RINGER: A PROGRAM TO DETECT MOLECULAR MOTIONS BY AUTOMATIC ELECTRON DENSITY SAMPLING

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BRIEF DESCRIPTION

Ringer distinguishes flexible regions from rigid regions of biomolecules such as drug receptors. To assess the generality and significance of the weak secondary peaks of uniquely modeled residues, we ran Ringer on 402 high-resolution (<=1.5 Å) crystal structures from the Protein Data Bank. Omit electron-density maps were analyzed to reduce the effects of model bias. When applied after refinement is considered complete, Ringer discovers polymorphism at over 3.5 times the frequency that is currently modeled in the PDB. Multiple conformers are found for >18% of unbranched residues in a test set of 402 high-resolution structures, in addition to the 5.1% that are already modeled.

More than a method for enhancing crystallographic refinement, however, Ringer is best used as a tool for systematically detecting low-occupancy structural features. The hidden conformational substates identified using Ringer provide clues to the functional roles of protein structural polymorphism and to assess the response of protein side chain distributions to perturbations including ligand binding, temperature changes and mutations. In calmodulin, for example, Ringer identifies side chains that undergo conformational population inversions and side-chain rigidification upon peptide binding, linking the structure to dynamic properties. Similarly, in human proline isomerase, Ringer was used to define the nature of a coupled conformational switch in the free-enzyme that defines motions that occur during turnover. In both cases, the alternate conformations identified by Ringer provided structural insights not available from any other experimental technique.

Link to overview of Ringer software

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OTHER INFORMATION

CATEGORIZED AS

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