New Hot Paper Comments

By Nicola Bellomo

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Nicola Bellomo answers a few questions about this month's new hot paper in the field of Mathematics.

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Field: Mathematics

Article Title: Mathematical topics on the modelling complex multicellular systems and tumor immune cells competition
Authors: **Bellomo, N**;Bellouquid, A;Delitala, M
Journal: MATH MODEL METHOD APPL SCI
Volume: 14
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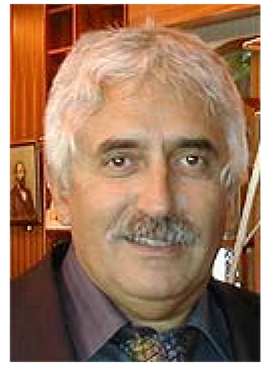
ST: Why do you think your paper is highly cited?

This paper deals with one of the most challenging research perspectives of this century: the mathematical description of living matter. The scientific community is aware that a great revolution of the 21^{st} century will be the mathematical formalization of phenomena belonging to living matter, whereas the revolution of the past two centuries has been the development of such an approach related to inert matter.

Indeed, it is a fascinating perspective, one which will capture the intellectual energy of several scientists in the fields of mathematics and physics. This essentially means that the heuristic experimental approach which is the traditional investigation method in biological sciences will be gradually enhanced by new methods and paradigms generated by a deep interaction with mathematical sciences.



"Systems in biology cannot be simply observed and interpreted at a macroscopic level."

ST: Does it describe a new discovery, methodology, or synthesis of knowledge?

It proposes a new mathematical theory, specifically a kinetic theory of large systems of active particles. An active particle is an object, identified at the microscopic scale, whose state is defined not only by geometrical and mechanical variables—for instance, position and velocity, as in the case of classical particles—but also by an additional variable suitable to describe their social and/or biological functions.

The overall description of the system is portrayed by a distribution function over the above-mentioned microscopic state. Suitable moments of the above distribution function provide useful information on the gross quantities characterizing the overall behavior of the system. The mathematical theory provides the conceptual framework to model the evolution of the distribution function.

ST: Could you summarize the significance of your paper in layman's terms?

Living systems can be regarded as constituted by many interacting active particles—i.e., cells in a vertebrate. Mathematical models can attempt to describe relevant biological phenomena—i.e., the competition between tumor and immune cells. The derivation of specific models, such as those dealt with in the paper, must take into account the technical difficulties in dealing with the mathematical description of living matter.

The following indications are extracted from:

H.L. Hartwell, J.J. Hopfield, S. Leibner, and A.W. Murray, "From molecular to modular cell biology," *Nature* 402 (6761): C47-C52 Suppl.

S, DEC 2, 1999.

i) Although living systems obey the laws of physics and chemistry, the notion of function or purpose differentiate biology from other natural sciences. Indeed, what really distinguishes biology from physics are survival and reproduction, and the concomitant notion of function. These biological functions have the ability to modify conservation laws of classical mechanics.

ii) Biological systems are different from the physical or chemical systems analyzed by statistical mechanics or hydrodynamics. Statistical mechanics typically deals with systems containing many copies of few interacting components, whereas cells contain from millions to a few copies each of thousands of different components, each with specific interactions.

iii) Systems in biology cannot be simply observed and interpreted at a macroscopic level. A system constituted by millions of cells shows at the macroscopic level only the output of the cooperative and organized behaviors, which may not, or are not, singularly observed. It follows that the mathematical theory needs to be developed at a well-defined observation and representation scale, while it needs to be consistent with the whole set of scales which represent the system.

The mathematical approach proposed in this paper attempts to tackle the above difficulties. It is described extensively in the forthcoming book by my two younger co-authors of the paper: Abdelghani Bellouquid and Marcello Delitala, *Modelling Complex Biological Systems - A Kinetic Theory Approach*, Birkhauser, Boston, (2006).

ST: How did you become involved in this research, and were any problems encountered along the way?

I decided to deal with the topics of this paper after a scientific encounter with Lee Segel, a mathematician in the Department of Computer Science and Applied Mathematics at The Weizmann Institute of Science in Israel, who died a short time ago. He changed my mind concerning the attitude that a mathematician should have towards biology by explaining to me that mathematics should attempt to capture, through equations, a physical reality which is only partially observed at the experimental level.

Only in this case can interaction between mathematics and biology become effective. Shortly after, I had the opportunity of working with Guido Forni of the University of Torino in

Orbassano, Italy, who is a leading expert in immunology. He made me understand how cells interact through complex dialogues ruled at the sub-cellular level. For further discussion of our efforts, see the following articles:

N. Bellomo and G. Forni, "Dynamics of tumor interaction with the host immune system," *Mathematical and Computer Modelling* 20 (1): 107-122, JUL, 1994.

N. Bellomo and G. Forni, "Looking for new paradigms towards a biological-mathematical theory of complex multicellular systems," *Mathematical Models and Methods in Applied Sciences* 16, 2006.

ST: Are there any social or political implications for your research?

In the industrialized countries, cancer has now moved from seventh to second place in the league of fatal diseases, surpassed only by cardiovascular diseases. Indeed, the World Health Organization estimates that cancer kills approximately six million people every year. The mathematical kinetic theory for active particles may contribute to a deeper insight into the immune system, and a deeper understanding of immune competition may contribute to the struggle against cancer.

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