



Query Based Probabilistic Synapse Detection in Array Tomography



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Challenge

- Detect specific synaptic subtypes with confidence values using array tomography data

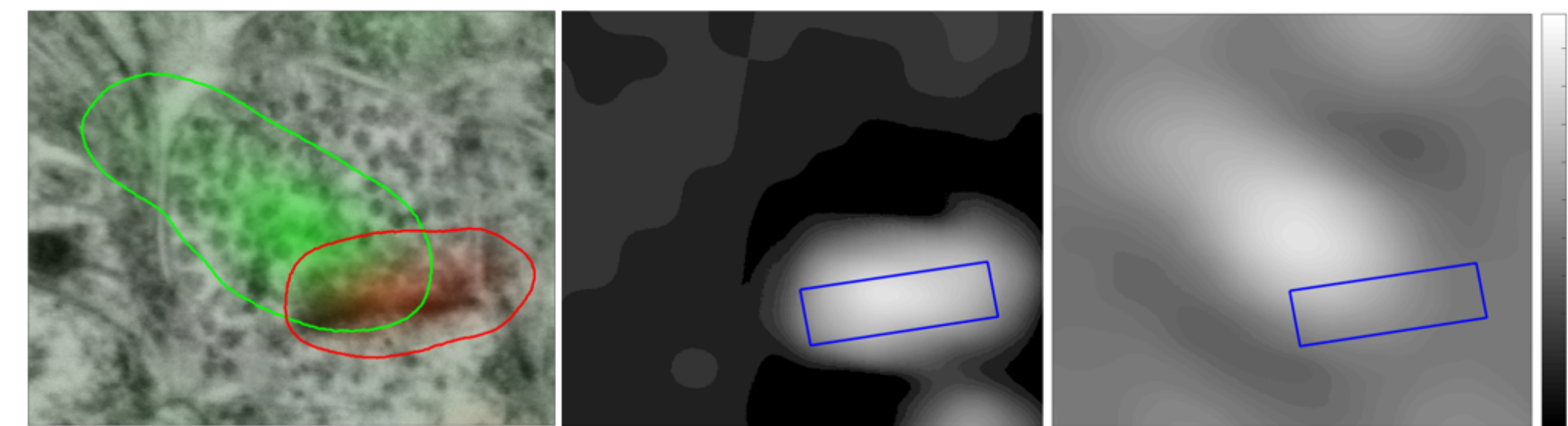


Figure 1: Left: PSD-95 (red) and Synapsin (green) data overlaid on EM data. Center: PSD-95 IF image. Right: Synapsin IF image. Synaptic cleft marked in blue.

Background

- What is a Synapse?

