Automating Variant Assessment using Structural Features

Adam Chamberlin, Min-Sun Park, Igor D. Petrik, Hsiao-Mei Lu, and R. Bryn Fenwick

Ambry Genetics, Aliso Viejo, CA, USA

Variant assessment is rapidly becoming a significant part of clinical diagnoses in both clinical and somatic diseases. As the number of uncategorized variants continues to grow, automated classification schemes will become more and more valuable. The application and automation of simple classification schemes using sequence, and ternary-structural features will be invaluable in prioritizing variants for assessment, classification and functional studies. Structural biology can provide a variety of features for variant assessment that can be leveraged in parallel with traditional methods such as *in-silico* predictions that rely on sequence primary-structure (Baugh et al., 2016). These features can include but are not exclusive to, structural motif identification, variant location in the domain (buried, surface, or interfacial), as well as information about the local environment of the variant (hydrogen bonding, ligand binding, back-bone conformation, etc), all of which provide invaluable insight into variant pathology (Pesaran et al., 2016; Ponzoni & Bahar, 2018). Here we present an automated method for leveraging structural features for variant assessment, which can be used as a tool to both propose appropriate categories for variants of interest and allow prioritization of variants for reporting and reassessment purposes.

Keywords: Protein structure, Bioinformatics, Genetic testing, Mathematical modeling, Mutation detection