Correlation-Based Search, Filtering, and Fast Fourier Transform

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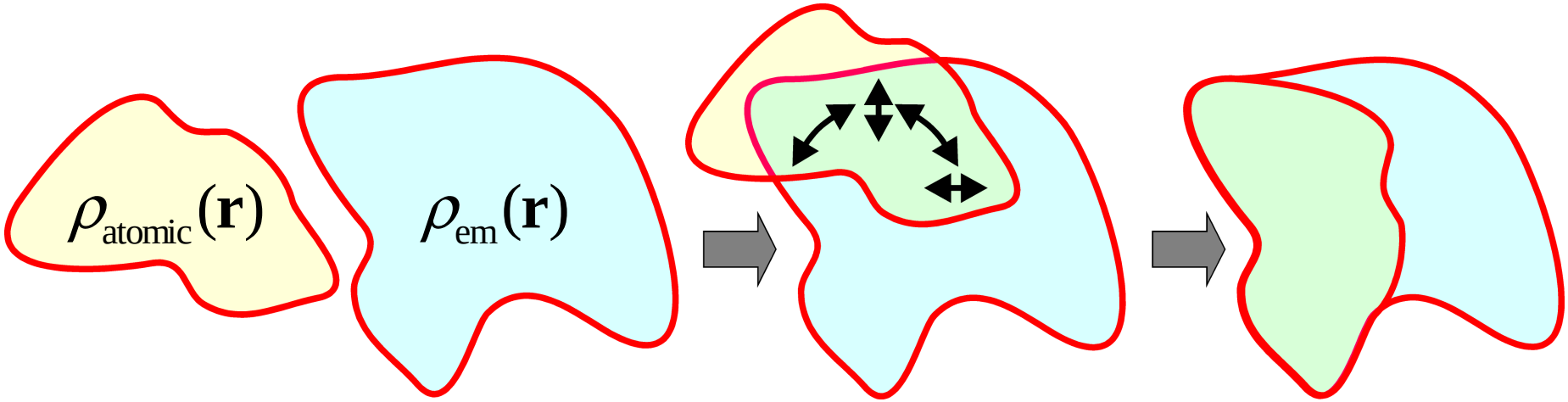
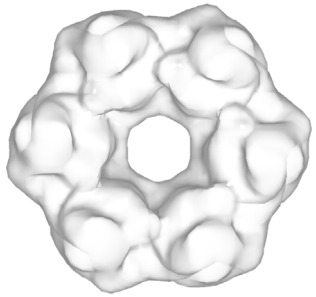
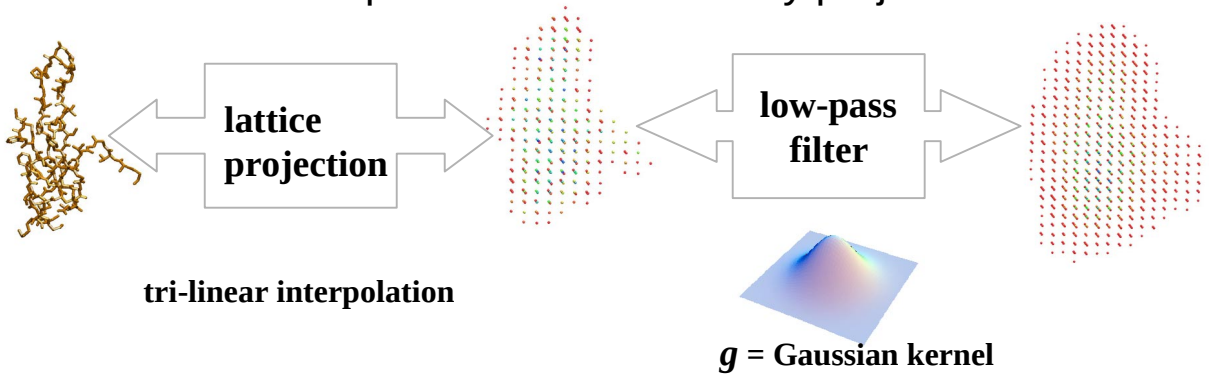


