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Cycle-Consistent Multi-Graph Matching for Self-Supervised Annotation of C.Elegans

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The subject

- *Caenorhabditis elegans* (a small worm)
- 1mm long, transparent body
- Stereotypical – always the same cells!

The data

- 3D microscope images
- Cell nuclei segmentations - 558 cells
- Ground truth cell label annotations



Previous State-of-the-Art

Labeled Worms

Corresponding cells (Label **Hyp11**)

Cell statistics

- Position
- Shape

Statistical Model "Atlas"

Unmatched label

↓ Transfer Labels ↓

Unlabeled Worm

→ Can we do this without labels?

Learn Huge Multi-Matchings without Labels

500

100

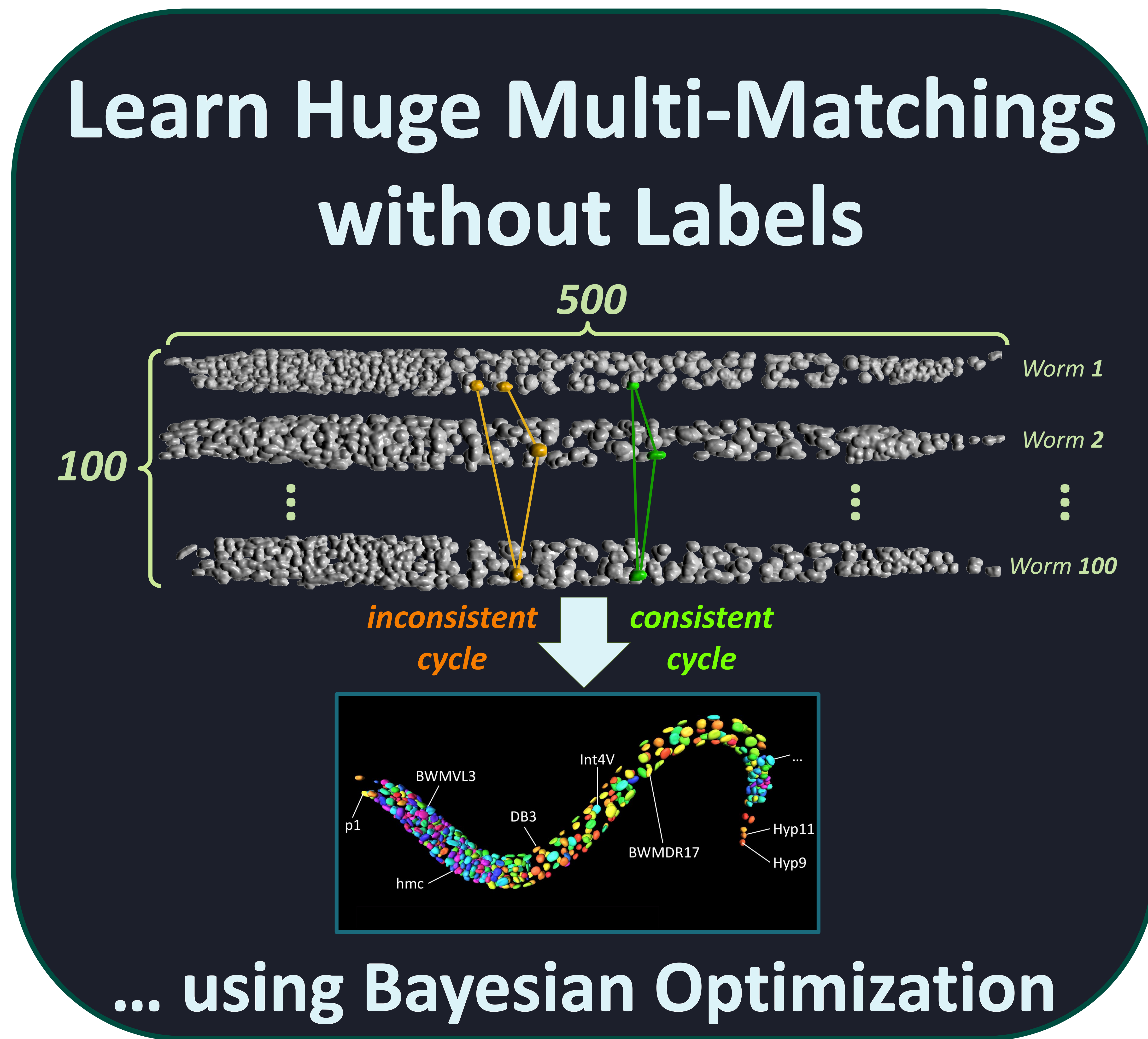
Worm 1

Worm 2

Worm 100

inconsistent cycle

consistent cycle



... using Bayesian Optimization

Our Pipeline

Step 1: Optimize Matching Parameters

1. Match all pairs independently
2. Measure cycle-inconsistency
3. Select new parameters reduce inconsistency
4. Repeat: Build matching problems

Step 2: Build Unsupervised Cell Atlas

Matching cost

Optimized parameters

Multi-Graph matching In union

Unsupervised "Atlas"

Bayesian Optimization

Black box function f

Given prev. results: Decide on new x

$f(x)$

Why Bayesian optimization?

- Piecewise constant objective → Zero gradients
- Limited dimensions – 12 parameters
- Expensive – 5 min per iteration

Step 1: Linear Terms
Linear assignment, dense

Step 2: Sparsity
Multi-objective

Step 3: Quadratic Terms
Graph matching, sparse

Graph Matching (NP-Hard)

Unlabeled Worm

Atlas

Restricted target region $\approx 3\sigma$

Idea

Corresponding cells from consistent multi-graph matching

Cell statistics

- Position
- Shape

Multi-Graph Matching

Goal

Min. sum over all pairwise graph matching problems

... Worm/Graph

... Pairwise graph matching problem

Loss

Inconsistent

consistent

min edit distance

"Synchronization": Fix cycle-errors from pairwise solving

Accuracy Multi-Graph Matching

Accuracy, %

Size of training set

Unsupervised Atlas

Pre-Atlas

Acc. with varying #worms

Atlas Accuracy, %

Size of training set

Unsupervised Atlas

Supervised Atlas

Results

Accuracy (average) ↑

Manual expert segmentation

Naïve unlearned	94.9%
Supervised	96.4%
Unsupervised	96.1%

Automated StarDist segmentation

Naïve unlearned	60.9%
Supervised	91.6%
Unsupervised	82.9%

Euclidean distances

Off-the-shelf segmentation

StarDist

Schmidt U. & Weigert M. et al. "Cell Detection with Star-convex Polygons" MICCAI 2018.