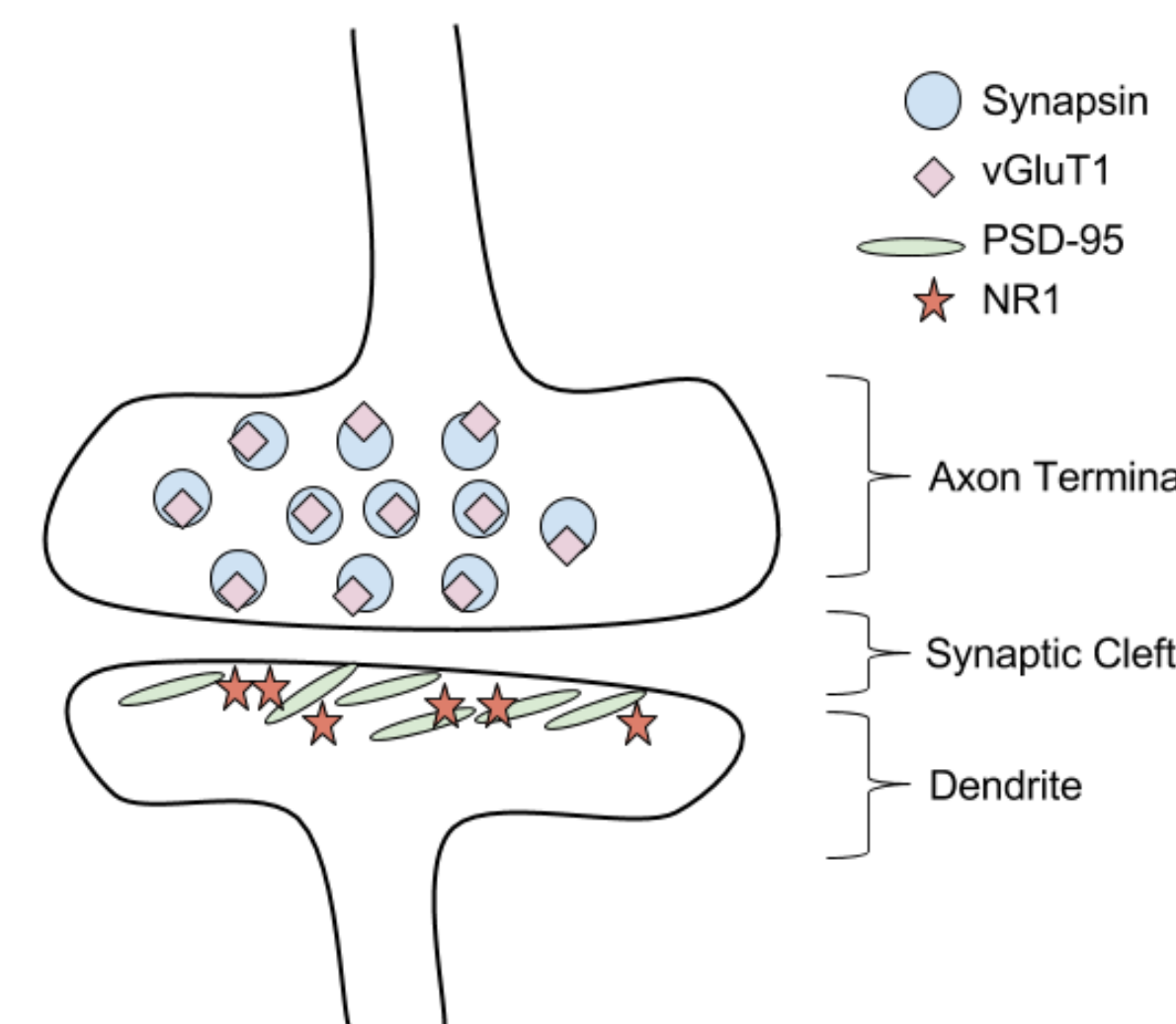


Figure 2: Molecular architecture of an excitatory PSD-95 expressing synapse depicted in a simplified cartoon form

