My Personal Journey In Mathematical Biology Medicine

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My long journey in mathematics as applied to biology and medicine began by a training in pure maths, geometry, that did not push me towards applications in any manner. At that time (late seventies), research in geometry was dominated by abstract concepts (e.g., sheaf cohomology), which had little to do with objects that one can touch. Conversely, having been trained in maths, I was demanding on understanding in depth how phenomena occur, not by principles, but by theorems, which will always remain the only way of *proving* results. I was not satisfied either with the idea to be a teacher all my life, although I had passed with success an application (the French agrégation) to obtain the right to teach at least in good conditions if I had to.

I was then available for something new. I have read somewhere that to fall in love, one has to be available for new things, and there should be many examples of this in literature. Well, it can be the same with science. I began with science, being more trained in this domain than in the other (love came a little later, but this is another story). Being thus available, and interested in working on not just transmitting, but as far as possible creating, knowledge in a field where some potential place for maths would exist, I considered different possibilities, among which the most obvious were offered by economics and by biology. I had not had any training in economics and I was very mediocre at biology, making very little sense of what I was taught in the lycée. But I had at the university the example of a geometer who, being one year ahead of me in mathematical studies, was at the same time studying medicine, and dealing with interesting geometrical problems coming from radiology. During my training for the *agrégation*, I had learnt to learn quickly and efficiently, I was not bad either at learning lists and I thought that I might be more useful as a doctor than as a teacher. I should also mention in the personal mental process that led me to medicine the movie by Akira Kurosawa "Akihige" (Red Beard), in which the character played by Toshiro Mifune is both able to break bones if necessary, as the master of martial arts he is, defeating a gang of ruffians who claim to prevent him from taking to his hospital a tuberculous prostitute from the brothel she works in, and later repair them, as the talented surgeon he also is. [When I tell this to my children, they seem to think that it is just one more odd thing of me.] Furthermore, during the summer preceding my first classes in medicine, I spent two months visiting Peru by myself, and the poverty I discovered there convinced me of the interest of being a physician rather than a teacher if one wants to be active and useful.

If I had not studied mathematics first, I might have become one of these "French doctors" for a time. Indeed, one can find real addiction in practicing first aid care or surgery, or even plain medicine when a fast and right diagnosis saves a life. What I discovered early in medicine were first very interesting classes in biology, anatomy and physiology - which then made sense to me, because they were meant to give the basic knowledge necessary to practice medicine - and also a close contact with real life. When you study maths, problems are generally designed in such a way that the student is guided by a succession of questions to the main result to be shown, and it would be unfair to put traps on the way towards the solution. Of course you have to keep in mind that apparently likely things are not true (e.g., that $\exp(A) * \exp(B)$ is not always equal to $\exp(A + B)$ for endomorphisms, etc.), but one learns to be cautious, and you can always count on proofs relying on theorems to sever between true and false. In medicine, nothing of the kind exists. Diagnosis is often difficult, and snares put on your way, just by hazards of life, are frequent. Doubt (popularized by medical TV serials) is also frequent, and no theorems exist to pull you out of it. What you can always reckon on is anatomy and physiology, but whereas anatomy is usually a faithful help, physiology is more ambiguous since its various negative feedbacks may be used to hypothesize one thing and its contrary. So that, confronted with clinical puzzles, rather that indulging in impassioned discussions as in TV serial staff meetings, physicians often apply therapeutic rules learnt in books, updated according to current treatments referenced by the Faculty.

Such generalized absence of theory with sound foundations left me unsatisfied as I had been, years earlier, by sheaf cohomology. I was again available (not in all domains, for I was then married with a newborn child) for discovering new things in maths and in medicine to find my own way. But how can you be useful to medicine when you have studied pure maths? I had in the course of my medical studies taken some time to learn classical statistics (teaching them at the same time, for there is no better way to learn than in teaching), which has always proved useful to me, be it only to understand how statistical tests are used in processing biological data. Being firstly recruited as a volunteer in the research institute that still hires me (on a permanent position now), and later detached in it from the national education service, I learnt at that time basics of signal processing and multidimensional statistical methods to deal with physiological recordings.

This was far from the mathematical modeling and analysis for medicine I am busy with now, but it was necessary to know what biological data are and what sort of physiological hypotheses one can propose from statistical processing of data, according to a well-designed method, to answer a pathophysiological question. The first study I led then was the core of my MD thesis, and it was later extended to more such studies. It was also very useful to me to establish contacts with medical teams, showing that I could provide them with new methods of investigation. Being hired for a prolonged detachment in my institute, I could then begin to get involved in more theoretical studies. It began with cardiac electrophysiology. After some time (ten years), I met an oncologist interested in mathematical modeling, not to understand better cancer treatments by the use of theorems, but to see what new insights mathematical models could bring to his therapeutic practice.

Limited as these expectations may seem, they are not so frequent and show some open-mindedness that allowed me to establish a long-lasting collaboration (twelve years). From it, my regular participation in lab meetings resulted in biological and therapeutic control questions that led me to design models of tumor growth control by drugs, and later to enter in contact with specialists of optimal control, with whom I still work on theoretical optimization of treatments by anticancer drugs. Presently, understanding resistance in cancer to overcome it by optimized time schedules of combinations of drugs is one of my major goals. This also leads me now to try and take advantage, at the genomic era (which includes epigenetics), of data on intracellular signaling pathways, to connect them with cell fate at the level of cell populations, the right level to observe cancer progression and its control by drugs.

Let the reader take this personal journey as a complement to the "Perspective" short paper I published last year in the May issue of this newsletter, and to a paper I published three years ago in Acta Biotheoretica on "Commitment of mathematicians in medicine". I hope that it shows an example of a way of career that may be followed - or on the contrary, that must be absolutely avoided! Example or quixotic counterexample, I will go on searching for theorems to found clinical practice (see on this a perspective I wrote in 2013 for J. Math. Biol.), and if I may have contributed to finding some in the future, I shall be happy with my journey.

About The Author:

Jean Clairambault, PhD, MD, trained - in that order - in mathematics and in medicine, is presently a senior scientist ("directeur de recherche") at INRIA and Laboratoire Jacques-Louis Lions, Pierre et Marie Curie University in Paris. His current interests in research are the emergence of drug resistance in cancer and the evolution from premalignant cell populations to tumors, together with therapeutic optimization methods using combined drug delivery strategies to overcome such evolutions at the cell population level. Website: `http://www.rocq.inria.fr/bang/JC/Jean_Clairambault_en.html`.