A hierarchical elastic network model for unsupervised EM density map segmentation

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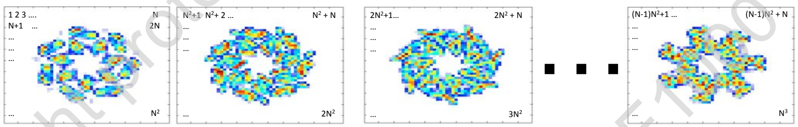
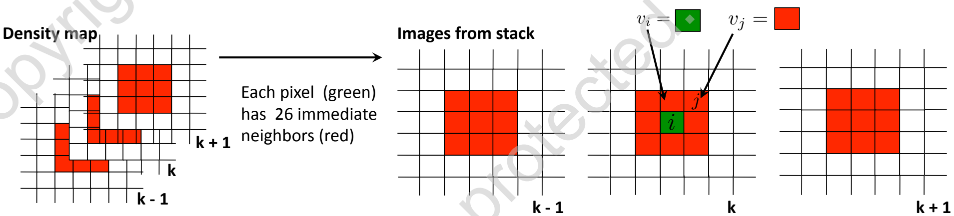
Hierarchical Elastic Network Model

We propose an unsupervised hierarchical elastic network model (hENM) based on a Markov diffusion process [1] to segment electron density maps into meaningful sub-regions, thereby highlighting different levels of structural and functional organization found in Cryo-EM density maps [2,3].

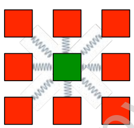
1 Consider each cross-section of the $N \times N \times N$ density map as an image with $N \times N$ pixels and a total of $n_{pixel} = N^3$ pixels.



Let $\vec{x}_i$ be the location of pixel i in Cartesian coordinates, and v_i be its intensity value.



2 Connect each pixel to its 26 neighbors with a spring.

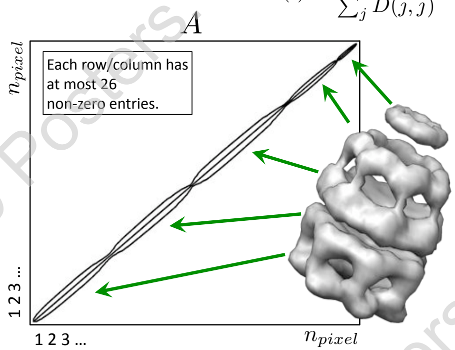


3 Give each spring an *affinity* (spring constant) to denote the likelihood of two pixels belonging to the same region [4,5]:

$$a_{ij} = \frac{1}{||\vec{x}_i - \vec{x}_j||} e^{-\beta(v_i - v_j)^2}$$

where β is proportional to the median of the distribution $|v_i - v_j|$.

4 Form symmetric $n_{pixel} \times n_{pixel}$ affinity matrix $A = (a_{ij})$, degree matrix D, Markov transition matrix M (see next step), and the stationary distribution $\vec{\pi}$ of the Markov chain: $\vec{\pi}(i) = \frac{D(i,i)}{\sum_j D(j,j)}$.



5 Hierarchically segment with hENM [6,7,8]:

Let $t = 0$, $A_0 = A$, $n_0 = n_{pixel}$, $D_0 = D$, and $\vec{\pi}_0 = \vec{\pi}$.

While $n_t > 1$:

$$D_{t-1}(i,j) = \begin{cases} \sum_{j=1}^{n_{t-1}} A_{t-1}(i,j) & i = j \\ 0 & i \neq j \end{cases}$$ degree matrix

$$M_{t-1} = A_{t-1} D_{t-1}^{-1}$$ Markov transition matrix

$$M_{t-1}^d = M_{t-1} \times M_{t-1}$$ diffusion

Choose K_t, a subset of n_t columns of M_{t-1}^d based on $\vec{\pi}_{t-1}$

$$\vec{\pi}_{t-1} = K_t \vec{\pi}_t$$ solve for next stationary distribution

$$A_t = \text{diag}(\vec{\pi}_t) K_t^T \text{diag}(K_t \vec{\pi}_t)^{-1} \text{diag}(\vec{\pi}_t)$$ next affinity matrix

$n_t =$ number of nodes in A_t

$t = t + 1$

End.

6 Perform soft clustering at each level of hierarchy by computing $W_t(i,j)$, which gives the probability that pixel i belongs to segment j at level t of the hierarchy:

$$W_t(i,j) = \frac{K_t(i,j)\vec{\pi}_t(j)}{\sum_{k=1}^{n_t} K_t(i,k)\vec{\pi}_t(k)}.$$

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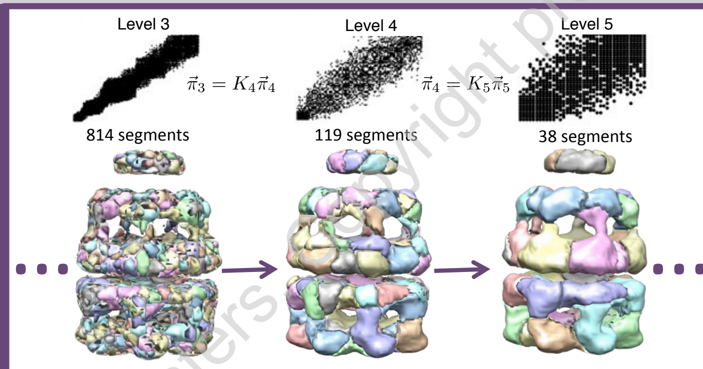
* Used for visualization

e.g. Hierarchical Segmentation of 23.5Å GroEL+GroES map



Results: Segmentation of 2010 Cryo-EM Modeling Challenge Targets