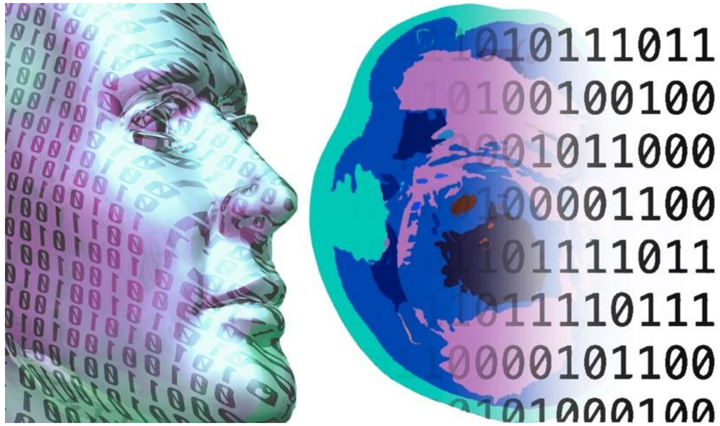
DiffKillR

Smita Krishnaswamy



DiffKillR: Killing and Recreating Diffeomorphisms for Cell Annotation in Dense Microscopy Images

Chen Liu[1*] **Danqi Liao**[1*] **Alejandro Parada-Mayorga**[2*]
Alejandro Ribeiro[3] **Marcello DiStasio**[1] **Smita Krishnaswamy**[1]

[1]Yale University [2]University of Colorado Denver [3]University of Pennsylvania

* These authors are joint first authors.
Please direct correspondence to: `smita.krishnaswamy@yale.edu`.

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- Motivation
- Background
- Methods
  - **DiffKillR**: **Kill**ing and **R**ecreating **Diff**eomorphisms
  - **DiffeoInvariantNet** and **DiffeoMappingNet**
- Experiments & Results
  - Sanity Checks for **DiffeoInvariantNet** and **DiffeoMappingNet**
  - Three Applications on Microscopy Images

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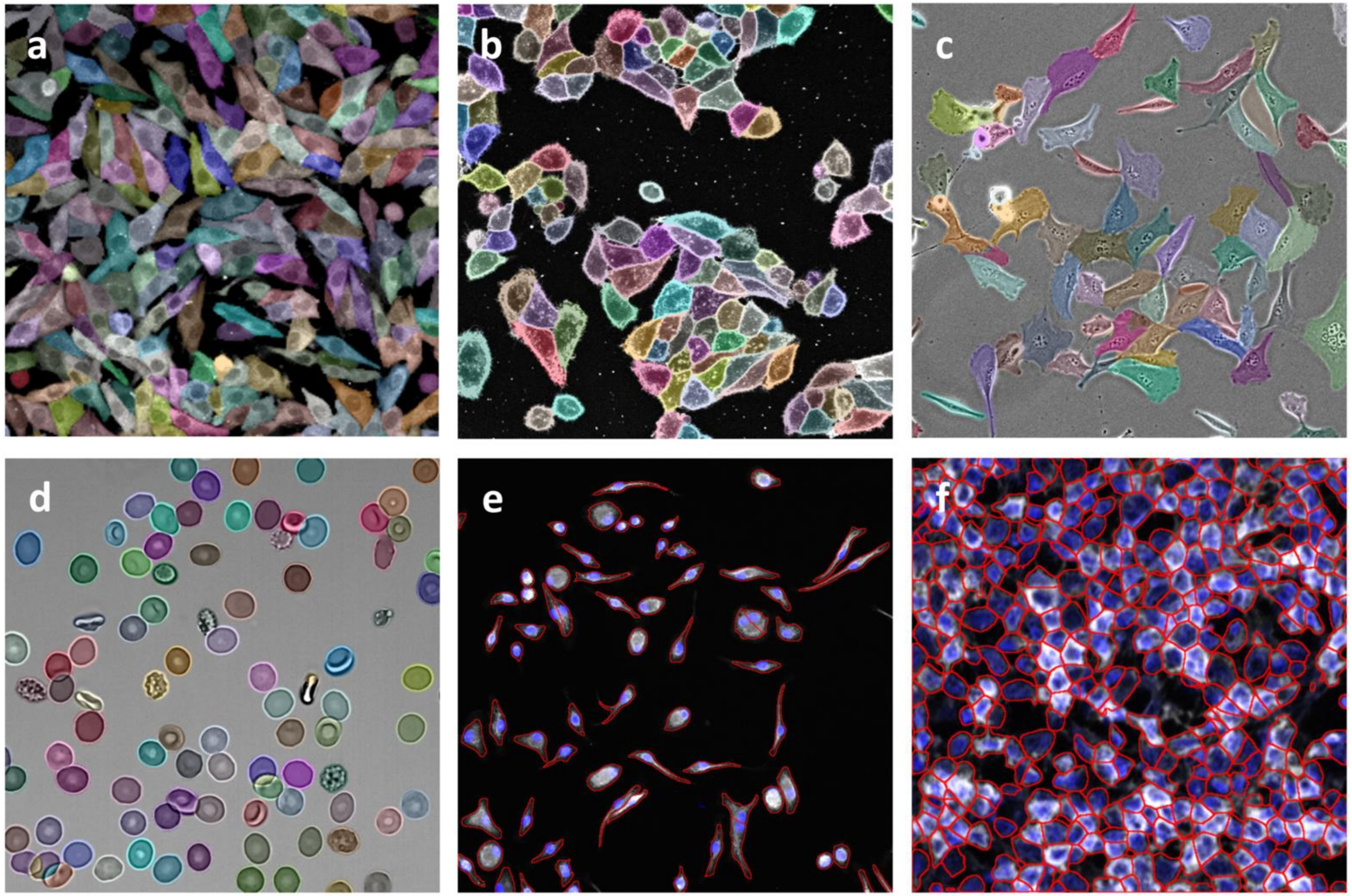

