A CONTROLLED CHAOTIC ATTRACTOR CONTROLS LIFE

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DANCING TO WHICH TUNE?

In answer to the question *What is controlling life?* a growing bulk of evidence reveals that it is not any part of those systems that regulate the generation of energy. In order to discern the kinetic relationships between energy production and consumption it is necessary to work either with single cells or with populations that are synchronously growing and dividing to avoid the time-averaging inherent in non-synchronous ensembles. Only when this is done can the temporal order of metabolism be dissected [1].

In experiments with a diversity of lower eukaryotes (yeasts and protozoa) we measured the O_2 consumption during the growth and division of organisms in synchronous cultures. During each division cycle, biomass doubles, as does respiratory rate. But the increase is discontinuous; large amplitude oscillations are observed. Experiments with uncouplers of conservation indicate that as the organisms grow, they cycle between energized and de-energized status (3-4) [2]. Thus energy generation is periodic; further experiments show that the period of the oscillation differs from one organism to another; in yeast (*Candida utilis*) it is 30 min [3], whereas in *Acanthamoeba castellanii* it is 69 min at 30 ^{o}C [4]. Where we have studied the temperature-dependence of the oscillations we have always found their periods to be temperature-compensated [5] with Q_{10} values not much greater than unity [6]. We asked the question what is controlling these oscillations? Both the characteristic (slow) time constants (order of hours), and the phase relationships between respiration and adenine nucleotide pools (ADP and J_{O_2} are in phase), indicate that ADP derived from biosynthetic reactions (especially the processes of protein and RNA synthesis) limits respiratory rates. Frequent and careful measurement of accumulating total cellular protein and RNA again reveals oscillatory expression (periodic turnover) [7]. Thus we have concluded that in organisms growing at near-maximum rates, mitochondrial dynamics is governed by the inherently more ponderous needs of biosynthetic functions with their long slow feed back loops [8,9]. It may thus come as a disappointment to bioenergeticists that their favorite organelles dance to a slow tune, whilst the piper plays the music elsewhere.

THE ULTRADIAN CLOCK

Temperature compensation of period is indicative of a clock; we have called this intracellular clock the *Ultradian Clock* [10], by analogy with the Circadian Clock which functions to synchronize the organism with its environment [11,12].

The mechanism of this rhythm (*i.e.* self-sustained endogenous oscillation) which provides internal time-sense like that of the circadian clock is not elucidated. This is a tough problem; for the 24 h clock all the powerful armory of molecular biology and the availability (for a quarter of a century) of clock mutants has not definitely pinpointed any of the gears of the mechanism or the putative

