

Biophysical Contributions and Challenges in Oncology

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Editorial

Students of the life sciences (and hence oncology) have long recognized that biology obeys the same chemical and physical laws that govern all aspects of our universe. Indeed, the lines between a monolithic biology have become quite blurred between biochemistry and biophysics, the latter involving the implementation of physics methods or physics principles to the study of life and its processes. The German-American physicist, Max Delbruck, after arriving in the U.S., soon applied his physics training to biological problems. He is considered by some to be one of the founding fathers of modern molecular biology [1]. His contributions began at a time before the structure of DNA was known and Harold Varmus [2], from a plenary lecture at the American Physical Society in 1999, summarized those fundamental questions that were being asked at that time: What is the physical form in which hereditary information is stored? How is it reproduced when a cell divides? How is that information reasserted during sexual reproduction? How does that information change when mutations occur? Answers to these questions were sought employing bacteria and bacteriophage interactions-a simple model from which our knowledge of genetics was greatly advanced. In the past, physicists have made major contributions in the areas of biological energetics, enzyme and reaction kinetics, oxidation-reduction potentials, osmotic pressure and diffusion, optics, surfaces and interfaces, viscosity and liquid flow, ion transport, structure and elasticity, energetics of photoreaction centers, as well as many other areas pertinent to the study of life. Zhou [3] has summarized major research advances that have led to Nobel Prize winning contributions. Beginning with the discovery of X-rays and their diffraction by crystals that, in turn, led to the new analytical tool of X-ray crystallography. This advance made possible the determination of DNA and protein structures, the structure of photosynthetic reaction centers, ion channels, and ribosome and RNA polymerase II structures. Nuclear Magnetic Resonance Spectroscopy and the development of the Electron Microscope are examples of other contributions by physicists that have made possible the study of life, and its processes, in a detail not previously afforded and extended our horizons of investigation and depth of knowledge.

A Special issue of the Journal (J Integr Oncol, 2016, S1), titled "Oncology and Biophysics: A need for Integration" again emphasizes the need for renewed application of physics' tools and intellect to complex biological problems. Opportunities already exist, with several outstanding Biophysics Centers across the nation offering access to faculty with expertise and availability for collaborations on worthy projects. Indeed, the NIH maintains a Biophysics Core Facility at the National Heart, Lung, and Blood Institute that provides consultations, training, professional collaborations and instrument access. As an example of the benefits, the author was the beneficiary of just such collaboration while on sabbatical in the U.K. Our previous work had

anti-carcinogenic influence of butylated centered on the hydroxytoluene (BHT) on UV-induced skin cancer in mice. While on sabbatical I was allowed access to a linear accelerator at the Christie Cancer Hospital in Manchester. This allowed my colleagues and I to conduct time-resolved spectroscopy, pulse radiolysis, and to determine the reactivity with various radical species [4] - one step closer to understanding the potential mechanism of the anti-carcinogenic effect of BHT. In addition, a redox mechanism, based upon one-electron transfer rate constants, suggested interactions between tocopherol, beta-carotene, and vitamin C in which the carotenoid radical cation, a strongly oxidizing radical, would be repaired by vitamin C. If left unrepaired, this radical might account for the pro-carcinogenic activity of beta-carotene [5]. The melding of physical data with animal dietary/UV-carcinogenesis studies supported an interaction with tocopherol but not with vitamin C, leading to the conclusion that other carotenoids, their isomers, or, as yet unidentified phytochemicals must be responsible for beta-carotene radical cation repair [6]. These same types of time-resolved studies have been made available to researchers at many sites (usually through NAS grants to Universities) where Van de Graaff accelerators have been constructed.

There are two further points that I would like to address in closing. The first was raised by Varmus [2]. i.e., and can be a severe, hindrance for the integration of physics and biology. That is self-identification linked to what appears on your graduate diploma. I have found this particularly irksome on the part of grant reviewers. If your diploma doesn't say "Immunology" you can't extend your research into that area. This is the case with biophysics and thus it is important to seek strong collaborations in this field if it is required to advance your research area. This ties in with my second point. My graduate mentor, Harry Wheeler, emphasized to his graduate students that it was "the problem" upon which one must remain focused - you could always learn new methods and instrumentation if the "problem" required. In the past I have seen well trained graduates in a special area of instrumentation that sought a problem upon which to ply their expertise. This is, of course, antipodal to the philosophy of graduate education stated above, but one can take advantage of such expertise when applied to "the problem", i.e., conquering cancer. Finally, one of the greatest contributions of physicist to biology has been the unwavering spirit that exceedingly complex problems can be solved.

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Page 2 of 2