Image Credit to
Cellpose: deep learning-based, generic cell segmentation

Microscopy Image Analysis

- **Heterogeneous**
  - shape
  - appearance
  - morphology
  - modality
- **Diverse Tasks**
  - Cell Counting
  - Orientation Prediction
  - Segmentation
    - nuclei
    - cytoplasm
    - subcellular structures
  - Many others
- **Extremely laborious**

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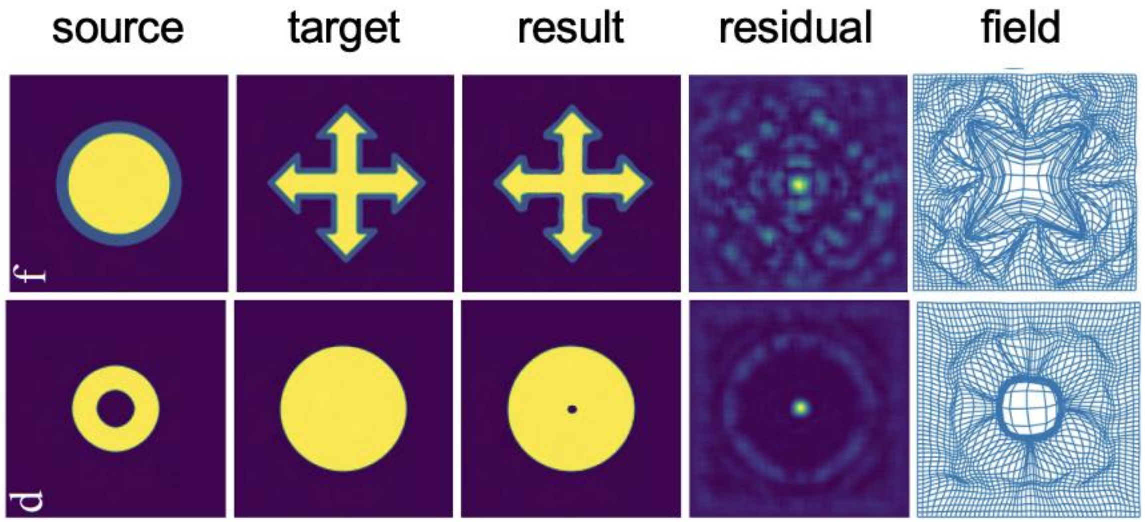
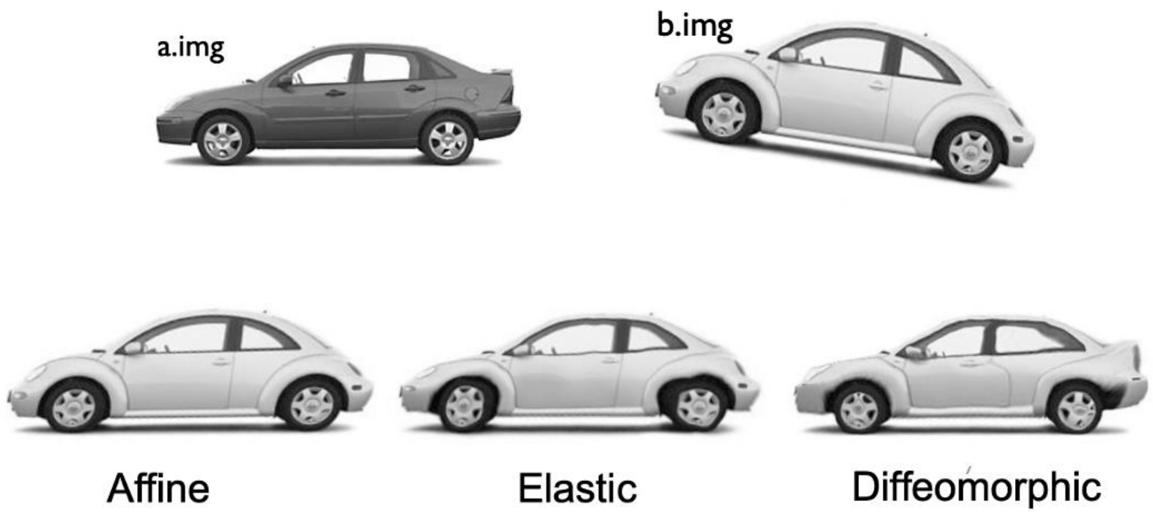
Diffeomorphisms

“A diffeomorphism is a map between manifolds which is differentiable and has a differentiable inverse.”



Examples of diffeomorphisms



Diffeomorphisms allow local warpings

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Methods (1/3): **DiffKillR**: **Kill**ing and **R**ecreating **Diff**eomorphisms

Intuition: Cells exhibit diverse shapes, poses, and morphometric features, but notably, **a small set of archetypes can represent most cells**.

Remark 1: When two cells are **sufficiently similar**, differing only by a diffeomorphism, we can compute the warping field between them. This enables a pixel-perfect mapping of annotation from one cell to the other.

Remark 2: To achieve this, we need a way to measure such “**similarity**” that is invariant to diffeomorphisms.

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Methods (2/3): **DiffKillR**: **Kill**ing and **R**ecreating **Diff**eomorphisms

DiffKillR is a novel framework that reframes cell annotation as the combination of **archetype matching** and **image registration** tasks.

1. Using a small set of annotated archetypes, DiffKillR efficiently propagates annotations across large microscopy images, reducing the need for extensive manual labeling.

2. More importantly, it is suitable for any type of pixel-level annotation.

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Methods (3/3): **Two Complementary Networks**

Remark 1: When two cells are **sufficiently similar**, differing only by a diffeomorphism, we can compute the warping field between them. This enables a pixel-perfect mapping of annotation from one cell to the other.

→ **DiffeoMappingNet**

Sensitive to Diffeomorphisms

Remark 2: To achieve this, we need a way to measure such "**similarity**" that is invariant to diffeomorphisms.

