

“Multiple sequence and structure alignments”

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Mechanistic analysis of the TrpRS mechanism has raised important questions concerning how binding interactions at the active site are coupled to the anticodon-binding site. Answers to these questions may be sought from correlated changes observed in multiple sequence alignments of the TrpRS family and, more generally, the class I aaRS superfamily. Cluster analysis of statistical D(DG) values associated with the multiple sequence alignment (Kim) reveal novel interactions between the signature catalytic peptides and other locations within class I aaRS. While pursuing multiple sequence alignments, we recognized that the sequence alignments were markedly improved by carefully aligning the known class I aaRS tertiary structures. Multiple structure alignments are currently a cumbersome process. To expedite multiple structure alignment, we have developed an algorithm that preserves considerable tertiary structure information in a simplified form (Roach, Sharma). The algorithm, based on consistent reduction of the edge structure of the Delaunay tessellation to a one-dimensional string, facilitates the use of existing software used for sequence alignment to compare 3D structures, speeding up such calculations by an order of magnitude. Principle Component Analysis (PCA) of aligned aaRS structures affords a method for approximating maximum parsimony structural trees. The resulting trees largely confirm the subclass organization derived from multiple sequence alignments for class I and class II aaRS. Notable exceptions, however, suggest that structural similarity does not parallel apparent genetic kinship.