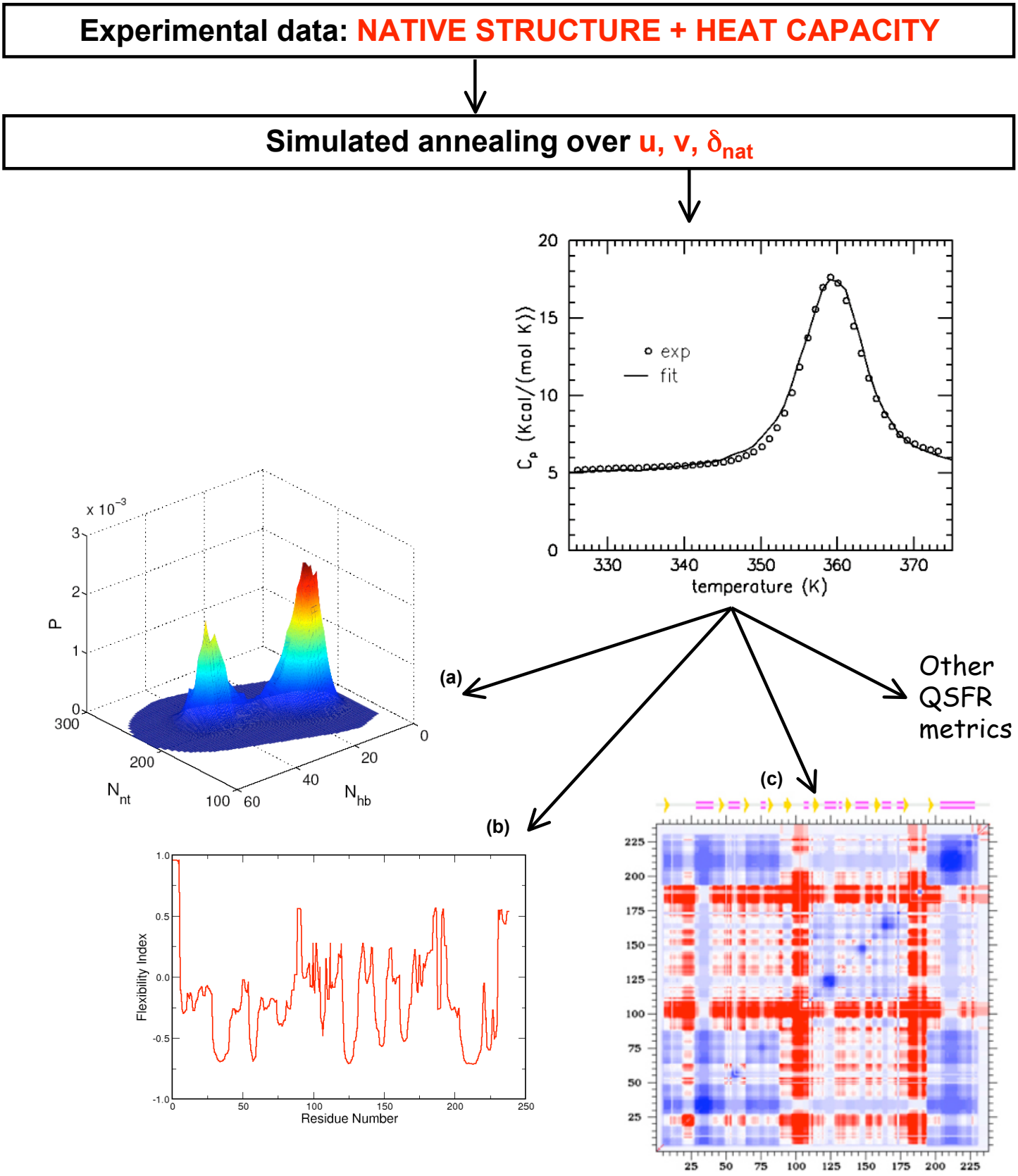

Supplementary Figure 1: A generic description of the workflow used by the mDCM. The mDCM begins with two pieces of input: (*i.*) the native structure of a protein and (*ii.*) an experimental heat capacity curve. A simulated annealing process is used to parameterize the model. With mDCM parameters in hand, a large number of mechanical and thermodynamic QSFR metrics can be computed. Three common examples are provided: (a) the free energy landscape (expressed here as probabilities), (b) backbone flexibility, and (c) cooperativity correlation. In the latter two cases, the values represent the thermodynamic average over the full ensemble; however, the mDCM also allows the user to average only specific sub-ensembles (i.e, the native basin only).