The hydrocarbon processing industry is in the midst of a major shift in feedstocks, structure, and products in response to rapidly changing energy sources and external driving forces associated with greenhouse gas emissions. Even amidst this rapidly changing landscape, fossil-based feedstocks, processing, and products will continue to be the status quo for the foreseeable future due to extensive existing investment. However, existing fossil-based plants with compatible equipment will begin the externality-induced transition over to bio- and e-refinery formats to leverage this existing infrastructure and logistical connections. Advanced separations play a role in this transition in several ways. First, modern separations can partner with existing technologies (e.g., distillation) to extend the time in which fossil-based processing remains competitive under modern externalities (e.g., CO$_2$). Moreover, energy- and capital-efficient separation technologies can reduce the effect of CO$_2$ and other emission mandates on fossil-based refining returns on energy invested. While bio- and e-refineries are often thought of as a “blank slate” for advanced separations technologies (thus bypassing the problem of working, amortized capital in existing plants), in fact, the adaptation of existing fossil-based refineries to renewable feedstocks suggests that the “hybrid” separation system paradigm is likely to be the standard for years to come. Nevertheless, these “green refineries” introduce many new separations challenges that are poorly addressed by conventional technologies. There are several unifying themes from a separations perspective in all three refinery archetypes (i.e., fossil, bio-, e-). Two themes that will be discussed in this seminar are “countering complexity” and “combatting dilution”, which represent perennial and emerging separations challenges, respectively. These themes are meant to highlight real-world deviations from the commonly thought of “binary” separation problems that the separations community typically grapple with. Taken together, these themes will be used to provide final thoughts on the design of the refinery of today, tomorrow, and the future.