Our lab uses an interdisciplinary approach that relies heavily on liquid chromatography–mass spectrometry (LC–MS) based metabolomics to understand medicinally and environmentally relevant microbial processes. The primary analytical platform is an Orbitrap MS with an electrospray ionization source, and the methods employed attempt to measure the concentration (pool size) of ~1000s of analytically tractable, yet chemically diverse, water and lipid soluble metabolites from all kingdoms of life. These methods measure at least one metabolite from all known carbon and nitrogen utilization pathways, the activated methyl cycle, all amino acid and nucleotide biosynthesis pathways, as well as lipids with diverse head groups; and the average coverage for each major pathway is ~65%. The utility of these metabolomics methods can be enhanced by monitoring the incorporation of stable isotope-labeled nutrient sources, either $^{15}$N or $^{13}$C, into the metabolome using kinetic flux profiling techniques (KFP). When coupled, pool size determination and KFP can be used to determine both the amounts of metabolites within and relative rates of flux through many biochemical pathways in vivo and allow a global snapshot of cellular metabolism to be obtained from a single set of experiments. Several vignettes from our work studying bacterial cell-cell signaling (quorum sensing), microbial nutrient cycling by marine organisms, and novel biochemical pathways in yeast will be discussed to highlight the utility of applying these metabolomics tools to probe complex biological systems and to provide insight into the mechanisms that consortia of microorganisms utilize to cooperatively and/or competitively dictate resource utilization.