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RELAXATION MODEL OF ADAPTATION*

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We consider the general properties of the process of adaptation on the assumption that this phenomenon has a biochemical basis. The hypothesis is advanced on the significant difference between the course of adaptation in the isolated system and in a complex of systems where oscillatory kinetics may be advantageous.

INTRODUCTION

ADAPTATION processes are widespread in biology and are encountered at the most varied levels of organization. The concept of adaptation is very wide and it appears improbable that there is just a single mechanism underlying all adaptation phenomena. However, it is possible that purely biochemical processes form the essence of a fairly wide group of phenomena of physiological adaptation (if we mean by the word "physiological" comparatively mild changes in conditions. Among them we see a narrower group striking the imagination by the clarity of its kinetic pattern.

The normally operating system with a minor change (for example, change in temperature by 4–6°C) in the conditions "suddenly dies away" and for long "does not give

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any signs of life". The impatient observer may consider the system dead but after a certain time (sometimes fairly considerable) the system just as suddenly renews work and operates "as though nothing had happened".

The expressions in quotation marks appear at first sight to be superfluous "literature" and undefined. However, they are most readily subject to formalization by expressing the idea of the relaxation nature of adaptation.

1. FAST AND SLOW VARIABLES

The word "sudden" is in essence the emotional equivalent of the statement that the reaction time of the observer is considerably greater than the time of "operation" of the observed system. But "suddenly" the system only changes state and it can maintain it for so long that the observer sometimes loses patience. Consequently, a sharp difference in the time scale is an internal property of the system and not a subjective evaluation of it by the observer. In the mathematical model this means the presence of a small parameter in the system

$$\varepsilon \cdot d\mathbf{w}/dt = \mathbf{a}(\mathbf{w}, \varepsilon) \tag{1.1}$$

and (in the simplest case) the possibility of choice of variables which leads to the breakdown of the systems into fast and slow:

$$\varepsilon \cdot d\mathbf{u}/dt = \mathbf{f}(\mathbf{u}, \mathbf{v}, \varepsilon), \tag{1.2}$$

$$d\mathbf{v}/dt = \mathbf{g}(\mathbf{u}, \mathbf{v}, \varepsilon). \tag{1.3}$$

The kinetics of such a system is determined as is known, by the properties of the surface of quasi-steady states obtained with the formal boundary transition $\varepsilon \to 0$:

$$0 = \mathbf{f}_0(\mathbf{u}, \mathbf{v}), \tag{1.4}$$

$$d\mathbf{v}/dt = \mathbf{g}_0(\mathbf{u}, \mathbf{v}). \tag{1.5}$$

This system makes it possible to find the fast variables as a function of the slow variables:

$$\mathbf{u} = \varphi(\mathbf{v}) \tag{1.6}$$

and substituting the values $\mathbf{u}$ in the equations for $\mathbf{v}$:

$$d\mathbf{v}/dt = \mathbf{g}_0(\varphi(\mathbf{v}), \mathbf{v}), \tag{1.7}$$

we trace the evolution of the low variables.

All this completely contains the "methods" of quasi-steady concentrations [1]. However, even in the classical work of Tikhonov [2] the condition of closeness of actual behaviour of systems to the limiting one was found.

This is the condition of stability of the quasi-steady point of the fast system.

Verification of this condition is in principle very simple although it may present considerable technical difficulties. The algorythm of the verification consists in the calculation of the matrix of the derivatives at the point of quasi-equilibrium.

$$A = \partial\mathbf{f}/\partial\mathbf{u}\big|_{\mathbf{f}(\mathbf{u},\mathbf{v})=0}, \tag{1.8}$$

and the search for its inherent values

$$\det|A-\lambda E|=0. \tag{1.9}$$

If all these numbers have negative real parts:

$$p_i=\mathrm{Re}\lambda_i<0, \tag{1.10}$$

then the system (1.2) is stable and the movement of the actual system occurs in the ε-neighbourhood of the trajectories of the system (1.5) lying on the surface (1.4) of quasi-steady states.

However, the condition of Tikhonov (1.10) is far from always fulfilled. We shall consider on the surface of the quasi-equilibrium the points at which the quality is fulfilled

$$\det\left|\frac{\partial \mathbf{f}}{\partial \mathbf{u}}\right|=0. \tag{1.11}$$

These points, called the points of disruption, form the boundary separating the region of stability from the region of instability. A series of studies by L. S. Pontryagin [3] and his followers have been concerned with the behaviour of the system close to the point of disruption. The essence of the phenomenon, the details of which are at present of no interest to us, is that the trajectories "are disrupted" from the surface of quasi-equilibrium and the quasi-steady approximation becomes crudely untrue.

