. If one would like to characterize the binding of a trans-activator such as Tat to HIV-1, one may argue that many isomeric and stereo-competitive forms exist, yet only one may be naturally occurring (with a higher probability) and hence more practically useful.

An example of how important this concept may be from an isomeric point of view is the bodies' response to isopropanol versus ethanol. From the stereospecific point of view, other examples commonly encountered include the competition between the two forms glucose (D-, and L-) exist, yet only one can be favorably used by our systems.

In the problem of HIV-1 suppression (or any other type of viral disease), one can use computational methods to first optimize (by some kind of molecular mechanics or dynamics methods) the two structures (HIV-1 and Tat), calculating their relative energies (HIV-1 relative to Tat since it is larger, and Tat can be given a value of zero). Next, the dealer (perhaps even the biologist or medical doctor!) can find several orientations (based on chirality, and other physical properties) of the HIV-1/Tat complex. The lowest in energy is thermodynamically favorable, and is an observable in nature. This can be completely exper-

imentally and theoretically characterized (ie, via partition functions, heat capacities, vibrational energies, etc).

But how can this affect anyone undergoing treatment? Simple, now you know the physical basis for the interaction, the next step is to find a *mediator* compound to break up this interaction. If we know that C261 is needed by Tat to bind to HIV-1 (more specifically the TAR region), one can simply locate (by a potential energy surface calculation) several analogues of a molecule into the mixture (the HIV-1/Tat complex), and calculate the relative energy. If the energy is very high, then the chances of forming it are nearly zero. If the energy is very low, then the mediator forms the desired target interaction (in this case suppression of Tat binding to HIV-1). The point of this is that physical methods can easily make their way into routing practices of biomedicine and biotechnology research.

One may ask how can these calculations be done on so large polymers? Consider the general form of the total energy of interacting ions and electrons as $E_{\text{tot}} = E_{\text{e-e}} + E_{\text{e-ion}} + E_{\text{ion-ion}}$. We can see from this simple interaction that the total energy is a sum of the kinetic energy of the interactions between the electrons, the sum of the potential energy of the interaction between the ion and electron, and the energy of the interaction between the ions. If we can then, average out all interactions with a density of a particular group (ie, Cysteine, tyrosine, etc), we can easily compute the energies of even the largest complexes by using *densities*, which is fairly easy to do once the corresponding groups are well characterized (the amino acid chain sequences).

Even statistical thermodynamics and mechanics allow for any useful medical data to be obtained. It has been shown recently that understanding of the evolution of the composition and structure of living beings can be based on the thermodynamic study of hierarchic structures at different levels.

Consider the second law of thermodynamics, which is one of the general laws of nature that defines direction and completeness (degree of transformation or extent of a process) of the real thermodynamic processes. It states that the entropy of a system will increase (in an isolated system) when the number of spontaneous (irreversible)

processes increases. However, biosystems are continuously “fed” by energy-rich compounds synthesized in nonspontaneous processes. From this viewpoint, biosystems do not spontaneously “move away” from some “vague equilibrium,” as is generally accepted, but rather exist in a stationary state of matter circulation. In this relative circulation, the thermodynamically unstable compounds are continuously generated upon exposure to an external energy source. Obviously, the sun, which is not only an external energy source but it is primary to existence, is the driving force of nonspontaneous processes of matter circulation on earth (although other energy sources exist as well, such as atmospheric discharges, volcanic activity, etc).

For most cases, however, thermodynamic results do allow for the calculations of the spontaneous degradation of biomolecules that results in the “recovery” of compounds that are thermodynamically stable (under earth conditions) into the matter exchange cycle, making them a routine in a variety of biologically related problems. If we are going to obtain a probable structure from quantum mechanics, thermodynamics is then needed to characterize this complex by computing various physical properties.

All in all, practical medical problems are becoming an area of interest to many branches of physical science research. Quantum and statistical mechanics are making their way into many modern experimental research labs, and are deeply impacting the way by which many do research. They allow for a very rapid comparison of many potential drug agents without wasting the time, energy, and resources needed for preliminary test runs. Although, the era of computational drug design and bioquantum mechanics is just beginning to make its way up to the scientific ladder, there is so much potential for its use and applications that it is definitely an area where many scientists need to begin to make some serious investments to master these methods. Modern resources make it possible for the original formulations of Schrödinger, Hartree, Fermi, and others to be put to the test of more practical open-ended problems. Just as the early physicists were put to the test of developing models to understand fundamental questions of nature, today’s scientists are given the prospect of using old tools in an extremely novel context. Only the future will tell how far this dream will be fulfilled. So what is medicine, or science for that matter? The answer is simple. *Life*.

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