A Typical Exhaustive Search Scenario

$\rho_{\mathrm{em}}(\mathbf{r})$ target density on lattice

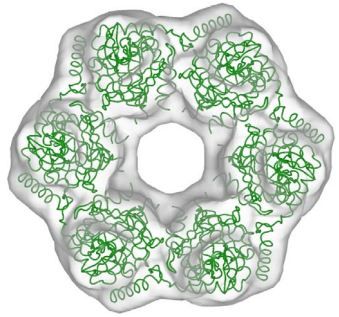


$\rho_{\mathrm{atomic}}(\mathbf{rR})$ rotated probe molecule density projected to the lattice:



$$g \otimes \rho_{\mathrm{atomic}}(\mathbf{rR}) \equiv \rho_{\mathrm{calc}}(\mathbf{r})$$

$$C(\mathbf{T}) = \int \rho_{\mathrm{em}}(\mathbf{r}) \times \rho_{\mathrm{calc}}(\mathbf{r}+\mathbf{T})\ \mathrm{d}^3\mathrm{r}$$

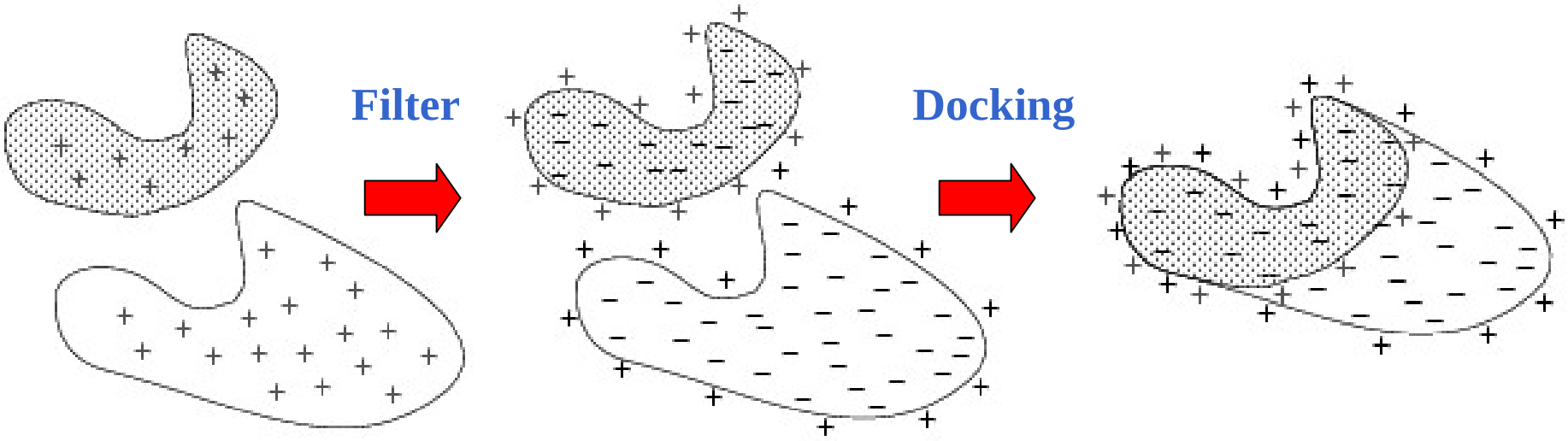


Fitting criterion: e,g, linear cross-correlation, evaluate for every rotation **R** and translation **T**

Enhancing the Fitting Contrast with Density Filtering

For low-resolution smooth density maps (e.g. from EM) we wish to enhance the *fitting contrast* (difference between correct and spurious fits) by adding "contour" information to the criterion.