→ **DiffeoInvariantNet**

Invariant to Diffeomorphisms

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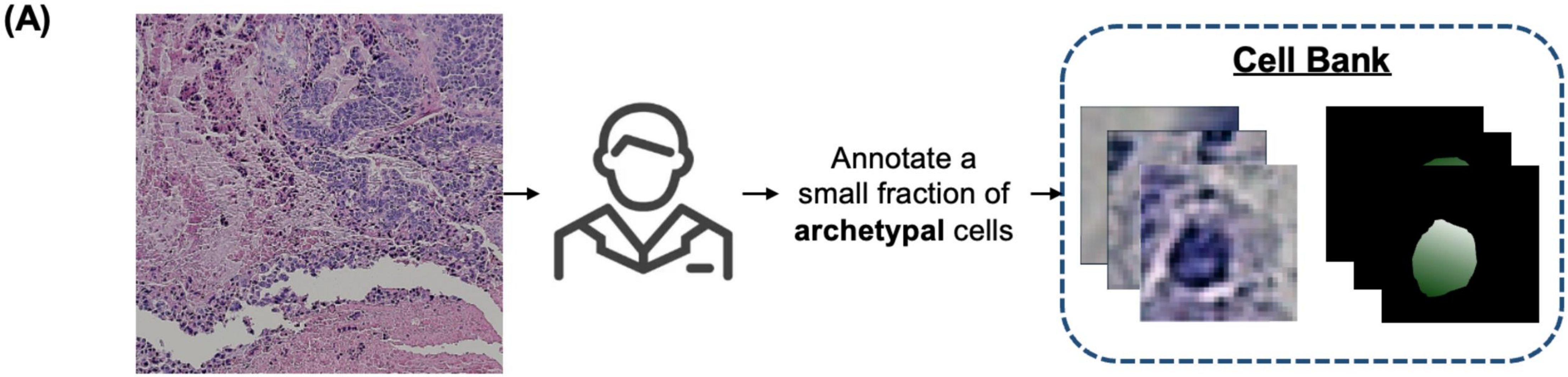
Workflow (1/3): A small set of annotated cells forms a cell bank.

We call them "archetypal" cells, but in practice randomly annotating would be sufficient.



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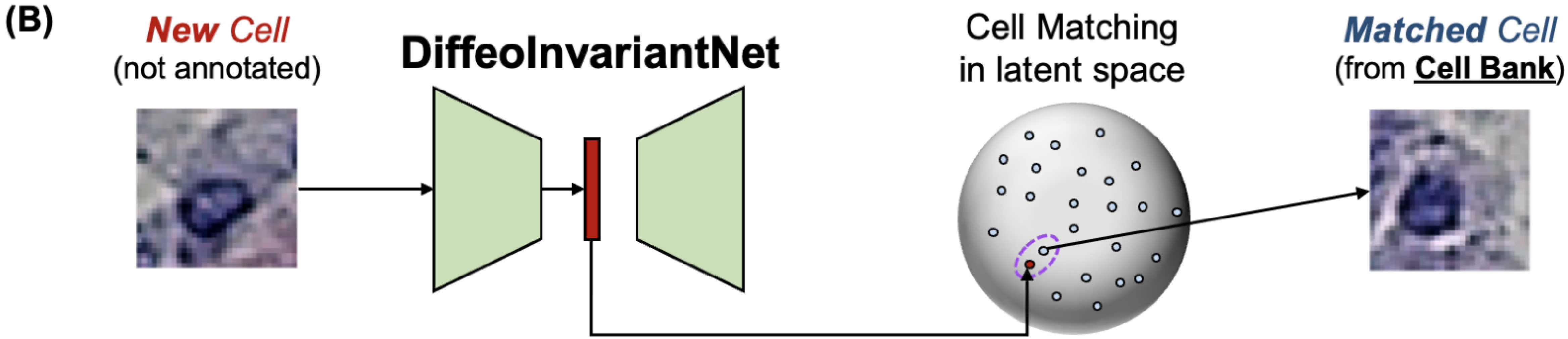
Workflow (2/3): DiffeoInvariantNet learns a latent space that is invariant to common diffeomorphisms. For each new cell, it finds the closest archetypal cell within the cell bank.



