Cronin, L., and Walker, S. I. (2016) Beyond prebiotic chemistry. *Science*, 352(6290), pp. 1174-1175.

Beyond prebiotic chemistry

What dynamic network properties allow the emergence of life?

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How can matter transition from the non-living to the living state? The answer is essential for understanding the origins of life on Earth and for identifying promising targets in the search for life on other planets. Most studies have focused on the likely chemistry of RNA (1), protein (2), lipid, or metabolic "worlds" (3) and autocatalytic sets (4), including attempts to make life in the lab. But these efforts may be too narrowly focused on the biochemistry of life as we know it today. A radical re-think is necessary—one that goes beyond investigations into plausible chemical scenarios to explore not just new chemistries, but also new physical processes and driving forces. Such investigations could lead to a physical understanding not only of the origin of life but also of life itself, as well as to new tools for designing artificial biology.

A transition from the limited function and memory possible in a soup of weakly interacting molecules to more strongly interacting networks was essential for the emergence of life on Earth. Left unattended, chemistry becomes more dilute and disordered. A route to complexity and enrichment that could lead to the development of evolvable units seems to be required quickly to avoid this serious issue. Yet, most research efforts have focused on detailing precise chemical mechanisms for producing high yields of individual bio-inspired products, without addressing the processes necessary to form increasingly complex molecules and networks.

What happens to our traditional perspectives if we do not restrict attention to the chemical substrates of known life? The development of networks over time may be more important than the specific chemical nature of their molecular components. Even RNA can form cooperative networks, diversifying its potential role in the earliest evolving chemistries (*7*). Autocatalytic networks can evolve in the absence of genes (*4*), but much more work needs to be done to understand the messier heredity of chemical systems. The first networks would have had to be simple, challenging the notion that highly complex and improbable molecules are needed to jump-start life. The molecular constituents of simple networks are more likely to arise by chance than the highly evolved molecules of extant life. Starting from networks composed of simple molecules could therefore dramatically reduce the time necessary for the emergence of life, and potentially increase the probability of an origins event,

A concept of information relevant to biological organization may be essential to identifying these networked processes. Adami and LaBar have described life at a basic level as "information that copies itself" (*8*). Given that life not only copies information but also uses information to construct itself, we might instead describe the start of life as "simple machines that can construct slightly more complicated machines." Focusing on information moves the narrative even further away from a chemistry-specific model than focusing on networks alone, but may perhaps provide our best shot at uncovering universal "laws of life" that work not just for biology of known chemistry, but also for putative artificial and alien life. For example, information-theoretic measures have recently been shown to distinguish biological networks from random, even in cases where the biological networks share important network properties with random networks, such as common topological features (*9*). Life requires chemistry, but it is the dynamical properties of that chemistry—including both the temporal and spatial organization of molecular networks and their information management—from which the properties of the living state emerge.

Another way to reconceptualize the problem is to consider life's emergence as a phase transition in the origin of the biosphere as a whole. This phase transition manifests as a sudden change in the way that chemistry is able to process and use information and to utilize free energy. It requires new approaches to understanding how the organization of energy flows can lead to the emergence of increasingly complex networks over time (*6*). Heterogeneity in the early Earth environment played a very important role in facilitating the emergence of life by helping to sustain, select, and drive the emergence of organized systems that could persist over time. For example, pores in rocks may have influenced chemical selection, leading to increasingly life-like chemistries over time (*10*).

One important order parameter in characterizing life's origin as a phase transition is the homochirality. Jafarpour *et al.* have shown that homochirality emerges spontaneously as a symmetry-breaking process in models of noisy autocatalytic systems, a result that could be experimentally tested *(5)*. Insights may also come from studying other transitions in the biosphere where organization has emerged from messy dynamical systems, including the origins of social systems *(11)*. Such comparisons could yield insights into universal properties of dynamic networks.

However, speculation should be restricted to the development of experimentally testable hypotheses that address key questions and provide a focus for progress. First, how did evolution begin if the machinery for evolution was not in place? Experimental studies addressing this question could evaluate the evolvability and robustness in molecular networks or systems with a lower molecular complexity than a full-blown ribosome. Second, can the emergence of life be substrate-independent? Answers may come from investigation of evolvable chemical pathways in the laboratory that are based on alternative polymers. This includes demonstrating how *function* can be transferred between molecules with different chemical make-up while preserving the overall network structure. Third, at what point in the historical origins of life did the current chemistry of life get selected? Could more than one version of biology exist on Earth today or in the past? This could in principle be tested in one-pot experiments that include *in-vitro* competition between alternative chemical scenarios for early life.

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In more abstract terms, it remains unclear whether life's origin, evolution, and understanding the living state will be understood within a common conceptual paradigm, or will be shown to involve different processes (*12*, *13*). Here, practical issues become important in connecting these areas. For example, how complex must a chemical signature need to be before it can be considered a biosignature? Looking for complex objects that could not form randomly in an environment, but arise only as a result of life-like machinery, might help in classifying potential biosignatures and the processes that generate them. Earth's complex inorganic and organic worlds are certainly highly connected in this respect, with even Earth's mineral diversity in part dictated by life (*14*).

Progress will be made by challenging all historical prerequisites assumed to be important in the origin of life. We should be considering measurable routes to developing new physics and chemistry to understand life's origins and the living state. Not only is a new understanding of what it means for a physical system to be 'alive' possible, but a new multinational project to search for new life on Earth *(15)*, generate new life in the lab or *in silico*, and to explore the potential for new life on other worlds *(16)*, can potentially be connected in deep and novel ways. What is needed is for researchers to challenge our own dogmas and intrinsic bias, and be willing to work across boundaries to construct a new model for the living state,, inspiring an era of 'big science' focused on origins and the development of new life forms resulting from theory-driven experiments.

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Acknowledgements: This perspective was inspired in part by a workshop held at the Carnegie Institution for Science in Washington DC, Nov. 9th – 15th 2015 and we thank the contributors to this conference.