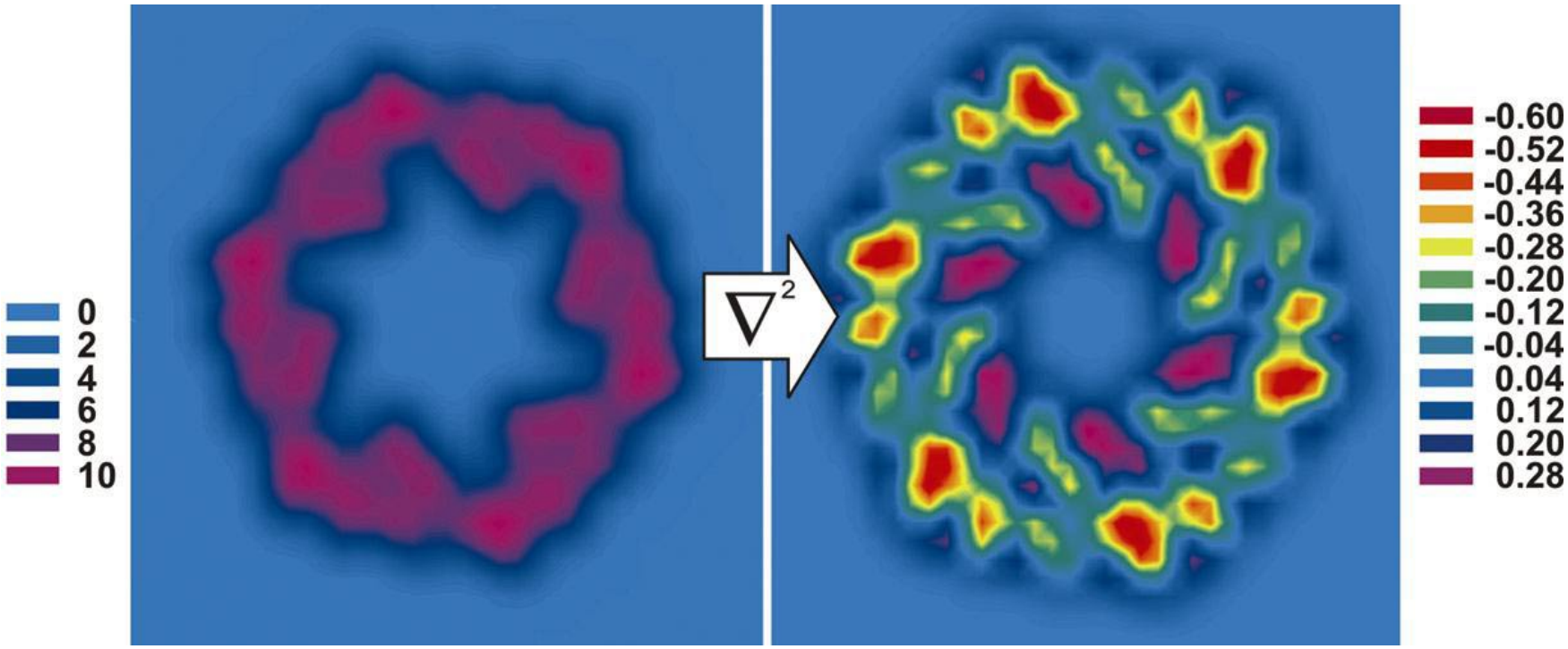
A suitable filter would assign negative values to the interior, positive values to the molecular contour. Both volume and contour matches would provide positive contributions to the correlation criterion:



How can we characterize the molecular "contour" in a low-resolution map?

Laplacian filter

$$\nabla^2 = \frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2} + \frac{\partial^2}{\partial z^2}$$