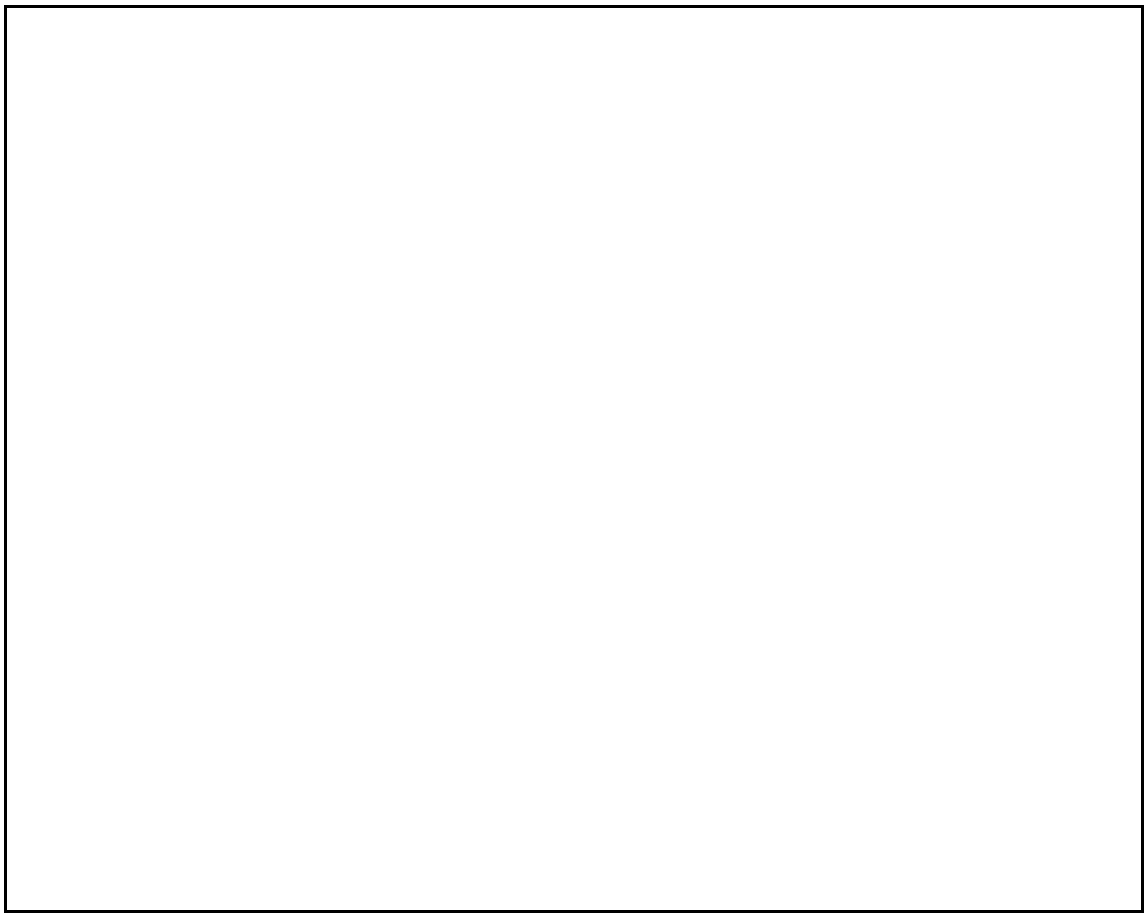

Fig. 1. Modification or disruption of control circuitry (by genetic or environmental means or by surgery) leads to ultradian or aperiodic (chaotic?) performance.

central oscillator, although recent experiments appear to approach the heart of the matter [13,14]. Current models incorporate post-transcriptional delays in an autoregulated feedback loop where the clock gene (e.g. *per* in *Drosophila melanogaster*) is modulated cyclicly; thus the *per* mRNA is modulated by its own translation product, which also cycles with a 24 h period. We have suggested [15] that this minimal limit-cycle model is sufficient but not adequate to explain the rich dynamic behavior observed in mutant flies. More than two variables can lead to quasi-periodic or chaotic dynamics. A recent simple model of the circadian system [16] shows chaotic dynamics. In most situations, chaos is regarded as a nuisance, since the onset of chaotic operation sets a limit to the range of useful operation. Why then have some living systems incorporated chaotic functions? Explanations have invoked unpredictability as advantageous in the search for novelty in form and function.

WHAT IS THE USE OF CHAOS?

An answer to the question *What is the use of chaos?* became much easier for non-living systems when Ott and co-workers [17] pointed out that exploitation of chaos becomes possible when it can be controlled; it would be most surprising if the advantages of controlled chaos had not been made available to the evolving organism [18]. These benefits are not inconsiderable; instead of a fixed period limit

cycle, the controlled attractor provides a single multi-oscillator capable of tuneable outputs of variable frequencies. Such a system can rapidly be switched from one state to another, thereby providing multiple use of a single configuration. It can be shown that a controlled chaotic oscillator can quickly and easily be tuned to optimal system performance, and is robust to external noise. Controlled chaos can lead to system diversity and to the development of complexity.

Several methods for the control of chaos are now recognized in physical systems [19]: none of these require novel control elements in terms of previously recognized principles of metabolic control (feedback inhibition, feed-forward activation and time delay). The continuous control of chaos by self-controlling feedback, developed in numerical simulations [20] for electronic circuitry (Tamasevicius A., personal communication), provides an excellent example of the simplicity and applicability of these principles to metabolic circuitry. We conjecture that normal operation of the chaotic attractor in its optimized controlled state provides the stabilized periodic orbit of the central circadian pacemaker and it is the outputs of this central oscillator that drive both ultradian and circadian rhythms (Fig. 1). Removal of control leads to aperiodic or arrhythmic operation. Less drastic interference (*e.g.* in *Drosophila* in the presence of D O or in other *per* mutants) may give arrhythmic, quasiperiodic or short period (ultradian) periodicity [21]. Switching from circadian to ultradian operation has been reported for lower eukaryotes as well as for humans [22].

The hypothesis that a controlled chaotic attractor may provide the central oscillator responsible for the generation of circadian and ultradian rhythms and hence of life itself (homeodynamics [23]) may be tested by seeking chaotic dynamics in those systems where controls have been disrupted.

Biological oscillations are an expression of information processing which requires both fluidity for signal processing as well as stability for information storage [24]. In higher-order, complex, self-adaptive systems the dynamics of information processing has gained control over the dynamics of energy transformations [25].

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