Introduction

In the present note a crude first sketch will be attempted of a Gibbs-ensemble view of large, open biochemical networks. The network finally in issue is of course the one in nature that is the interior of the living organism, a great cauldron of $10^5$ or $10^6$ or more chemical species in a continual state of intra-action and of interchange with the exterior. It is not the regime of some $10^{16}$ interacting atoms per cell over which ensembles are to be built, but just this lower-order regime of $10^6$ chemical species whose concentrations are the dynamical variables in coupled motion under those strong differential laws called chemical kinetics. The reason is that the $10^6$ "chemical coordinates" in the "chemical dynamics" here stand within effective observational reach while embracing at once the central biochemical phenomena, like enzyme catalysis. The aim is to move on down still further from the $10^6$ reduced coordinates to some few ensemble moduli toward global oversight of biological process. The ensemble, as merely methodological tool for scanning differential systems, seems worth trying at the still certainly complex reduced level of chemical dynamics.

Suppose we look with purely chemical eye into the cellular interior, assaying steadily over a very long time the concentration (or total number of molecules) of some selected few of the numerous biochemical types. The assay will be a kind of noise that must be expected to show on the one hand short-term and probably somewhat erratic fluctuations, and on the other hand longer-term near-periodicities corresponding to cell splitting. In this myopic chemical view, however, the stunning morphology of the splitting does not enter explicitly; only the single-cell chemical interior on through one (any one) long linear chain of the morphological descendants comes under observation; it is just the single cell-in-continuo, as one entity pulsating in time over very many morphological cell-lifetimes, that is under analysis.

Now granting the uniformity of the exterior, it is clear that the long-time interior biochemical assay of the single cell-in-continuo also will have a certain uniformity, viz., the ups and downs of concentration present something like a stationary record in the curve of concentration-vs-time: two long strips of the curve are substantially the same in their mean characteristics, and it cannot be told which strip preceded which — as for any stationary process, you cannot tell what time it is, the process being time-translationally invariant in the mean. The stationarity is of course the
feature that hints to a possible ensemble approach. By contrast with the cell-in-continuo, the closed chemical complex may show some swings in concentrations, but as the system inevitably glides to equilibrium the non-stationarity becomes grossly evident, there is no question at all in distinguishing the remote future behavior from the remote past.

There are of course in this picture serious counter-indications to an ensemble attempt. At any level of observation, including the above micro-chemical one, the near-periodicity associated to cell division is going to have to show through significantly. This appears to be very anergodic, very contrary, seemingly, to the whole idea of getting at time averages through ensemble averages. The cell-in-continuo does make biochemical noise, but also, on a grosser time-scale, does run with reasonable regularity, a noisy clock that rings the hours moderately well though ticking the seconds poorly. Plainly at least two quite different time scales have to enter the theoretical description (or, ensemble-wise, at least two ensemble moduli will be needed), with the long scale appropriately sharp while still allowing an estimate for its experimentally significant unsharpness. Out of respect for the strength of known chemical laws, it will not do to fabricate ad hoc "biochemical oscillators" here; the issue is, rather, to test whether open chemical kinetics as a cogent theory of time-evolution of chemical populations in non-equilibrium is itself equal to the task of portraying the cell-in-continuo.

Open kinetics

Let us write down the laws of mass-action controlling chemical concentrations $z_1, z_2, \ldots, z_n$ under rules for reactions of the most primitive but universal types, and augment them with terms allowing material influxes and outfluxes in the simplest reasonable way:

\[ \dot{z}_i = e_i - \sigma_i z_i + k_{ia} z_a + K_{ab}^1 z_a z_b = Z_i(z). \]  

[summation on repeated Greek indices understood]

The first term $e_i$ permits growth of species $i$ due to influx from the exterior; owing to an assumed constant exterior, the input rate $e_i$ is itself properly taken as constant. The second term describes outward transport of $i$ to the exterior at a rate naturally proportional to the interior concentration $z_i$. The third and fourth terms are the conventional mass-action laws for the fundamental reaction types: $k_{ij} z_i$ ($k_{ij} \leq 0$) tells of $i$-decrease owing to all possible types of chemical decay, for instance all the decompositions $i \rightarrow a + b$ and isomerizations $i \rightarrow i'$; while $k_{ij} z_i$ ($k_{ij} \geq 0$) describes $i$-increase due to the like of $j \rightarrow i + a$ (including isomerization $j \rightarrow i$). Similarly, terms like $K_{ab}^1 z_a z_b$ ($K_{ab}^1 \geq 0$) describe $i$-increase from $a + b \rightarrow i$, and $K_{ia}^1 z_a z_i$ ($K_{ia}^1 \leq 0$) $i$-decrease from, typically, $i + a \rightarrow j$. None other than these elementary conventional steps in $k, K$ need be considered, as anything more complicated can be built up from them through introduction of suitable chemical complexes, intermediates, excited states and the like, albeit at the expense of greater chemical speciation: the quadratic non-linearity in the differential laws seems as high as it is ever necessary to go, and it expresses anyway that it is binary collisions that can be taken as fundamental. The universal format seems easily worth any extra speciation.

The principal "bio" component of the kinetics is deposited in the transport terms $e_i - \sigma_i z_i$. If we strike these out, the remainder in $k, K$ is ordinary closed-system kinetics where any starting configuration $z(0)$ in $z$-space ends up at some static equilibrium endpoint $z(\infty)$. Are the simple transport terms equal to preventing such stasis? The answer seems to be Yes: it has been shown by Chance and by Higgins [1] by computer that the simple transport terms, in modest networks,