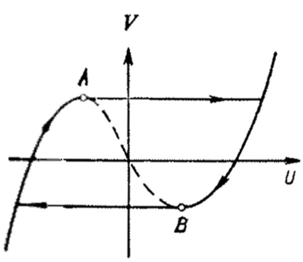

FIG. 1

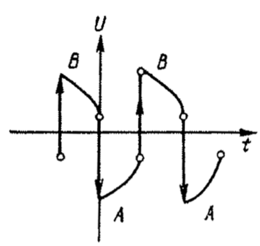

FIG. 2

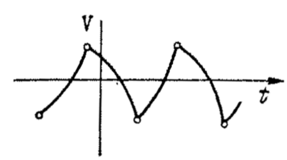

FIG. 3

FIG. 1. "Torn trajectory" of relaxation oscillations. Broken line isolates region of instability in the quasi-equilibrium curve. A and B—points of disruption.

FIG. 2. "Jumps" of fast variable from branch A to branch B and back.

FIG. 3. Breaks in experimental curve "denoting" existence of fast stage.

This can be clearly seen from the very simple example of the system of two equations arising from the van den Pol equation.

The qualitative pattern of the relaxation oscillations is completely determined by the presence of the region of instability on the surface of quasi-equilibrium and by the character of the slow movement (in the direction towards the point of disruption!) in the stable parts of this surface. (In the plane the point of disruption coincide with the boundaries of the zones of monotonicity of the quasi-equilibrium curve.)

It is very instructive to compare the behaviour of the fast and slow variables. The fast variables perform characteristic "jumps" from one state (branch A) to another (branch B) necessarily causing an association with sudden "movement" of the system after the last phase in adaptation.

The slow variables remain continuous but at the points corresponding to the ruptures of the fast variables in the graphs of the slow variables characteristics breaks form.

The relaxation oscillations are taken as an illustration not only because of their wide popularity but also because this is a very plausible scheme of the work of the adaptive mechanism in certain extreme conditions. However, more about this below.

2. OBSERVED AND HIDDEN PARAMETERS

The vital activity of the system studied is usually judged from a few clearly visible signs of the type of growth, or movement or the consumption of substrates. The depth processes are relatively inaccessible and experimental intervention (even with the modest aim of observation) often ends in death of the system. Even in *in vitro* experiments continuous recording is a difficult technical problem [4], and usually one-single value z is observed which is a fairly complex function of the concentrations (light absorption, redox potential, evolution of gases, etc.).

$$z = F(\mathbf{u}, \mathbf{v}), \tag{2.1}$$

and often depends in an unknown fashion on the concentrations.

If z is the observed value and the variables $\mathbf{u}$ and $\mathbf{v}$ are the hidden variables relating to the relaxation system then the graph of z usually has characteristic breaks typical of fast variables.

The breaks will be absent only in the exceptional case when the observed value depends only on the slow variables and does not depend at all on the fast ones.

However, there exists a wide class of methods of recording involving the accumulation of the reaction products. In these cases the observed value z is connected with the determining variables $\mathbf{u}$ and $\mathbf{v}$ by the differential equation

$$dz/dt = F(\mathbf{u}, \mathbf{v}, z), \tag{2.2}$$

which is a particular case of the equation for a slow variable. The only difference to that the variable z in our case does not come into the system (1.1) and may be found only after the main system has been integrated. In essence all this is a precise mathematical formulation of the hypothesis: measurements are made so meticulously that they do not introduce distortions not the course of the process.

Thus, the difference between the ruptures and breaks in the experimental curve characterizes not the property of the system but the method of recording. Typical of these classical methods of recording (for example, observation of growth) is less accuracy, the need for accumulation and consequently, breaks in the experimental curve, often perceived subjectively as "error" of the experiment with the resulting endeavour to "smooth" the curve. This explains the interest which the mathematician shows in low inertial methods of continuous recording isolating clearly, in jumps, the most interesting determining aspect of the phenomenon—its relaxation character.

3. RELAXATION MODEL. STATE OF ACTIVITY AND REST

A simple relaxation model of adaptation may be constructed with one fast variable which is also the single observed value z. The second variable y is slow. It is curious that even these minimum assumptions allow us to construct a quite meaningful model:

$$dy/dt=b(y,z,\varepsilon), \qquad \varepsilon\cdot dz/dt=c(y,z,\varepsilon). \tag{3.1}$$

All the subsequent analysis is based on two main premises. The first is that the phenomenon is only described by a mathematical model. The second is that the system has a working state and a state of rest which differ to the observer.