- Array Tomography (AT) Pipeline

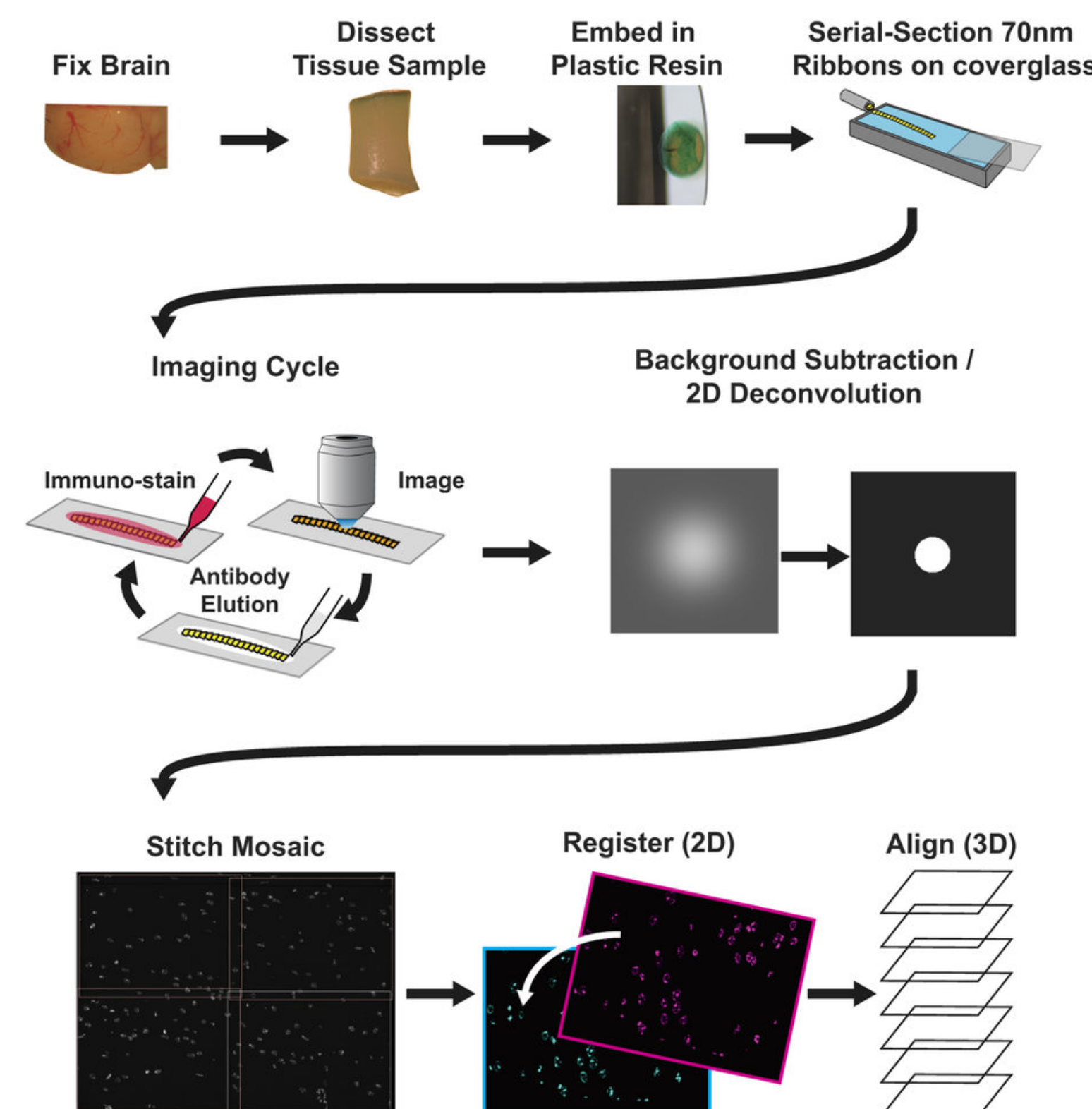
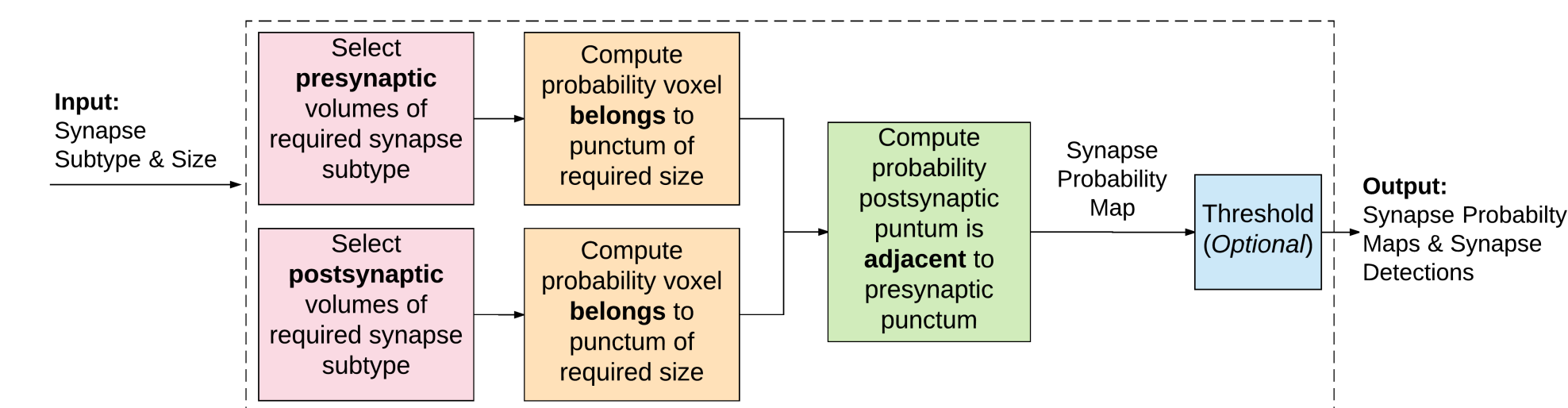


Figure 3: Array Tomography Methodology [6]

Action

- Overview of Proposed Method



- Step 1: Foreground Probability.** Model background p_B from the raw data. Foreground probability is one minus the background.

