# Dynamic concepts in biology

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The purpose of this first conference, the productivity of photosynthesis systems, is very well summarized in its title: models and methods. It is to discuss methods to extract facts and information from nature, especially regarding the functioning of organisms that contribute to primary production and to develop models that enable us to use this information in a meaningful way.

## Theory and models

Hardly any would challenge the theorem that the purpose of any theory is to summarize and predict. However, this is not the only purpose and probably not the most important in a world where so many changes occur through human efforts and our interests shift from stationary situations to non-stationary processes. An acceptable theory at the present time should also provide relevant information for management purposes.

Now it appears that even under conditions where all basic principles and data regarding the system are known, our ability to reason is often too rudimentary to come to useful results, especially where non-stationary processes in space and time are involved. For instance, although the aerodynamic behaviour of seeds and the dynamic conditions in the air should be known in detail, it would be extremely difficult to predict even the most likely distribution of seeds originating from a point source; the prediction of the actual distribution in an actual situation would not be considered at all.

At present it is my prejudice that part of the difficulties we encounter in our attempts to apply knowledge may be overcome by the use of simulation. The word prejudice I use on purpose, because I think that the approach in spite of its increasing numbers of advocates, has still to prove itself.

Simulation in this context may be defined as the building of models and the study of their behaviour. Models being schematic representations of systems, which in their turn comprise a part of reality, defined by its boundaries. This definition is so broad that it is worthwhile to attempt a further classification. Since the art of model-building is not very much advanced in our science, I will illustrate this classification by means of examples borrowed from classical dynamics.

### Demonstrative models

These models cannot be used for experimentation that replaces experimentation with nature, but only for demonstration. The classical example is a planetarium, which mechanism is completely different from reality. These planetariums may be used to familiarize an astronaut with the sky, but cannot be used to study the dynamics of a space flight. The representation of the behaviour of a plant community by a set of curves that are obtained by the most refined technique of statistical analyses of a large number of observations is a still more rudimentary example of a demonstrative model.

### Scale model

Examples are hydro-dynamic models of rivers and aero-dynamic models of air planes. The equations of movement in these models are the same as in reality and are realized in the same way, only at a more convenient scale. These models, which are visually similar to the simulated system, are possible because theory is far enough advanced to change the scales of time and space without changing flow patterns, and necessary because a complete mathematical treatment, even with the most modern mathematical instruments and tools, is not feasible. The models do not provide a solution, but they are replacements of reality, facilitating experimentation.

In other scale models the equations of movement are the same, but the mechanism is different. It is, for instance, possible to simulate the non-stationary movement of ground-water by means of models in which the aquifer is replaced by lead and the water by heat. These type of scale models are often of limited use, because the analogy with reality that is of interest, is not complete. Heat models of water-flow in soil are for instance of limited use because there is no analogy of gravity. Scale models seem impossible to realize in biology: the worlds in which Gulliver travelled were, even before his visit, full of contractions.

### Analogue models

More abstract, but at the same time more flexible than scale models are electronic models, designed to eliminate the discrepancy between the simplicity of formulating the basic processes of dynamic systems and the impossibility of arriving at an analytical solution. An analogue model of a falling apple could consist out of two condensors. The first condensor is loaded with a current proportional to the acceleration, so that the voltage is proportional to the speed of the apple. The second is loaded with a current proportional to the voltage on the first, so that its voltage is analogous to the fallen distance. The dynamic principles in reality and the electronic principles of the model are known to such an extent that scaling of variables between model and real system is possible and thus to arrive at quantitative answers.

Analogue models and the simulated system are visually not similar. However, if the equations of movement of the model and of the real system are the same, the answers obtained with the model are correct and do not need any verification.

The integration on the condensors is continuous and occurs in parallel like the processes of the real world, so that the time that it takes to perform a simulation does not depend on the size of the system to be simulated.

Analogue computers, developed on these principles are very useful for the simulation of continuous systems, but are not without disadvantages. The user has to adapt the scale of each variable such that the circuit elements are not overloaded and used throughout their full range and has to live with the inaccuracy of the circuit elements.

**Simulation languages for digital machines**

These problems do not occur when continuous systems are simulated on digital machines for which purpose special simulation languages have been developed. The use of these languages must be preferred to the use of analogous machines if a number of changes in the system to be simulated are discontinuous, many empirical relations have to be introduced in the model and changes at a certain instant of time do not only depend on the state of the system, but also on its history. These situations occur in many biological systems and it is beyond doubt that for their simulation digital computers with proper simulation languages must be preferred.

A digital machine, which has the restriction that all operations are discreet and occur in a fixed order, seems the most unsuitable machine for the simulation of continuous systems in which all changes occur in parallel fashion. The main purpose of all simulation languages for continuous systems is to circumvent these two restrictions.

