Combining high throughput combinatorial synthesis/screening with machine learning for drug and biomaterials discovery

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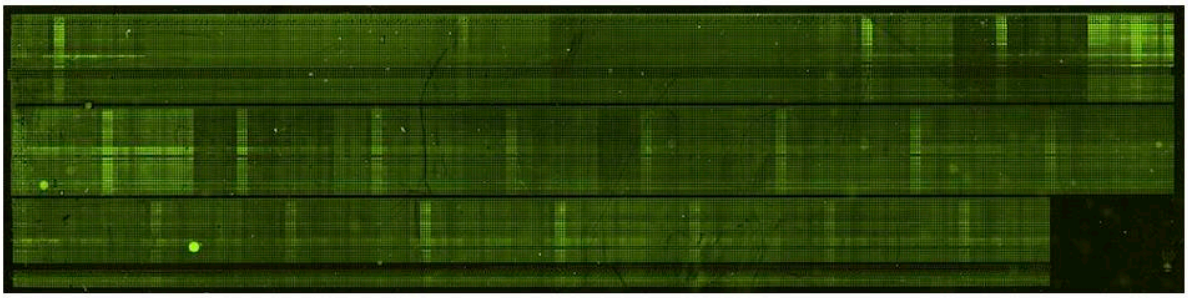
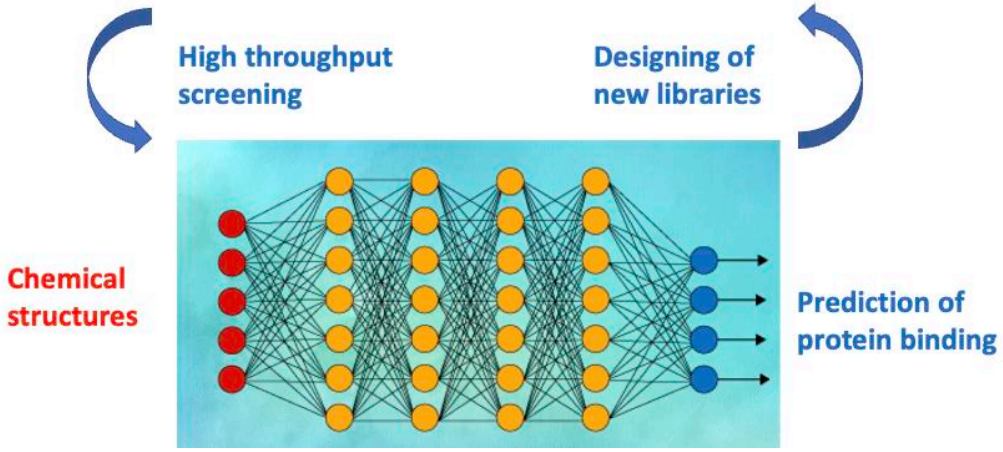
Project description

Fundamentally, drug screening and discovery are limited by our capability to synthesize new compounds and test them. The throughput of synthesizing new compounds in conventional medicinal chemistry projects is below 1 compound per day. As an important breakthrough from our lab, we have recently reported an amphiphilic coating of glass surface on which small droplets of polar aprotic organic solvents can be deposited with an enhanced contact angle and inhibited motion to permit fully automated multiple rounds of the combinatorial synthesis of small-molecule compounds and peptides. This amphiphilic coating can be switched into a hydrophilic network for protein- and cell-based screening. Employing this in situ synthesis method, chemical space can be probed via array technology with unprecedented speed for various applications, such as lead discovery/optimization in medicinal chemistry and biomaterial development. For example, by combining our knowledge in rational design of natural product derivatives, a 20,000-member library of immunosuppressive drug cyclosporin A can be synthesized on a single glass slide to probe their interaction with fluorescently labelled protein immunophilin.





The large library sizes of small molecule array have provided us great tools to discover binding molecules, however, also present challenges to process and analyze the resulting information. In this project, by coupling machine learning with on-demand high throughput library synthesis and screening, reinforcement learning algorithm can be developed to explore the chemical space of unprecedented size and diversity. We are particularly interested in protein targets involving in the stimulation, inhibition and regulation of immune system.