$$p_B(x, y, z) = \frac{1}{\sigma_B \sqrt{2\pi}} \int_{v(x,y,z)}^{\infty} e^{-\frac{(t-\mu_B)^2}{2\sigma_B^2}} dt. \quad (1)$$

$$p_F(x, y, z) = 1 - p_B(x, y, z). \quad (2)$$

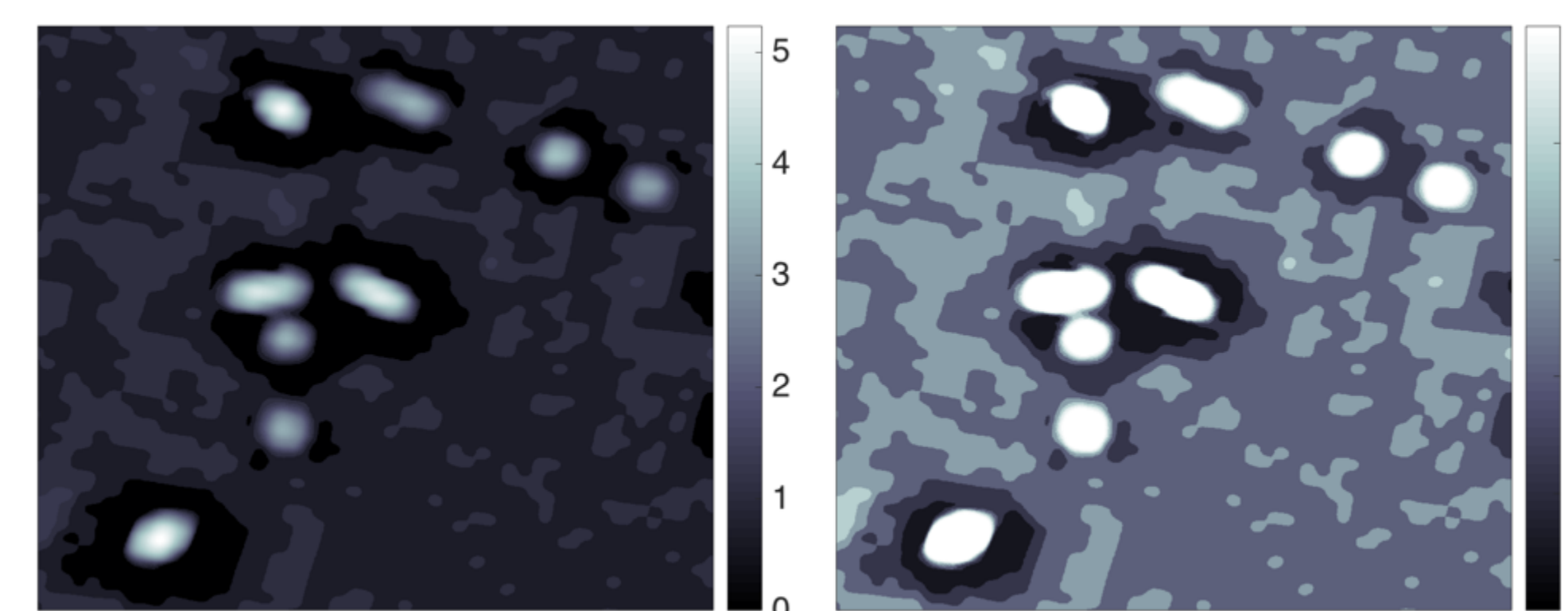


Figure 4: Cutout of size $5.268 \times 5.827 \mu m$ of the logarithm of the IF raw data (left) and the corresponding image of the foreground probability map (right) of one slice of the PSD-95 antibody.

- Step 2: 2D Puncta Probability.** Output is probability a voxel belongs to a group of high probability voxels.

$$p_P(x, y, z) = \prod_{i=x-W}^{x+W} \prod_{j=y-W}^{y+W} p_F(i, j, z), \quad (3)$$

where, p_F is the foreground probability and W is the expected size of a punctum.

