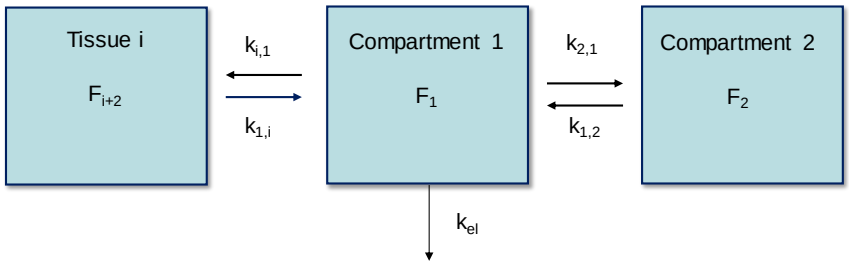
Kinetics

The term "**kinetics**" refers to very broad areas of common life as well as science. Here, the movement of material objects into space, which belongs to mechanics, and the mixture of solids, liquids or gases under the laws of diffusion and entropy will not be considered. "Kinetics" deals with the evolution of simpler systems composed of atoms or molecules transforming in time by radioactive decay, chemical or enzymatic reactions or molecular complexation and with the behavior of chemical or biological components in living organisms. If this assemblage may seem heteroclite, it is actually quite natural because all these kinetics can be described by **systems of ordinary differential equations**, in which unknown functions depend only of a single variable, time, as opposed to partial differential equations, which involve several independent variables including time and space variables and require other study tools.

In particular, we are interested here in an approach to the kinetic modelling of these systems by the introduction of **compartments**, i.e. spaces containing each a component whose spatial distribution in the compartment is homogeneous and instantaneous and exchanging these components with each other according to the density (concentration) of the components in the compartments.

These **multi-compartment mathematical models** therefore consider only one parameter per compartment, such as the quantity of a component or its concentration in a compartment whose volume is assumed to be constant over time.

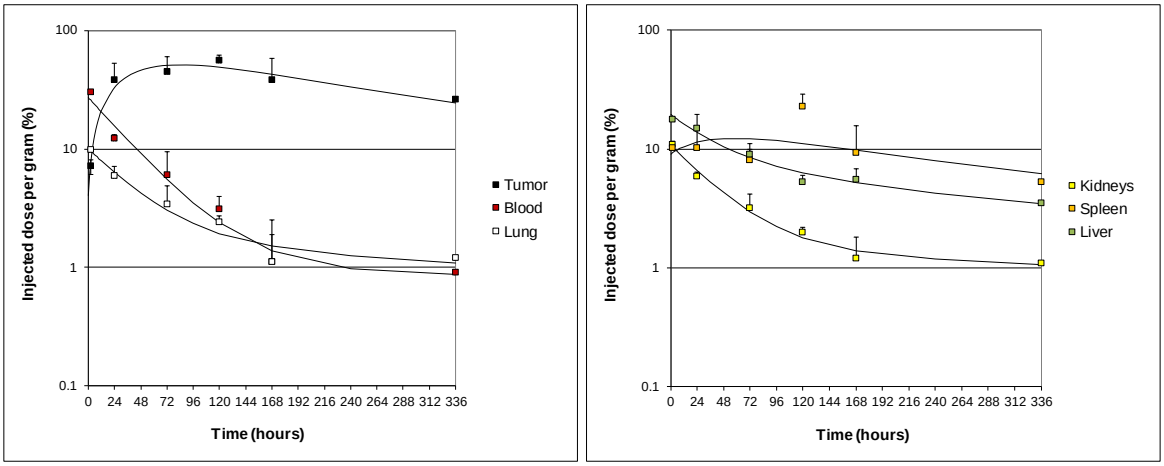


Although the compartmental approach was first developed to study the pharmacokinetics of drugs and tracers[i], this way of treating kinetic systems is convenient and powerful. The aim is to avoid having to develop analytical solutions, sometimes complex, of differential equations. The system is described by writing down these equations and letting the software solve them, numerically, using validated calculation methods. Then the kinetic simulation step may easily be followed by the estimation of parameters that provide the best fit between simulation and experimental data.

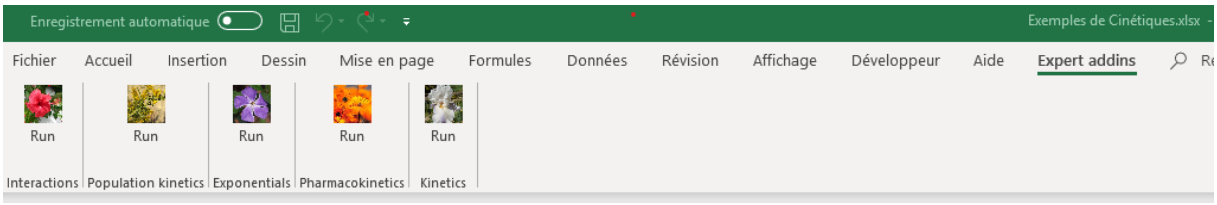
In this second step, the question of the identifiability of the parameters is left to the theorists[ii] in favor of a pragmatic approach allowed by the flexibility of the software. The model can be modified very quickly and it is very easy to test whether the adjustment of the parameters converges correctly or not. Indeed, thanks to the computing power of the computers that we all currently have, the two steps, simulation and adjustment, are executed by the program in a few seconds.

This software is largely inspired from WinSAAM[iii] and its predecessors SAAM and ConSAAM, with whom the author familiarized at the NCI Laboratory of Mathematical Biology, in Bethesda, MD, in the years 1984 and 1985 thanks to John Jacquez, Dave Covell and John Weinstein. Let them be thanked. WinSAAM is still one of the most powerful platforms for this type of calculations, but it may be considered difficult to use because of its interface that remains influenced by the good old punched

cards. To make these compartment modeling approaches more accessible, the author undertook to create the software **"Kinetics",** which deals with the same questions in the environment of **Excel spreadsheets,** familiar to experimenters, physicists, chemists, biologists or pharmacologists. The programming tools are no longer Fortran, but Visual Basic supported by a dynamic link library written in Pascal. Developed without access to the sources of SAAM, this software is free for use and distribution under the conditions that these are not for profit, that the Arronax GIP is thanked for the communication or publication of any results obtained using it and that beneficiaries of the transfer of this software undertake to respect the previous conditions. All files needed to use "Kinetics" are in the compressed file below. Sources can be obtained by express request to barbet@arronax-nantes.fr.



This software is in fact one of a series that allow simulations and adjustments of parameters of multiple molecular equilibriums, titration and speciation ("Interactions"), adjustment of exponentials ("Exponentials", "Pharmacokinetics") and of population kinetics studies, ("Populations Kinetics") all working from an Excel spreadsheet and available from the Arronax-Nantes web site.



[i] Jacquez JA, Compartmental Analysis in Biology and Medicine, 2nd ed., The University of Michigan Press, 1985.
[ii] Jacquez JA. Identifiability and parameter estimation. JPEN J Parenter Enteral Nutr. 1991, 15:55S-59S.
[iii] Novotny JA, Greif P, Boston RC. WinSAAM: application and explanation of use. Adv Exp Med Biol. 2003, 537:343-51