For this purpose it is recognized that in any system changes of state do not depend on each other, but each is related to the state of the system at the moment. For instance, the growth of the leaves of a plant does not depend on the photosynthesis rate, but on the amount of carbohydrates that are present. If, however, the photosynthesis rate changes to zero at the onset of darkness, carbohydrates are being depleted and this results in a decrease of the growth rate of the leaves. In other words, the dependence of the growth rate on the photosynthesis rate is a consequence of the operation of the system and does not reflect a direct relation between both rates.

The fact that rates are not mutually dependent, but depend on the state of the system enables a sorting routine to be introduced for the equations that describe the system. Starting from the known state of the system – at the onset characterized by the initial conditions – the equations are sorted in computational order. Then each rate is calculated independent of the others and then all rates are realized over a small time interval. In this way, the program is executed in a semi-parallel fashion.

This updating, or integration, has to occur with finite time steps, because otherwise the simulation is never finished. The systematic errors resulting from this can be maintained within acceptable limits by choosing a suitable method of integration.

There are various centralized integration methods. In simple languages, the integration is performed according to the point-slope method of Euler (new value of state = old value of state + time step × rate of change). Other languages use more sophisticated methods in which the size of the time step depends on the rate of change:

with fast changes the time steps are small and with slow changes the time steps are large, chosen in such a way that the error of integration is not unduly high.

Since the acceleration of a falling apple is constant ($g$ = 981 cm sec$^{-2}$), the velocity is the integral of the acceleration, and the fallen distance the integral of the velocity, the fall of the apple could be simulated in one of the simulation languages (CSMP 360) as follows.

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VELOC = INTGRL (0.,981.)
DIST = INTGRL (0., VELOC)
PRINT VELOC, DIST
TIMER FINTIM = 100. PRDEL = 10.
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The INTEGRAL statement for the VELOCity means that at time zero the velocity is zero, and that the rate of change is 981 cm sec$^{-2}$. The INTEGRAL statement for the DISTance fallen, states that this distance is zero at time 0. and that the rate of change is equal to the velocity. When these statements are read by the computer, its printer produces a list of the values of velocity and the distance fallen at intervals of 10 seconds up to a time of 100 seconds.

It is possible to program this simple system because the principles of the dynamics of a falling body, and the numerical value for the acceleration of a falling body at the earth's surface are known. The succesfull space flights of recent years have been made possible, because the flights can be accurately simulated in advance, but it cannot be stressed enough that this is only possible, because Newton and his successors provided the space-technicians which such a sound basis to start from.

### The strategy of model-building in biology

The biologist concerns himself with dynamic systems which are undoubtedly more complex than those of the technician. The question arises whether our knowledge of principles is sufficient to embark on the design and construction of simulation models. From the engineering point of view the answer to this question has to be in the negative; the biological principles which have to form the base of model-building are too fragmentary to embark on straightforward model-building along the same lines as in the physical sciences.

Instead of being fatalistic about it, this should stimulate us to formulate our own strategies of model-building, and I will use the rest of this lecture for such an attempt.

Foremost we have to realize that in biology various levels of knowledge may be distinguished which are characterized by the level of organization within the systems or by the relaxation times of phenomena, that is the time necessary for the recovery from small disturbances. For instance, the concentration of intermediates in the respiratory chain may be adapted within a minute to concentration changes of glucose, and relaxation times of hours have been observed for disturbances in the enzyme level. It may take a plant some days to adapt to a new temperature regime, a pasture with perennial ryegrass a few months to recover from frost damage, and a forest years to recover after a period of shifting cultivation.

Roughly speaking, the relaxation times of biological phenomena are a factor $10^7$

apart. The areas of biological specialization in this whole spectrum of relaxation times concern molecules, cell-structures, cells, tissues, organs, individuals, populations and communities. Hence, there are about 6 or 7 levels of knowledge, and this leads to the conclusion that a specialist has to restrict himself to phenomena with relaxation times that are only a factor of 10 to 100 apart to work fruitfully. That is, each fruitfully within its own domain; the flipside of the coin being that the communication between specialists of different levels of knowledge is inadequate.

Now I believe that the simulation in the biological sciences has to be used to fill the gap that exists between specialists at various 'levels' and that we may come to a strategy of model-building in biology when we keep this purpose in mind. To build a model we have to consider and to join two levels of knowledge. The level with the short relaxation times is then the level which provides the explanation or the explanatory level and the one with the long relaxation times, the level which is to be explained or the explainable level.

