The chemistry at interfaces dominates the properties of systems as diverse as nanoparticle luminescence and antibiotic resistance. Despite the large difference in samples, there is commonality in the challenges presented by isolating the relatively small signals at these unique boundaries. Using a suite of nonlinear spectroscopic and microscopic techniques, we are probing both material and biological surfaces and the molecules that interact with them in new ways. For example, we have developed the ability to directly measure surface states on quantum dots using electronic sum frequency generation microspectroscopy. The broad energetic distribution of signal we measure provides evidence for the existence of both deep and shallow traps. In other work, our probing of membrane-associated small molecules with living microbial cells reveals unexpected behavior that may help explain their resistance to current drugs. Overall, our efforts open up new pathways of exploration and understanding of interfacial complexity.