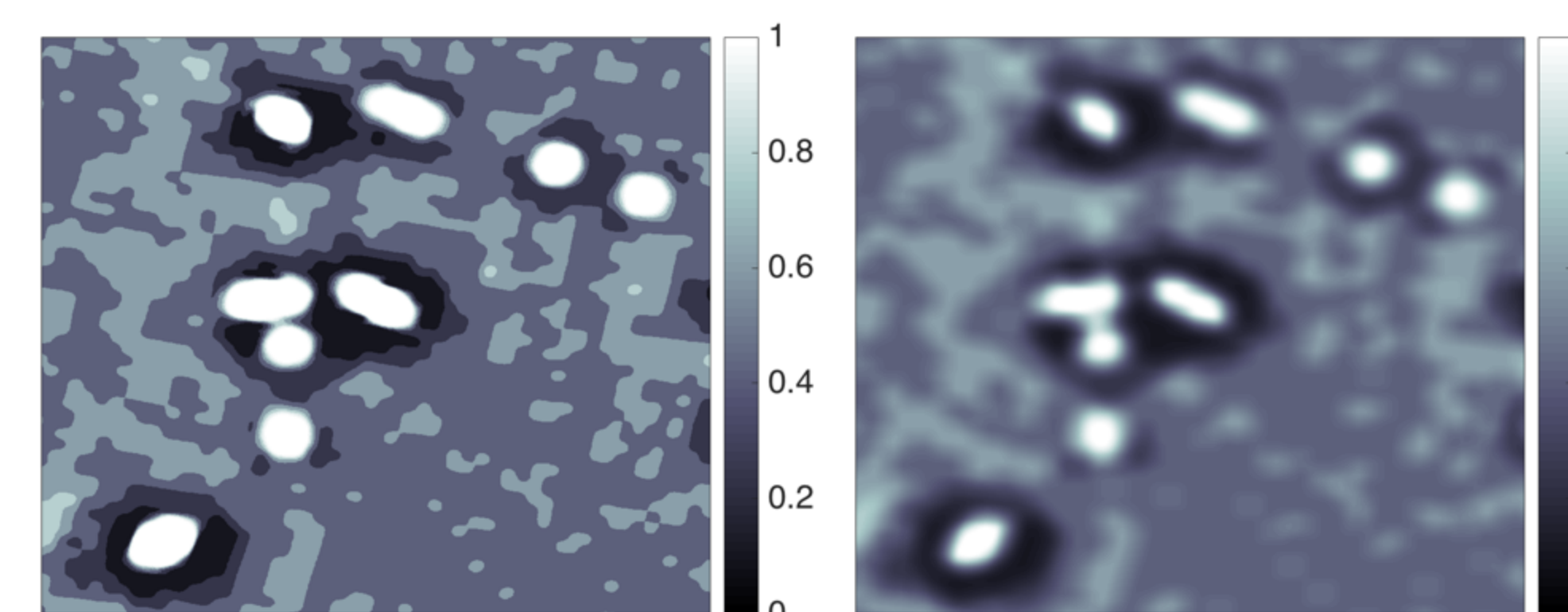


Figure 5: (Left) Probability map from step one. (Right) Corresponding probability map of each pixel belonging to a 2D punctum.

- Step 3: 3D Puncta Probability** Punctum which do not span multiple slices are down weighted by a factor, $f(x, y, z)$

$$f(x, y, z) = \exp \left\{ - \sum_{j=j_{start}}^{j=j_{end}} [p_P(x, y, z) - p_P(x, y, z + j)]^2 \right\} \quad (4)$$