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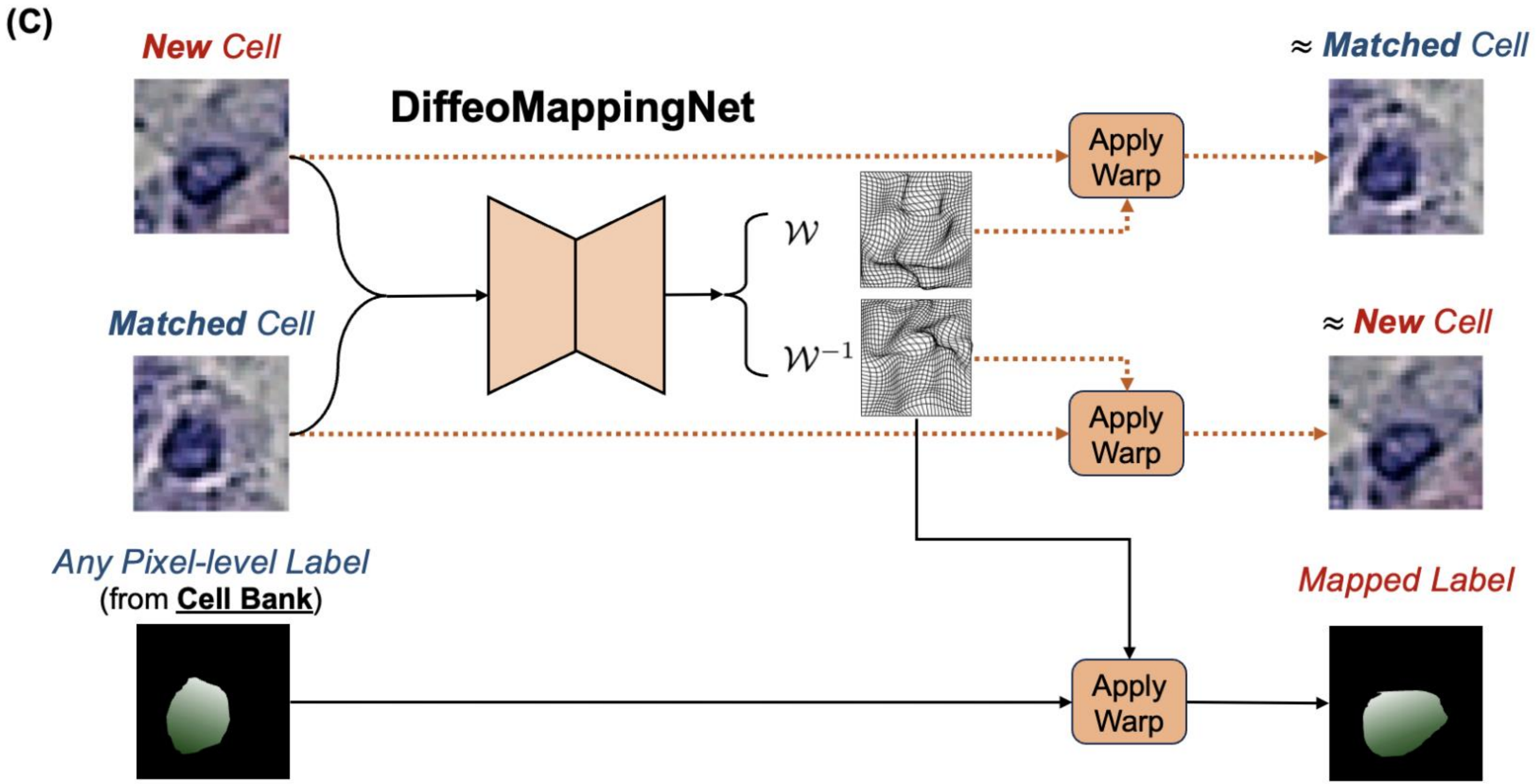
Workflow (3/3): DiffeoMappingNet transforms the label to the new cell using the pairwise diffeomorphism computed via image registration.