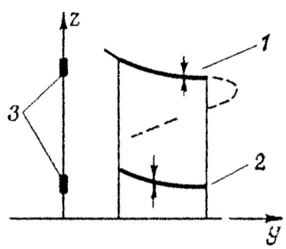

FIG. 4. Two branches of quasi-equilibrium curve: z—observed value; y—internal variable; 1—state of activity, 2—state of rest (shock), 3—experimental characterization of resting and activity state.

Since the single observed value is the variable z, then this means that the curve of quasi-equilibrium

$$c(y,z,\varepsilon)=0 \tag{3.2}$$

has at least two different roots

$$z_0=f(y,\varepsilon), \qquad z_1=g(y,\varepsilon), \tag{3.3}$$

one of which corresponds to rest and the other to the active regime.

(Change in the scale of measurements of z

$$z=(1-\zeta)f+\zeta g,$$

$$\zeta=(z-f)/(g-f)$$

leads the general case to the situation "yes—no" when the value $\xi=1$ corresponds to activity and $\xi=0$ to rest. Qualitative statements of the type "moves", "does not move" therefore may be considered a special case of normalizing of the observed value.)

Mathematically, this means that the curve $c(y,z,\varepsilon)=0$ in the plane (y,z) has at least two branches in a certain zone of change of the internal variable y.

The very possibility of observing the states of activity and rest denotes the stability of both these states in relation to fast movement. But, from this logically follows the existence of an intermediate state unstable in relation to the fast movement.

This intermediate state is difficult or even impossible to record since even a very small change in it rapidly (in the period of the order ε) throws over the system either to quasi-equilibrium of activity or to the quasi-equilibrium of rest. However, the role of this state is very important since it divides the plane (y, z) into the zone of extension of states of activity and the zone of extension of states of rest.

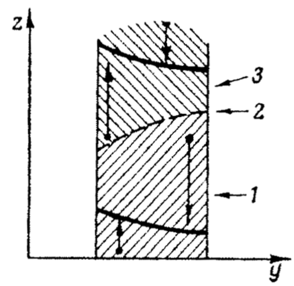

FIG. 5

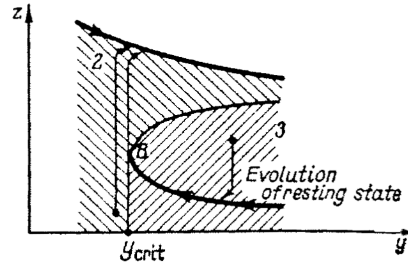

FIG. 6

FIG. 5. State of unstable quasi-equilibrium separating zone of activity from resting zone: *1*—resting zone, *2*—boundary—unstable quasi-equilibrium, *3*—zone of activity.

FIG. 6. Spontaneous renewal of activity: *1*—loss of stability of state, *2*—activity zone, *3*—resting zone; *4*—evolution of resting state.

The next step of the analysis is to take into account the evolution of the system in the "state" of rest. From experiments it is known that the system "present" at rest, may "spontaneously" renew activity. The simplest interpretation of this fact is that the judgement of the state of the system merely from the observed value is too crude. The internal unobserved (for the given methods of recording) variable in fact slowly shifts along the line of rest to the intersection with the separation line.

At this moment the state of rest loses stability in relation to the fast movement and the system in a short time comes into a state of activity. The point y_{crit} in Fig. 6 corresponds precisely to such a critical state in which the system does not have a resting state and may be stable only in the state of activity.

The hidden variable y undergoes at the moment of the jump insignificant changes. However, the rate of its movement

$$dy/dt = b(y, z, \varepsilon), \tag{3.4}$$

depending on the fast variable z changes significantly. The slow changes in y will of course, continue but the character of evolution in the state of activity usually differs from the state of rest. Mathematically, this is expressed in the fact that the equation for y in the resting state

$$dy/dt \approx b\big(y, f(y)\big), \tag{3.5}$$

generally speaking is quite dissimilar to the equation in the state of activity.

$$dy/dt \approx b\big(y, g(y)\big). \tag{3.6}$$

For example, change in the direction of movement y is quite probable.

The analysis so far made refers to the mechanism of return of the adaptive system to the state of activity. The maintenance of this state allows of still simpler interpretation.

