Computational systems biology methods enable rational design of cell factories on a genome-scale and thus accelerate the engineering of cells for the production of valuable chemicals and proteins. Unfortunately, for the majority of these methods' implementations are either not published, rely on proprietary software, or do not provide documented interfaces, which has precluded their mainstream adoption in the field. In this work we present cameo, a platform-independent software that enables in silico design of cell factories and targets both experienced modelers as well as users new to the field. It is written in Python and implements state-of-the-art methods for enumerating and prioritizing knock-out, knock-in, over-expression, and down-regulation strategies and combinations thereof. Cameo is an open source software project and is freely available under the Apache License 2.0. A dedicated website including documentation, examples, and installation instructions can be found at http://cameo.bio. Users can also give cameo a try at http://try.cameo.bio.