The knowledge of the phenomena and processes on the explanatory level are summarized in a model which behaviour is used to predict the phenomena and processes on the explainable level. Since the relaxation times at both levels are a factor 100 apart, it is possible to formulate the phenonema on the explanatory level in terms of rate equations, so that for the building of models it is possible to use the techniques developed in the physical sciences. For instance, in a model of the growth of plants and crops the measurements of the rates of photosynthesis, respiration, growth and development measured in plant physiology have to be used to simulate the behaviour of the whole plant or the crop in course of time, while the models on ion uptake by roots are based on rate measurements in physical chemistry and enzymology.

## Verification of models

All knowledge on the explanatory level is not of the same quality. To illustrate this, we consider the simulation of ion uptake by growing roots from soil. The equations that govern the diffusion and mass flow of ions in the soil and their mutual interaction are derived from physical and chemical principles. Hence, the knowledge necessary to simulate the concentrations at the root surface, as far as affected by the properties of the soil, may be so sufficiently detailed and trustworthy that verification of results of the model on the explainable level is not necessary. However, the equations that are used to describe how the rate of uptake of the ions by the root depend on the concentration at the root surface are derived from non-binding opinions regarding the physiological uptake mechanism of ions. This aspect of the model must therefore be verified by doing experiments with the model and the actual system, both, on the explainable level.

It will often be found that the results obtained with experimenting with the model and the actual system do not agree. In that case, the model may be adjusted such that a better agreement is obtained. Since there are many parameters and many equations involved this is not difficult. However, it is a disastrous way of working because the

model degenerates then from an explanatory model in a demonstrative model which cannot be used anymore for extrapolation, and the technique reduces into the most cumbersome and subjective technique of curve fitting that can be imagined.

The proper way of action when discrepancies between the operation of the model and the actual system are found, is to locate by means of experimenting with the model and further study, which parts of the model are of most doubtfull value. The principles of this part are then improved upon by a study on the explanatory level. Hence, instead of adjusting equations and parameters for ion uptake to fit the facts, the physiology of ion uptake should be studied again and opinions in this field should be revaluated. Alternate opinions on the explanatory level can then be introduced, and their consequences on the explainable level studied by experimenting with the model and the actual system.

The evaluation and verification of the phenomena on the explanatory level is restricted to the design and redesign phase of modelling, and during the use of the model the verification on the explainable level should have priority. A model on both levels not at variance with the observed phenomena, is acceptable.

This way of working at two levels of knowledge and of joining both by means of simulation models has to be developed by the biologist himself. He cannot borrow very much from the chemist and the physicist, because they are not much in need of this way of working, nor from the mathematician because no mathematical problems are involved. He will not get much help from sociologists and economists because in their disciplines levels of knowledge with different relaxation times are hardly developed as yet, although this may improve in future.

**Two- and multi-stage models**

A simulation model that joins two successive levels of knowledge may be called a one-stage model. These are in general of manageable size, and because the relaxation times of both levels are a factor of 100–1000 apart it is possible to advance in time with steps in the order of 1/1000 of the length of the simulated period. To be more specific, a model to simulate the growth of a crop in its vegetative stage is operated for a time span of about 50 days, so that time may be advanced in steps of 1/20 of a day. This means that every 1/20th of a day, the rates of photosynthesis, respiration, transpiration growth, etc., are calculated from the state of the crop, characterized by the amount of reserves, amount, area and architecture of the leaves, amount and activity of the rootsystem, etc., on one hand, and the external parameters characterized by radiation, temperature of the leaf and root zone, humidity, etc., on the other hand.

This may be done then on basis of relevant measurements under controlled conditions.

In two-stage models three levels of knowledge are linked, they are built in cascade and may be verified also at three levels. It would be possible, and probably advisable to base calculations of photosynthesis and respiration rates not only on measurements of these rates under controlled conditions, but also on biochemical knowledge of

these processes.

The amount of detail that is necessary for these two-stage models is large and because the relaxation times at both extreme levels are a factor 10,000 apart, it may be only possible to advance in time with steps of 1/10,000 of the total time span to be simulated or even smaller.

Hence, these two-stage models have already a tendency to outgrow present day computers and budgets. Practically, it is only possible to use a hierarchical approach, that is to incorporate more basic biochemical knowledge by building models of sections of the system and to introduce the outcome of these simulations into a one-stage model. Whether this is done by means of analytical equations, so called laws or multi-entry tables, is not a matter of principle, but of convenience.

Seven-stage simulation models by means of which eco-systems may be explained on basis of the molecular sciences are impossible large and detailed and it is naieve to pursue their construction. Likewise, it is naieve to pursue construction of simulation models which are supposed to simulate complex-eco-systems like forests as a whole.

Success in this field is only possible when we have the common sense to recognize that we know only bits and pieces of nature around us and restrict ourselves to quantitative and dynamic analyses of the simplest ecological systems that can be made or found in biology.