Although conventional high throughput screening (HTS) has enabled the discovery of numerous leads, the difficulties faced during optimization, poor hit rates, and false positives has allowed room for fragment based drug design (FBDD). Comparatively speaking, FBDD uses smaller, more chemically diverse libraries to detect weak interacting inhibitors. Such diversity is achieved by using small compounds that are more likely to interact promiscuously with various proteins. Lead detection via FBDD allows for more feasible optimization as compared to conventional HTS.\(^1\)\(^2\) Despite such advantages, FBDD is limited by the lack of sensitive assays available for screening. Scientists at Abbott were able to overcome this problem by using SAR by NMR. Here, nuclear magnetic resonance (NMR) spectroscopy is used to detect the binding of two or more compounds to proximal sites within a protein followed by optimization and linking. Ligand binding is characterized by a comparison of NMR spectra generated for protein in presence and absence of the ligand. SAR by NMR has been greatly utilized in lead discovery and development for numerous targets.\(^1\)-\(^4\) Most recently, SAR by NMR has played a crucial role in the design of an ABT-737, a nanomolar inhibitor of the Bcl-2 family of proteins.\(^5\) Despite great success, the design of ABT-737 has emphasized the limitations of SAR by NMR, particularly in the design of suitable linkers.


