

## TECHNICAL PERSPECTIVE #3 SIGNAL TRANSDUCTION AND NON-LINEARITY

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In the sequence of events which may lead from field exposure to biological effects, the biophysical transduction process plays the crucial role. Actually, there must be two distinct steps to this process. First, there has to be a physical interaction mechanism in which the fields affect a chemical process. Then there must be an amplification of the effect by biological means. Because of the extremely low energies involved, we have to assume that the transduction involves non-equilibrium states and that the dynamics is non-linear.

Linear dynamics is ubiquitous in physics. Newton's equations, Maxwell's and Schroedinger's equations are all linear. They are immensely successful in describing reality, but they are essentially equations of forces in vacuum. As soon as things get more complex, in any qualitative phenomenon, such as the transition from laminar to turbulent flow, or in phase changes from gas to liquid to solid, non-linearity becomes crucial.

Even the classic many-body problem is inherently non-linear. For example, the solar system, apparently such a model of deterministic clockwork, is actually chaotic. Uncertainty of a mere kilometer in position grows to a distance equal to the radius of the earth's orbit in 100 million years. Going backwards in time, only half way through the Cretaceous, the relative position of the planets becomes unpredictable and, as a result, so is the occurrence of ice ages on earth.

Linear dynamics is incapable of describing qualitative changes. Whenever there are phase changes, whenever structure arises, non-linear dynamics is responsible. Biology is notoriously non-linear. The very fact that biological phenomena are successfully described in qualitative terms indicates this. If it were not for non-linearity, we would all be quivering jellies.

Because many of us have very little familiarity with non-linear equations, let us look at the most simple instance of such a dynamical relationship. We do this purely as an example, to gain some insight into the qualitative features which could be expected. There are no pretensions that this model describes any specific biological feature.

The linear difference equation

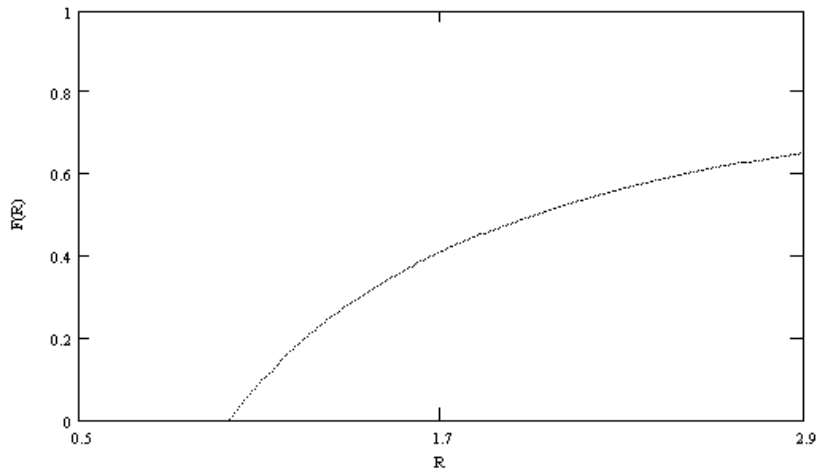
$$x_{n+1} = R * x_n$$

describes the exponential growth of a population of cells or the monthly increase of your bank account (with constant interest rate and no withdrawals, of course). But cell populations don't actually grow indefinitely. A more realistic equation, which takes into account the finite resources available is given by

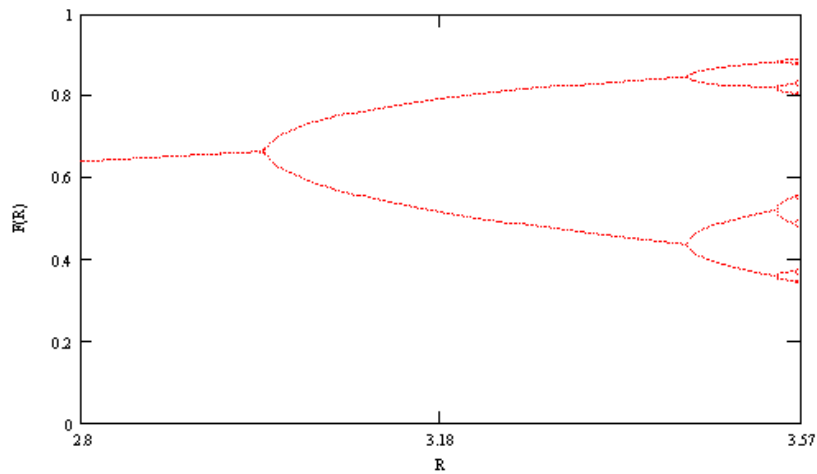
$$x_{n+1} = R * x_n * (1 - x_n)$$

This is a simple quadratic difference equation, which appears not too different from its linear counterpart. We observe that for R between 0 and 4 the value of x will stay finite, no matter how many iterations we make. Let's consider the limiting value of x as a 'function' of the parameter R, say F(R). We will see that F(R) shows an astonishing amount of structure.

