I will discuss how the interplay of environmental variables, such as temperature and redox conditions, as well as availability of organic and inorganic energy substrates determine the population size and community structure of microorganisms in deeply buried sediments and crustal environments. I will show how rates of biomolecule-damaging reactions, e.g. amino acid racemization, DNA depurination, and the energetic cost of biomolecule repair are direct consequences of the temperature and redox environment and that therefore temperature and redox conditions exert a key influence on microbial population size in subsurface environments. In addition, I will discuss the role the chemical composition of microbial energy substrates has in determining the community structure of microorganisms. I will present the hypothesis that the macromolecular composition of biogenic organic compounds is a key determinant of microbial community structure in the majority of subseafloor sediments, whereas in subseafloor crustal environments and deep sediments in proximity to seismically and geothermally active zones the composition of geogenic inorganic and small organic molecules is the main driver of microbial community structure. I will conclude with an outlook on important scientific goals and drilling targets of future subsurface microbiological research, and demonstrate how scientific observations and hypotheses resulting from ocean drilling expeditions are challenging fundamental microbiological concepts and transforming our understanding of life on Earth and beyond.