Mathematical Modelling and Simulation in Biomedicine

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INTRODUCTION.- Mathematical techniques are increasingly used to address problems in biomedical sciences. Indeed, statistical analysis have long since been acknowledged as essential for experiments validation. On the other hand, computer simulations allow to perform a wealth of in silico experiments, whereby the consequences of clearly stated hypotheses can be easily explored. In addition, mathematical modelling is becoming a method of choice when it comes to identify main agents in complex scenarios. In the following lectures some examples will be discussed to show how mathematical modelling, analysis and simulation, used as a complement to (but not as a substitute of) well-established biomedical techniques can be used to gain insight into complex systems of biological interest.

Lecture 1. Comprehensive vs minimal models: Emergent behaviours in immune response

The astonishing efficiency and availability of computer simulations has greatly stimulated the formulation and study of complex models in biomedicine. Indeed, large systems of equations can now be simulated, which in principle allows for simultaneous consideration of many biological processes in the models proposed. However, uncertainty about parameter values, and hence about the comparative importance of the features they represent, set serious limitations to the practical relevance of such comprehensive models.

In this lecture a minimal mathematical model will be presented to describe key features of the immune response to acute infections . In particular, the way in which a large population of T-cells (lymphocytes) is first generated (clonal expansion) and then dispensed with (clonal contraction) will be obtained as an emergent population effect arising from individual T-cell decisions, encoded in a simple deterministic algorithm. Further extensions, and limitations, of the approach presented will also be discussed.

Lecture 2. Mathematical problems in radiotherapy: Accounting for tumour heterogeneity

Radiotherapy, the use of ionizing radiation to destroy solid tumours, is a treatment of choice for more than 50 percent of cancer patients. A key issue to be addressed in any radiotherapy treatment is how to achieve significant tumour control with a minimum of induced side effects on neighbouring healthy tissues and organs at risk. As a consequence of scientific and technological advances made during last century, radiotherapy has proved successful in a large percentage of cases. However, as any other therapy currently available, it still yields poor results in the treatment of tumours at a disseminated stage.

In this lecture mathematical methods in radiotherapy will be described. Particular attention will be paid to modelling tumour heterogeneity, manifested in the presence of several phenotypes with different radiosensitivities within a tumour, and to the manner in which dosimetries accounting for such heterogeneity can be suggested.

Lecture 3. Pattern formation in vasculogenesis

The vascular system is the first fully functional system in vertebrates, since its performance is needed for nutrient distribution and waste removal as embryo grows. Unfolding of the vascular system first proceeds by vasculogenesis, that is by the formation of a full vascular bed with vessels of different sizes and calibres. Early in this process, isolated cell progenitors (angioblasts) begin to coalesce and assemble into a reticular pattern, a template for subsequent deployment of blood vessel networks. Later on, functional vessels will be remodelled by means of angiogenesis, a regulatory process that acts over an already existing vasculature.

In this lecture mathematical models will be described that have been used to elucidate the role of chemical signals in the unfolding of filamentary structures corresponding to an early vasculature, a process characterised by well-defined space and time scales. Particular attention will be paid to discussing insight provided by mathematical modelling in ascertaining key mechanisms involved in that process.