FFT Acceleration of the Translational Search

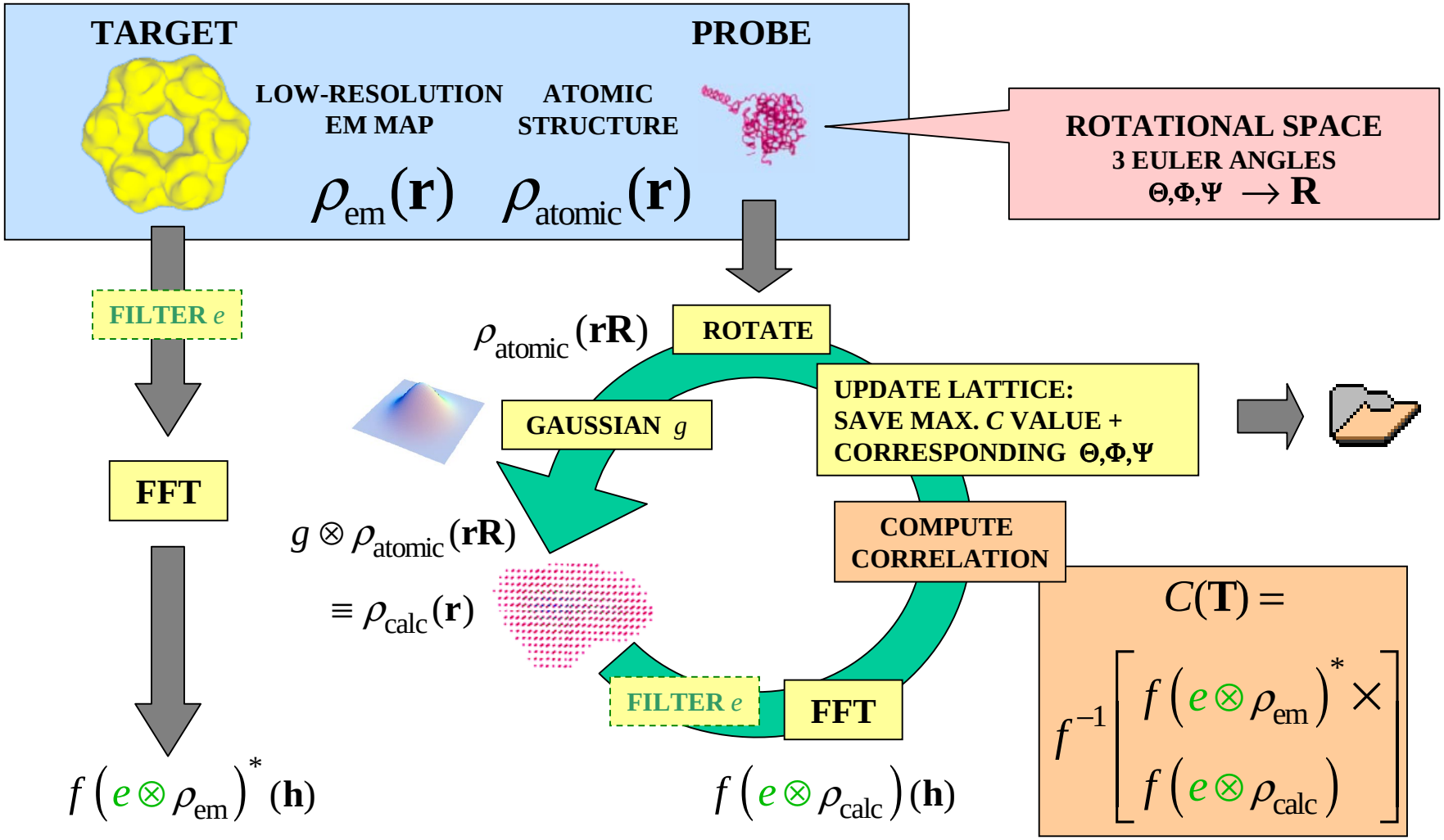
$$C(\mathbf{T}) = \int \left(e \otimes \rho_{\text{em}}\right)(\mathbf{r}) \times \left(e \otimes \rho_{\text{calc}}\right)(\mathbf{r}+\mathbf{T})\ \mathrm{d}^3\mathrm{r} = f^{-1}\left[f\left(e \otimes \rho_{\text{em}}\right)^* \times f\left(e \otimes \rho_{\text{calc}}\right) \right]$$

Fourier Convolution Theorem:

Direct approach (top): N^2 multiplications
FFT approach (bottom): N log N multiplications

(N = number of voxels,
f = Fourier Transform,
e = optional filter, e.g. Laplacian)

The 6D Search Algorithm (CoLoRes)

