



Supplementary Fig. 1: Network properties of mutational hotspots in comparison to population variants. **A**, Distribution of hotspots and population variants on proteins with regard to protein interaction interfaces. Enrichment was calculated as the ratio of the observed fraction of hotspots/variants that occur on interaction interfaces over the fraction of interface residues on corresponding proteins (expected fraction). **B**, Average number of protein interactions affected by hotspots and population variants. **C**, Average edge betweenness of interactions affected by hotspots and population variants.