$$p_{3DP}(x, y, z) = p_P(x, y, z) f(x, y, z), \quad (5)$$

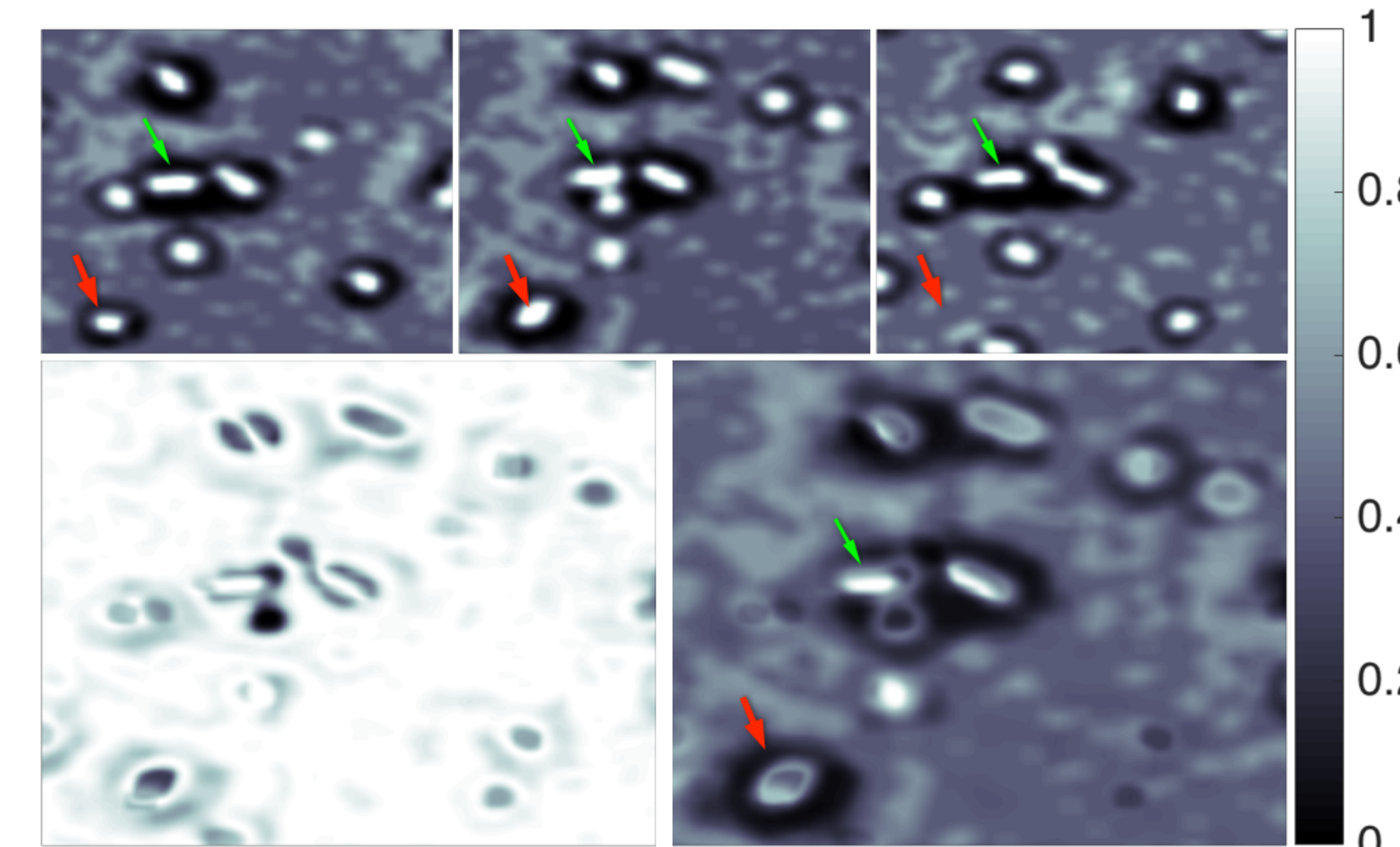


Figure 6: **Top:** Three consecutive slices of the 2D puncta probability. **Bottom:** Factor image given by Eq. (4) (left) and the corresponding 3D puncta probability (right) of the center slice in the top row. Each image is a cutout of size 2261×2501 pixels or $5.268 \times 5.827 \mu m$.

- Step 4: Presynaptic and Postsynaptic Puncta Adjacency.** For the final output, multiply the postsynaptic probability by the maximum presynaptic probability value in an adjacent region.

