Authors must submit a 120-word-maximum statement about the significance of their research paper written at a level understandable to an undergraduate-educated scientist outside their field of specialty. The primary goal of the Significance Statement is to explain the relevance of the work in broad context to a broad readership. The Significance Statement appears in the paper itself and is required for all research papers. For PNAS Plus papers only, a collection of such statements will appear in an issue of the journal, see www.pnas.org/site/authors/pnasplus faq.xhtml.

## Current length: 116 words

Advances in genome sequencing technology are providing the sequenced human genomes and exomes of large numbers of individuals, thereby identifying regions under evolutionary pressure. Although signs of such pressures manifest throughout the genome, the mechanisms responsible are often unclear. Allostery serves as a plausible mechanism in many cases. We take a generalized approach to this problem by using protein conformational changes to identify potential allosteric residues in large numbers of proteins, and then evaluating their conservation using various measures and sources of data, including human genomes. These residues are conserved both among humans and across species, and they may sometimes aid in interpreting disease-associated mutations. We also introduce a user-friendly software tool for implementing this method.