Bioprocessing offers a sustainable and green approach to the production of chemicals. However, a bottleneck in introducing bioprocesses is cell factory development, which is costly and time-consuming. A systems biology approach can expedite cell factory design by using genome-wide analyses alongside mathematical modeling to characterize and predict cellular physiology. This approach can drive cycles of design, build, test, and learn implemented by metabolic engineers to optimize the cell factory performance. Streamlining of the design phase requires a clearer understanding of metabolism and its regulation, which can be achieved using quantitative and integrated omic characterization, alongside more advanced analytical methods. We discuss here the current impact of systems biology and challenges of closing the gap between bioprocessing and more traditional methods of chemical production.