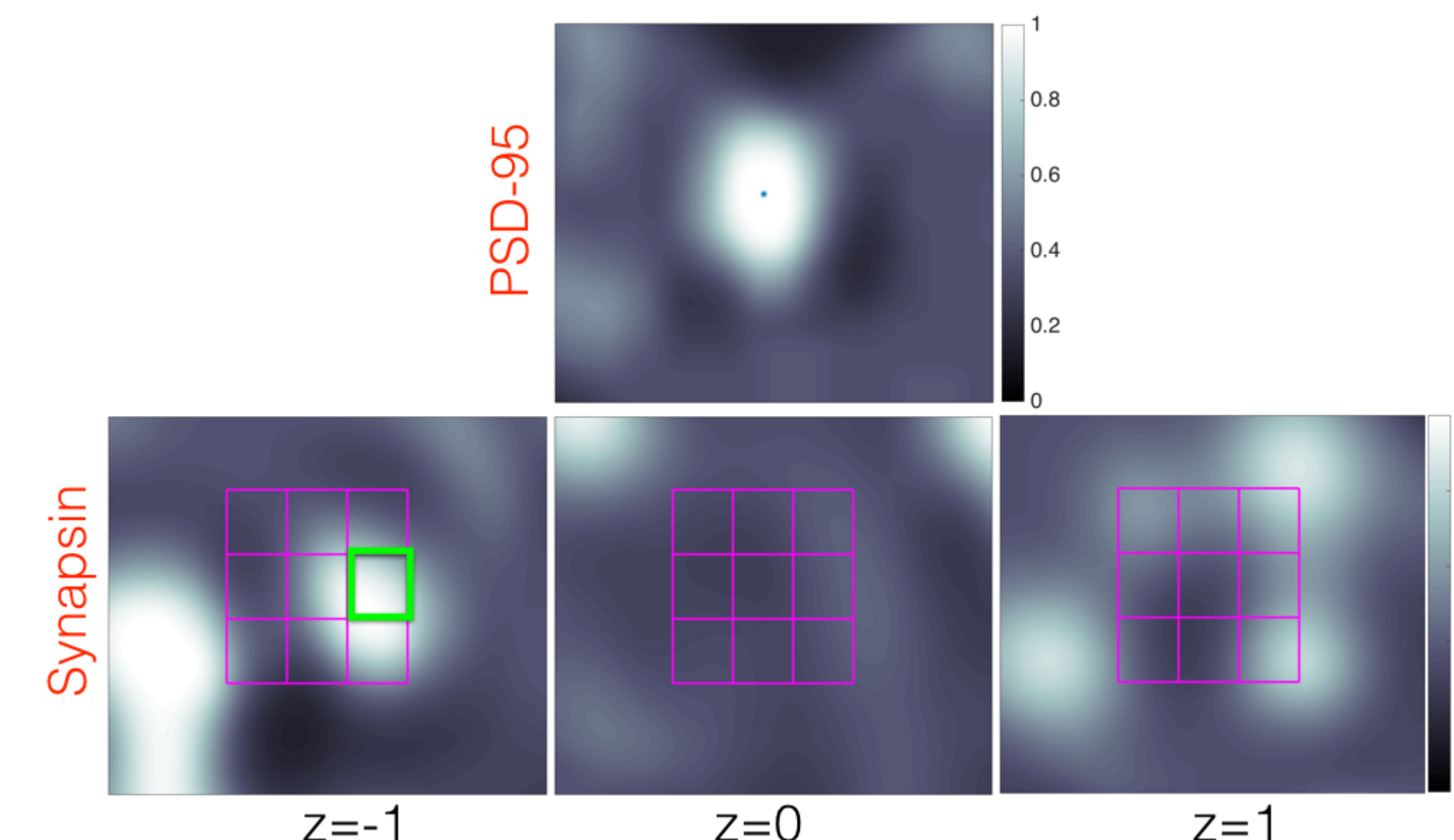


Figure 7: First row: cutout of PSD-95 Punctum with center pixel highlighted. Second row: synapsin cutouts with the search grid overlaid.

Resolution

- Sample Query:

Query	Presynaptic		Postsynaptic	
	Antibody	Puncta Size (x,y,z) μm	Antibody	Puncta Size (x,y,z) μm
1	Synapsin GABA	$0.2 \times 0.2 \times 0.21$ $0.2 \times 0.2 \times 0.07$	Gephyrin	$0.2 \times 0.2 \times 0.07$
2	Synapsin VGAT	$0.2 \times 0.2 \times 0.21$ $0.2 \times 0.2 \times 0.07$	Gephyrin	$0.2 \times 0.2 \times 0.07$
3	Synapsin GAD	$0.2 \times 0.2 \times 0.21$ $0.2 \times 0.2 \times 0.07$	Gephyrin	$0.2 \times 0.2 \times 0.07$

Figure 8: A set of inhibitory synapse subtypes

- Results:

Dataset	Excitatory				Inhibitory			
	EM		IF		EM		IF	
KDM-SYN-120905	Precision	Recall	Precision	Recall	Precision	Recall	Precision	Recall
KDM-SYN-140115	0.88	0.91	0.90	0.93	0.82	0.81	0.91	0.91
	0.92	0.94	0.93	0.95				

Figure 9: The relationship between the precision and recall values across a series of thresholds for each cAT dataset.

