

***Accelerating the discovery and invention of critical chemical transformations via Systems Chemistry.***

**Abstract.** The vast majority of druglike chemical space is unmapped and unreported. Small molecule drug development relies on the ability to use chemistry to navigate chemical space towards the discovery and optimization of a molecular structure that properly interacts with biological systems to achieve a desired effect. Albeit chemistry's integral role in exploring chemical space, fewer than five chemical transformations account for most reactions performed in medicinal chemistry. Bolstering the ability to efficiently reach the entirety of chemical space will greatly reduce the time and cost of resource intensive drug discovery campaigns. Continuing advances in computational and synthetic methods have considerably sped up the rate of reaction invention. Holistic drug development strategies that include the potential invention of any novel chemical transformation must be considered. Enumerative combinatorics algorithms can generate theoretical, chemically viable transformations between classes of substrates, the most promising of which will be targeted for rapid discovery utilizing state-of-the-art high throughput experimentation techniques.