To begin, the function F(R) is quite well behaved. Up until a threshold of R=0.5 it is equal to zero. After that it rises monotonically until R=3. This is a good classical function, quite similar, for example, to a dose-response function with a threshold value. In fact, an analytical expression can easily be given.

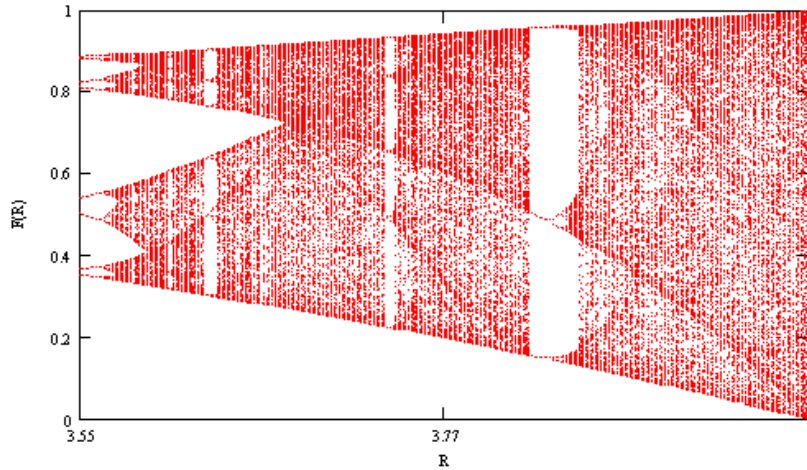


At R=3 something interesting happens: the function splits in two. Soon after it bifurcates again. And again, and again. Until it becomes a tangle of infinite ramifications. The simple function has become a fractal.

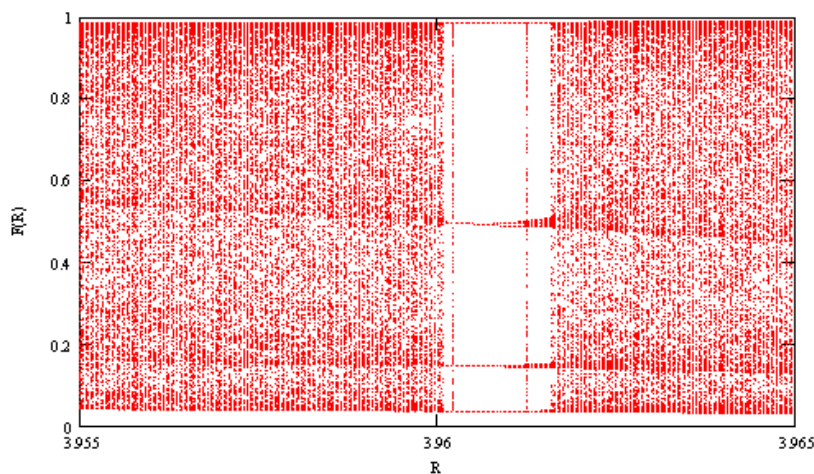


Many biological structures follow a fractal pattern: the branchings of a tree from a central trunk and the dendritic configuration of a root system, the sequence of bronchial ducts and the flow of blood through smaller and smaller arteries and capillaries.

But such multivariate functions also illustrate another biological feature: the existence of stable states. There are limit cycles, sometimes several of them, which draw dynamical variables to themselves regardless of initial conditions. These limit cycles thus represent states of homeostatic equilibrium. Linear dynamics is incapable of describing such intrinsically biological characteristics.



The fractal range of  $F(R)$  eventually culminates in yet another qualitatively distinct realm. Chaos breaks out. For larger values of  $R$  there is no defined solution  $F(R)$ . Instead, values fluctuate between given upper and lower limits in a way that appears random, though it is strictly deterministic. Unlike the linear case, however, initially small errors will grow indefinitely so that after a number of cycles the result becomes unpredictable.



The chaotic realm is by no means featureless. Throughout, there are windows where there are stable solutions with only a few values. Some of these windows are quite wide, but others are narrow and resonance-like.

We have considered the quadratic difference equation merely to gain insight into the qualitative characteristics of nonlinear dynamic relationships. We have found a range of features evocative of biologic systems. If such relationships lie at the heart of the interaction between fields and biological systems, and it is difficult to imagine that they are not, then it should not be surprising if we find dose-effect relationships that do not entirely conform to the linear preconceptions.