MEASURING A MITOTIC OSCILLATOR:
The ARC DISCONTINUITY*

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Mitosis occurs synchronously in up to $10^8$ nuclei in the syncytial plasmodium of *Physarum polycephalum*. Any two phases of the mitotic cycle may be mixed by fusing plasmodial pairs. A topological property of the synchronized phase of the fused pair as a function of parental phases, the arc discontinuity, characterizes the underlying oscillator, and indicates mitosis is controlled by a moderate relaxation oscillator which rotates more rapidly near its singularity than its limit cycle. A model oscillator is briefly described.

Mitosis is an event of short duration relative to the cell cycle. In no organism is the system controlling its regular periodicity known. If the “clock” which controls its timing is a continuous biochemical oscillator, we need to characterize its wave form both as an aid to discovery of the true control periodic processes from among many candidate periodic processes, and because the dynamic properties of the oscillator should be determinants of cell behaviors.

Students of circadian rhythms have long recognized that permanent phase resetting of a clock after experimental intervention is likely to reflect properties of the controlling oscillation itself rather than variables driven by the oscillator.

There are two broad types of macroscopic tools to examine phase resetting behavior; “external” perturbations such as light flashes, temperature shocks,

etc.; and “internal” perturbations obtained by fusion or mixing of two phases of the control oscillator itself.

Winfree (1972) has made elegant use of the former tool, which can yield a plot in the space of stimulus duration versus the phase perturbed, of all points having identical ultimate phase. Winfree calls such a set of points an isochron. Isochron structure in that space gives some insight into the wave form of the control processes.

I wish to consider a technique I call the arc discontinuity, which can be utilized whenever it is possible to mix, or couple two oscillators and obtain phase synchronization. This is experimentally possible in yeast suspensions undergoing glycolytic oscillations (Ghosh et al., 1971). Two aliquots of yeast in two phases can be mixed. After transients, they synchronize. In the myxomycete *Physarum polycephalum*, up to $10^8$ nuclei in a single syncytial cytoplasm undergo mitosis synchronously (Rusch et al., 1966). Two syncytial plasmodia at any two phases of the mitotic cycle can be fused; nuclei and cytoplasm mix and subsequently synchronize (ibid).

A property of both Physarum and the yeast glycolytic oscillator is that if any two neighboring phases are mixed, the fused pair ultimately synchronizes to a phase between the two neighboring parental phases on the shorter arc connecting them. This is strong presumptive evidence for an underlying continuous oscillator. Consider an arbitrary continuous chemical limit cycle in a state space $X$ and $Y$, rotating around a steady state $S$, with phase defined around the cycle, Figure 1(a). After Winfree (1972), I define the phase of states not on the cycle by the state on the cycle with which they ultimately synchronize. The $J$th isochron is then the locus of points which ultimately synchronize with a copy of the oscillator released at phase $J$. If rotation velocity is independent of amplitude away from $S$, isochrons are straight radial lines emanating from $S$ and crossing the limit cycle.

Consider any three neighboring phases on the cycle in the order $B$, $A$, $C$, in Figure 1(b). Mixing or fusion of $A$ and $B$ will, roughly, cause the representative points to move toward one another along the chord connecting them by mixing $X$ and $Y$ concentrations, until they synchronize and wind out to the limit cycle. The phase of the $AB$ mix will lie on the short arc between $A$ and $B$ which does not include $C$. The $AC$ mix will synchronize to a phase on the short arc which does not include $B$. While typical of continuous oscillators, synchronization to the shorter arc between two neighboring phases need not occur for all possible phases in discontinuous oscillators.

Let a sequence of experiments be performed holding the phases of $A$ and $C$ fixed, but moving $B$ successively around the phase circle away from $A$ and toward $C$. For each experiment, assess whether the phase of the $AB$ mix falls