If the set of equations has true positions of equilibrium, then they are situated on the curve of quasi-equilibrium since at the point of the true equilibrium both velocities go to zero:

$$\left.\begin{aligned} b(y,z,\varepsilon)&=0\\ c(y,z,\varepsilon)&=0\end{aligned}\right\} \tag{3.7}$$

both of the fast and slow movement. There may be several points of true equilibrium. They correspond to quite different regimes.

The stable point in the rest line corresponds to death of the system and the stable point in the line of activity to the stable vital activity of the system. Finally, the unstable points separate the portions of the quasi-steady line with different types of behaviour.

4. TYPES OF ACTION. EXAMPLE OF ADAPTIVE BEHAVIOUR

Further discussion is impossible without translating into the language of the model the most important experimental concept—the concept of action on the system. In the actual situation it may come about in the most varied ways: change in the temperature, mechanical damage, placing in heavy water, irradiation, etc. From the stand point of the model only one thing counts—during the action the description of the system by equations (3.1) is not suitable since the experimenter would have to be included in them.

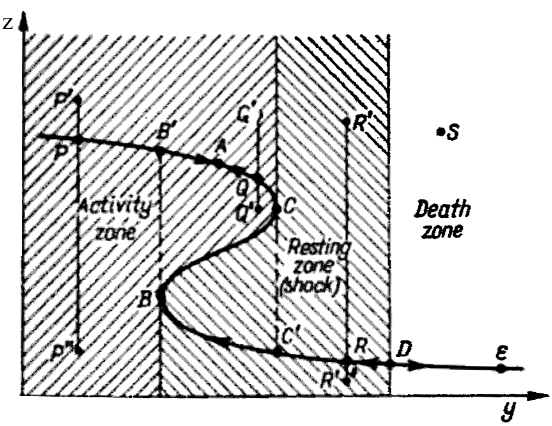

Fig. 7. Phasic portrait of adaptive system: *A*—point of stable activity; *D*—boundary of reversible changes.

The position changes when the action ceases and the system "is left to its own fate". At that moment the result of the action is that the system is in the non-equilibrium state. The further behaviour of the system and its adaptation are now determined only by the internal properties. Such a point of view, of course, means dispensing with analysis of the action (representing an independent task) and the concentration of attention on the mechanism of adaptation.

Mathematically this corresponds exactly to the task of Kosha (problem with initial data) for the system of equations (3.1). Therefore, hereafter by "action" we shall understand the transfer of the depicting point of the system to one of the points of its phasic plane. Moreover, we shall speak of the "action of P" meaning by this that the system is at point P as a result of a certain action.

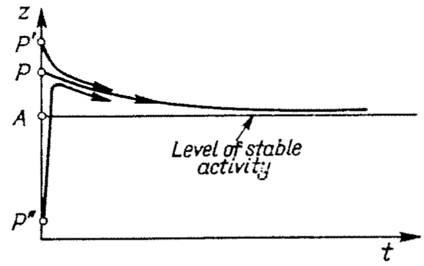

FIG. 8

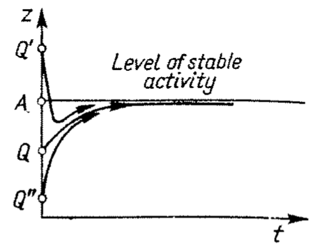

FIG. 9

FIG. 8. Maintenance of activity and passage to stable regime: agents P, P' and P''.

FIG. 9. Another possible type of passage to stable regime: agents Q, Q' and Q''.

The classification of the actions is from this point of view tantamount to the classification of the types of behaviour of the integral curves of the system, which corresponds to the division of the phasic plane of the system into regions of uniform behaviour. In the example illustrated in Fig. 7 there are three such regions: zones of activity,

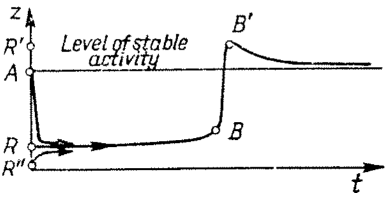

FIG. 10

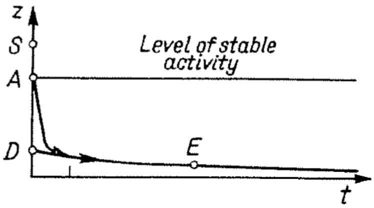

FIG. 11

FIG. 10. Lag-phase RB and evolution along the line $B'A$.

FIG. 11. Irreversible changes as a result of action of S: death of system.

rest and death of the system. We present some typical forms of behaviour during the observed value z on exposure to actions of various types. In all cases we observe a characteristic fast transitional process corresponding to the passage to the state of quasi equilibrium. The symbols in Fig. 8–11 correspond to the symbols in Fig. 7.