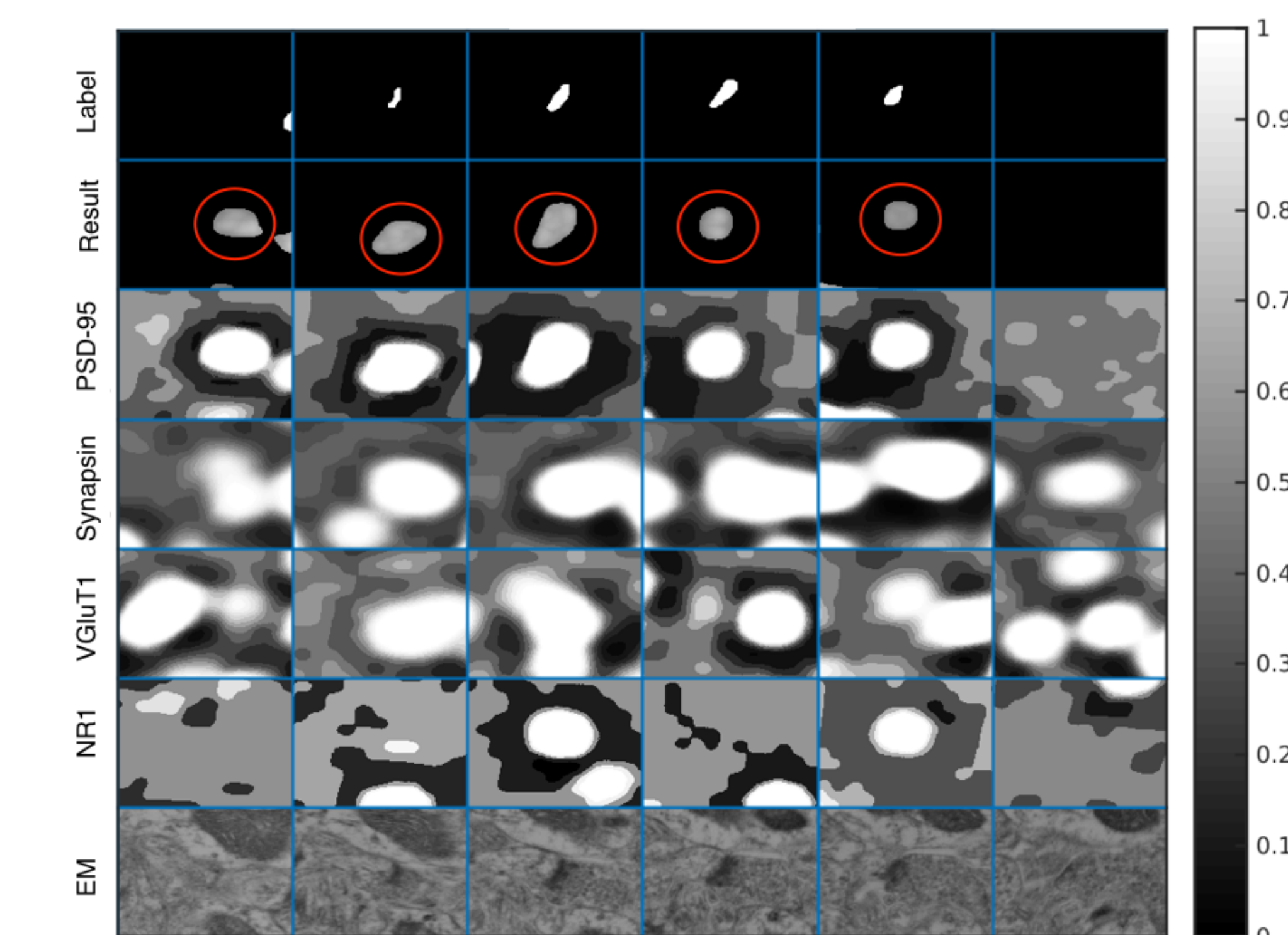


Figure 10: Synaptogram showing the distribution of IF data for an EM identified synapse. Each 'block' is $1.221 \mu m \times 1.233 \mu m$.

Acknowledgments

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