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Introduction: Without presupposing any particular molecular framework, the newly formed Laboratory for Agnostic Biosignatures (LAB) team is pursuing approaches to life detection that could help us identify unknowable, unfamiliar features and chemistries that may represent processes of life as-yet unrecognized.

Chemical Complexity: There are multiple ways to utilize high heritage instrumentation in more agnostic ways. For example, flight capable mass spectrometers have long been flown on spacecraft, designed to search primarily for patterns among the molecular weights of carbon-bearing organic molecules. However, mass spectrometers can also be configured to search for chemical complexity of any type of molecule (organic or inorganic) that would be unlikely or impossible to form spontaneously. Without making assumptions about the chemical structures of the molecules, recent work suggests there may be a threshold beyond which complex molecules are unlikely to form without supporting biological machinery [1].

Mass Spectra Agnostic Identification of Complexity (MAGIC): Methods used to characterize potential biosignatures of life on another planet involve mass spectrometers due to their high detection sensitivity and diagnostic fragmentation patterns associated with the analysis of known organic compounds. However, elucidating chemical structures from the mass spectrum of an unknown compound, and whether the sample contains signatures of unknown life forms, remains challenging. We propose several methods to agnostically infer biogenicity from mass spectral data: determine if a sample contains polymers, which have been proposed to play an essential role in biology by increasing the functional chemical space and providing storage for propagatable information; determine if molecular fragmentation patterns, or relative abundances of compounds in biotic samples are distinct from those of abiotic samples. We employ statistical methods involving data reduction and processing, such as Fourier transform and machine learning, by applying it to commercial and flight-instruments data. This project seeks to address the fundamental question as to whether biotic and abiotic samples can be classified solely based on their mass spectra.

Chemometric Approaches: Sequencing approaches, currently under development to search for nucleic acids and monitor terrestrial contamination [2-3], can also be utilized to explore sample complexity, regardless of whether life is based on nucleic acids [4]. This concept builds on the fact that oligonucleotides naturally form secondary and tertiary structures that can have affinity and specificity for a variety of molecules, from peptides and proteins [5], to a wide variety of small organic molecules [6,7], to inorganics such as mineral surfaces [8] and individual metals [9]. By accumulating large numbers of binding sequences that reflect different compounds in a mixture, statistical data analyses of oligonucleotide sequences and sequence counts enable patterns associated with increasing levels of complexity to be analyzed [Fig. 1]. This pattern recognition, known as "chemometrics," could be used to distinguish samples with chemistries suggestive of biology—to "read" patterns of molecules that arise from the vast amount of information stored on the surface of a primitive microbial cell, and to do it with great sensitivity.

Disequilibrium Redox Chemistries: Disequilibrium redox chemistries that are inconsistent with abiotic redox reactions could also be used as an indicator of active metabolism. Unexpected accumulations of chemical elements or isotopes could indicate life, as could patterns of energy transfer. Many microbes can utilize solid-phase minerals as an electron acceptor, e.g. insoluble Fe(III) oxides. An agnostic means of detecting this microbial activity is to use an inert, conductive electrode (e.g. graphite) in the environment. The current density and other electrical attributes produced by microbes are notably distinct from abiotic oxidation [10]; thus this signal could be used as an agnostic biosignature.

Probabilistic Approaches to Data Analysis: While it is necessary to broaden our scope and design inclusive life detection strategies, agnostic approaches may be less definitive than, say, uncovering a hopane or DNA sequence. A data interpretation scheme that considers expectations and likelihoods and establishes critical thresholds for life detection based upon probabilistic models is thereby key. For instance, a Bayesian network for which the output is the probability there is a biosignature in a measurement set (*i.e.*, P(biosignature | Data) could be utilized to assess the probability of life, and thus convert measurements into likelihoods and thresholds.

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