5. STABILITY AND ADAPTIVITY

The analysis made shows that the reaction of the system to external factors must be characterized by two different indices—stability and adaptivity.

The stability of the system is greater the farther is the point A from the "dangerous" point of disruption C. In this case considerable influences are necessary to "knock out" the system from the state of activity (Fig. 12).

Otherwise, adaptive systems "tolerate" strong influences. At first they "fall into a trance" but "rallying" restore the state of activity. The store of adaptivity is greater the greater the arc *BD* (Fig. 13).

It is instructive to compare the extreme situations—stability without adaptivity and adaptivity without stability.

The stable system without adaptivity (point *D* merged with point *B*) may tolerate strong influences retaining activity. However, any influence leading to shock is tanta-

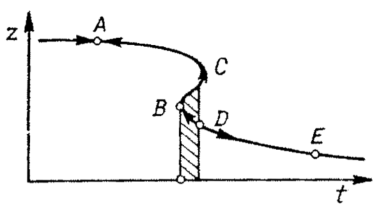

FIG. 12

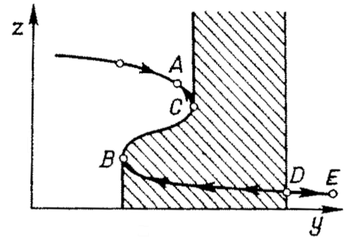

FIG. 13

FIG. 12. Stable but little adaptive system.

FIG. 13. Adaptive system with low stability store.

mount to the death of the system, since during evolution along the line *DE* irreversible changes develop in the system and it sometimes no longer returns to the state of activity.

On the other hand, a well-adaptive system without stability (point *A* on the arc *BC*) retains the ability to come out of the shock state. It however loses the ability to retain activity and periodically (an oscillatory regime develops wich in no wise differs from the relaxation oscillations depicted in Fig. 1) goes into shock spontaneously without external influence but all the same, the system does not die.

Consequently, stability and adaptivity are essentially different pathways of stabilization of the systems.

Stable systems operate more and more productively. They correspond well to favourable conditions but rapidly die in unfavourable conditions.

Adaptive systems operate worse and often "die out" but are capable of working in difficult conditions.

6. EVOLUTIONARY SIGNIFICANCE OF ADAPTIVE OSCILLATIONS

Until now, the term "evolution" has been used in the narrow technical sense—slow movements in the system (3.1).

A wider interpretation of this term—even slower change in the form of the right hand sides (in particular, of the coefficients) of the system of equations—corresponds better to the meaning which biologists impart to this word.

With such an interpretation one may raise the question of interaction of the system with the medium considering the system and the medium as parts of a wider system.

It is plausible that with such a posing of the problem one may demonstrate the gradual development of activity in poorly adaptive systems placed in an unfavourable (but not) destructive) medium.

On the other hand, adaptive systems in a favourable medium will increase in stability and working capacity, of course, through fall in adaptivity.

The expectation of the validity of such statements is all the more justified since a similar problem in discrete interpretation (games of automata) was raised by Tsetlin [5] and similar statements demonstrated.

We shall now consider a more general scheme taking into account the spatial inhomogeneity of the medium.

We shall assume that in a certain direction the conditions worsen and a boundary exists beyond which the conditions become fatal for the existing "colony" of systems, In such a situation an "adaptivity" gradient will gradually appear in the colony. Closer to the boundary the systems will become ever more adaptive "paying for this" with their stability. The new more adaptive systems can penetrate beyond the old boundary. This expansion will be arrested only by the exhaustion of the "store" of stability. At the new boundary, only systems adaptive without stability can exist. But we already know that in this case the system will inevitably become auto-oscillatory.

This circumstance produces a quite new situation for the colony as a whole. For the individual system (cell) auto-oscillations are an indication of extremely unfavourable conditions but for the colony as a whole they may be on organizing factor. In particular, the nearest neighours with their negligibly small stability store will be drawn into auto-oscillations. In such conditions resonance formations [6] of supracellular level are possible.

It is very tempting to compare the auto-oscillatory pattern formed with the spontaneous electrical activity of the nerve cell. Of course, the comparison must be literate in evolutionary terms. Comparison may be made either with objects standing at the boundary of the cell and multi-cellular organism or with the stage of embryogenesis at which the laying down of the nerve cells occurs. Comparison with evolutionary mature nerve cells where the original "distress" is morphologically fixed and has received the sense of a signal will hardly be productive.

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