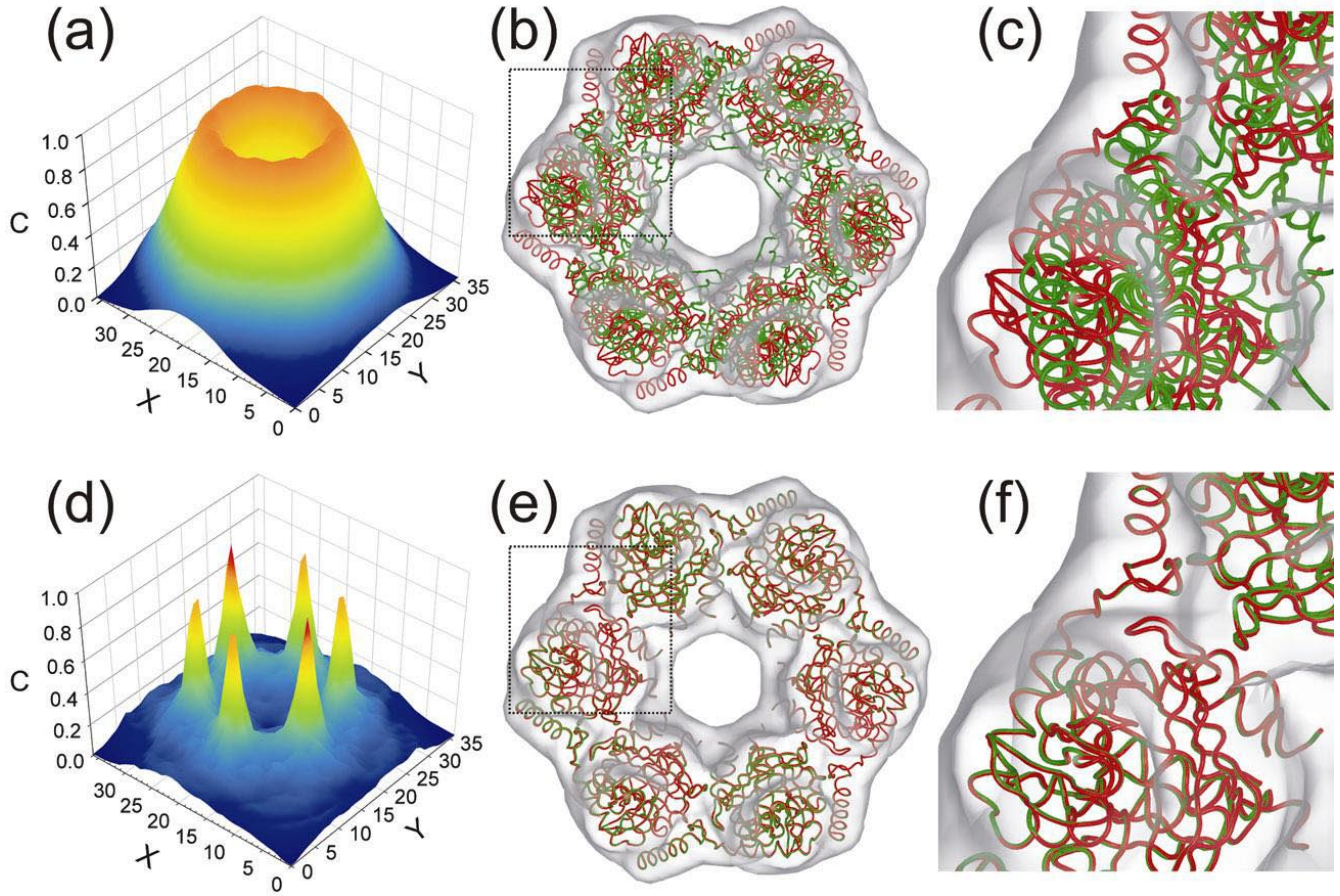


Effect of Filtering on Fitting Contrast

RecA (2REC.pdb), Grid size 6Å, resolution 15Å, 9^0 steps (30481 rotations)

standard cross-correlation

w/ Laplacian filtering



Only Laplacian filtering successfully restores the initial pose (red). Best docking results in either case are shown in green.

Reference

Pablo Chacón and Willy Wriggers.

Multi-Resolution Contour-Based Fitting of Macromolecular Structures.

J. Mol. Biol. 2002, 317:375-384.