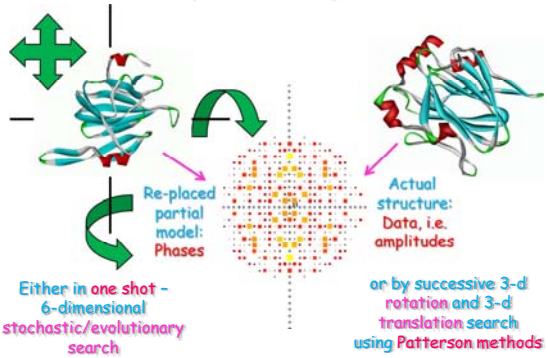
Molecular Re-Placement of a structurally similar search model



Either in one shot – 6-dimensional stochastic/evolutionary search

or by successive 3-d rotation and 3-d translation search using Patterson methods

Molecular replacement models

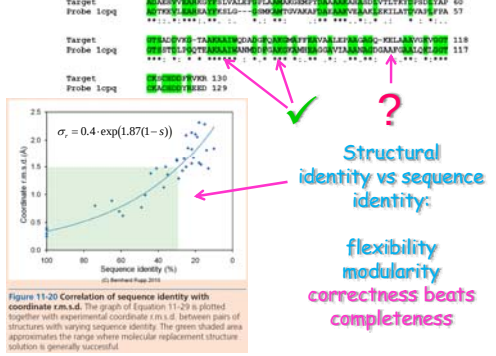
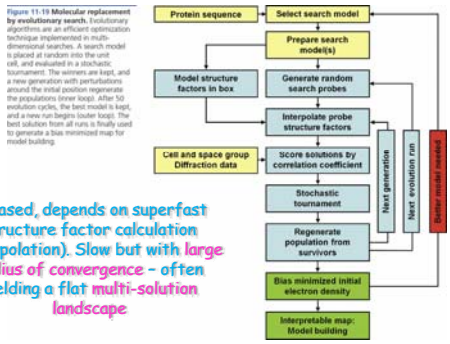


Figure 11-20 **Correlation of sequence identity with coordinate r.m.s.d.** The graph of Equation 11-29 is plotted together with experimental coordinate r.m.s.d. between pairs of structures with varying sequence identity. The green shaded area approximates the range where molecular replacement structure solution is generally successful.

Structural identity vs sequence identity:

flexibility
modularity
correctness beats completeness

Evolutionary 6-D multi-solution search: EPMR



F-based, depends on superfast structure factor calculation (interpolation). Slow but with large radius of convergence – often yielding a flat multi-solution landscape

Typical multi-solution landscape

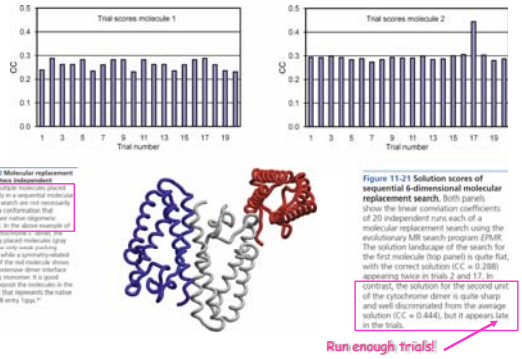
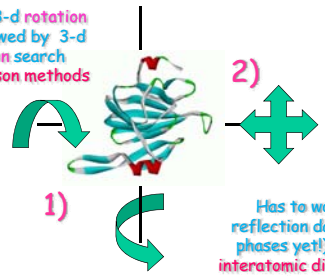


Figure 11-21 **Solution scores of sequential 6-dimensional molecular replacement search.** Both panels show the linear correlation coefficients of 20 independent runs each of a molecular replacement search using the evolutionary MR search program *EPMR*. The solution landscape of the search for the first molecule (top panel) is quite flat, with the correct solution (CC = 0.288) appearing twice in trials 2 and 17. In contrast, the solution for the second unit of the cytochrome dimer is quite sharp and well discriminated from the average solution (CC = 0.444), but it appears late in the trials.

Run enough trials!

Plan B: break up into rotation and translation part, use Patterson function

Successive 3-d rotation search followed by 3-d translation search using Patterson methods



Has to work with reflection data only (no phases yet!) –> done in interatomic distance space using Patterson methods

Finding molecule orientation: Patterson cross-rotation function

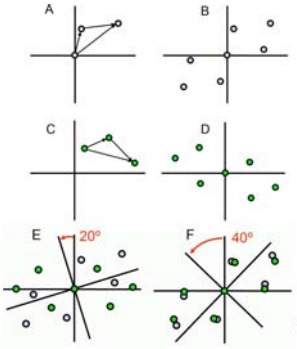


Figure 11-23 **Patterson cross-rotation search.** Panel A shows a search molecule positioned in a *P*1 box that is selected to be large enough to contain only intramolecular vectors. The Patterson map containing the intramolecular distance vectors of the search molecule is shown in panel B. The target molecule in an as-yet-unknown orientation and location in its unit cell (C), and the corresponding vectors are shown in the next map (D). Intermolecular vectors to neighboring molecules are omitted. Note that the intramolecular vector map is independent from the location of the target molecule, but it depends on the orientation and is correspondingly rotated. By successively rotating the search map (blue dots) and calculating the overlap function at each orientation, we can find the correct rotation angle(s), in this case about 45° (panels E and F).

$$\Re(\mathbf{R}) = \frac{1}{V}\int_{r_{min}}^{r_{max}} P_t(\mathbf{r}) \cdot P_s(\mathbf{R}^{\mathrm{T}}\mathbf{r})\mathrm{d}^3\mathbf{r}$$