Scientific theories, like many other things, have a lifetime. It is important to discard them when they are no longer useful, no matter how important they have been in history.

The ‘law of mass action’ is like that. The law of mass action defines a chemical reaction in the minds of most students of chemistry. They learn the law so young in their careers that they usually forget the crucial question. Are the constants of the law constant? If not, why do the constants vary?

In fact, the rate constants of the law of mass action are hardly ever constants when measured over a range of experimental conditions, specifically, as the concentration of other species in the system (not reactants and products) are changed, even as the concentration the reactants are changed.

In fact, if the reactants are ions in water, as are nearly all chemical reactions in biology, and a large number in classical chemistry, the rate constants can hardly ever be constant. The free energy of reactants is changed when background ions (that are not reactants or products) are changed because the screening of the reactants is changed. The ionic atmosphere changes the effective concentration in all ionic solutions. In simple solutions like dilute NaCl (less than 50 mM, for example) Debye-Hückel theory describes the ionic atmosphere. In the mixtures of ions in seawater or in the solutions inside and outside biological cells, divalents and interactions are beyond what Debye-Hückel can describe.

These effects are not small in the special conditions in which most chemical reactions occur. Biochemical reactions occur mostly in enzymes where the density of ionizable side chains is very large indeed (more than 10 M) because of the abundance of acid and base amino acids in enzyme active sites. In these conditions, reactants and products, and ions, are very crowded and nothing like ideal. Rate constants must then vary because the free energies of reactants then depend on every species present. Everything interacts with everything else and rate constants vary importantly with almost everything.

These ideas have been developed (and refereed) elsewhere and are in fact not new at all. Physical chemists have known that rate constants are not constants ‘forever’. What is not so well known are the consequences and possible remedies for this dysfunction of the law of mass action.

If the rate constants of a chemical reaction vary with conditions, the energies driving that reaction also vary, almost by definition. If we do not understand how the energies of a chemical reaction vary with conditions, or why they vary, we cannot use those energies to control the reaction. At least, we cannot use those energies in a planned and calculated way. We can only learn to control by trial and error.

Not all of science of science is like that. Not all of science depends so strongly on trial and error. The laws of some sciences are valid with little or no adjustment of parameters. We can argue that the fantastic development of semiconductor technology is possible only because the PNP (i.e., drift diffusion) equations do a good job of describing the properties of transistors, whether they are working as amplifiers, limiters, switches, exponentiators, or multipliers. We know that modern airplanes are possible because computational fluid dynamics can integrate the Navier-Stokes equations to predict incredibly complex flows and forces.

In my view, chemical and biochemical devices would be far easier to design and use if the law of mass action were replaced with something that actually works.

The replacement would need to involve location explicitly. Devices always have inputs and outputs so their descriptions must have different boundary conditions at different locations. The replacement would need to deal with flows. Devices usually need power supplies. Devices usually involve flow. In biology in particular flows are an essential feature of the living. Flows cease, and thermodynamic equilibrium occurs only at death. And the replacement of the law of mass action must deal with interactions in crowded conditions in which everything interacts with everything else, because these special conditions are so important in devices. Our electrochemical technology have enormous densities of reactants where they are important near electrodes; enzymes, ion channels, and nucleic acids have enormous number densities of ions near and in their ‘active sites.’

The law of mass action has not been replaced up to now, in my view, because a suitable replacement was not available. A promising candidate is now at hand, and its promise needs to be tested by extensive application, throughout the world where the law of mass action has been used, throughout the world where its constants had to be variables.

The replacement was developed to deal with complex problems of fluid mechanics extending classical variational principles of mechanics to systems with dissipation. Despite heroic efforts, Onsager and followers did not succeed in this attempt. But now it is possible to derive Navier Stokes equations from an energetic variational approach EnVarA that combines Hamiltonians with the dissipation functions of Rayleigh. The derivations are a matter of mathematics, and existence and uniqueness theorems exist, as well as many numerical results.

What is not mathematics are the energies and dissipations treated by EnVarA. These are a matter of physics, chemistry, and biology. The law of mass action needs to be replaced by a description of chemical reactions and the ionic solutions energies and dissipations accurate enough to allow design of devices.

I certainly do not know how to do that in general. But in a few special cases, we have been able to treat classical problems with a variational approach and convert dysfunctional equilibrium theories (that always used variable constants to describe (un)constant fields) with useful theories allowing flow and interactions.

I write to suggest that a similar approach might be useful far more generally. I write to suggest that the law of mass action needs to be repealed and replaced with an energetic variational approach able to deal with location, boundary conditions, and flows in a mathematically consistent and defined way.