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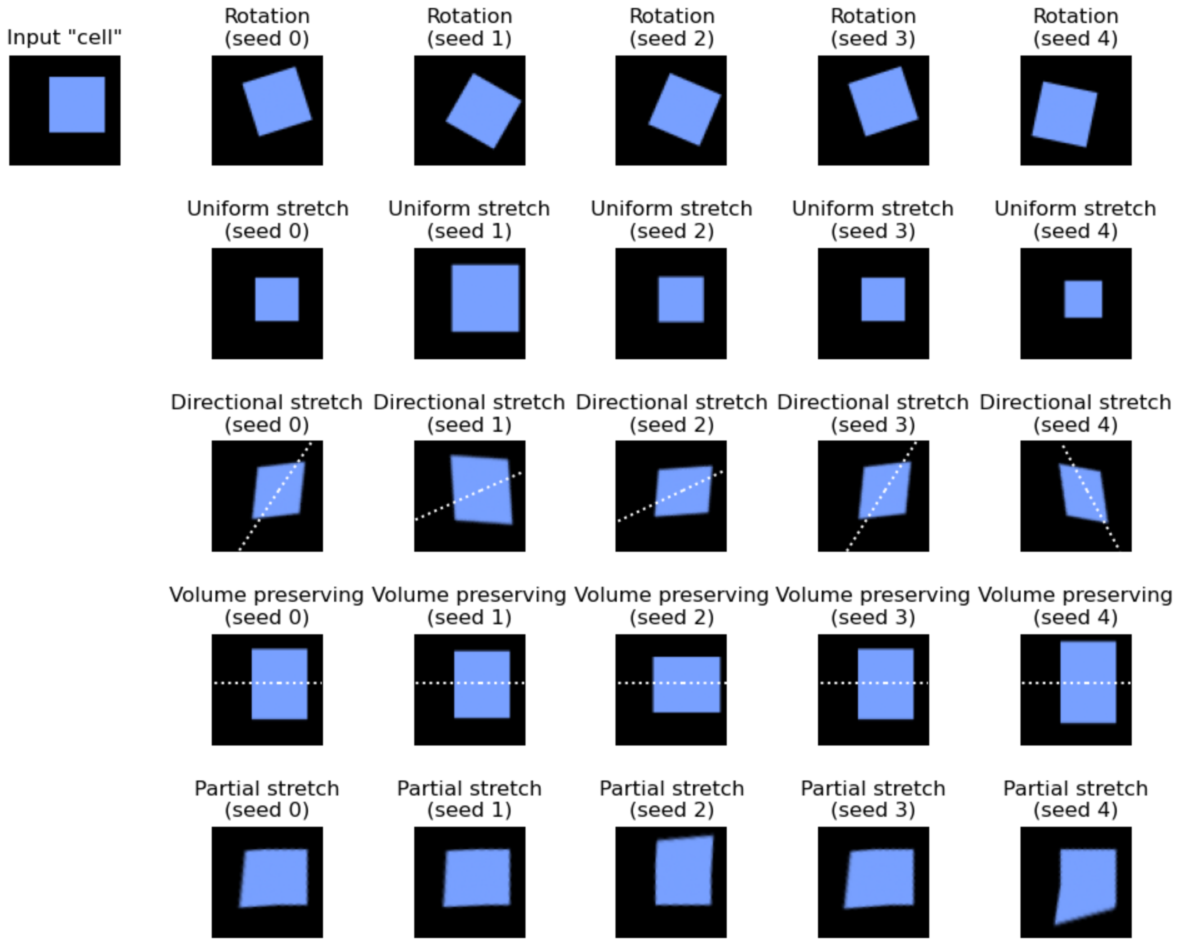
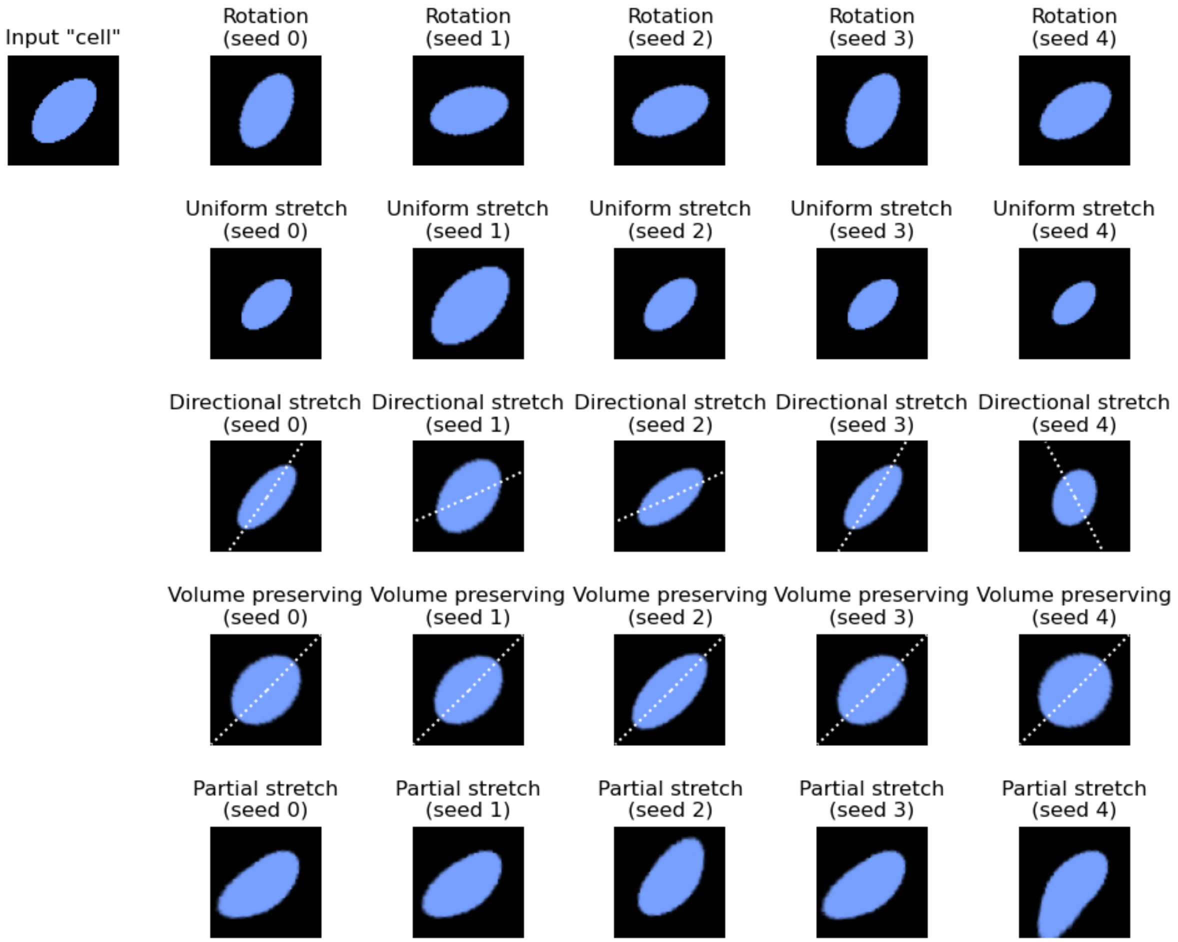
Introducing **realistic diffeomorphisms**





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Sanity Checks for DiffeoInvariantNet

→ Reasonable cell matching results

(matching cells augmented by a realistic diffeomorphism to its source)

TABLE I

CELL MATCHING ON HISTOLOGY IMAGES [30].

	MAP	1-neighbor Accuracy	3-neighbor Accuracy
Breast Cancer	0.954 ± 0.023	0.949 ± 0.009	0.912 ± 0.013
Colon Cancer	0.900 ± 0.004	0.845 ± 0.006	0.830 ± 0.007
Prostate Cancer	0.876 ± 0.012	0.799 ± 0.055	0.808 ± 0.015

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Sanity Checks for DiffeoMappingNet

→ Ablating DiffeoMappingNet architecture on Synthetic Shape Registration

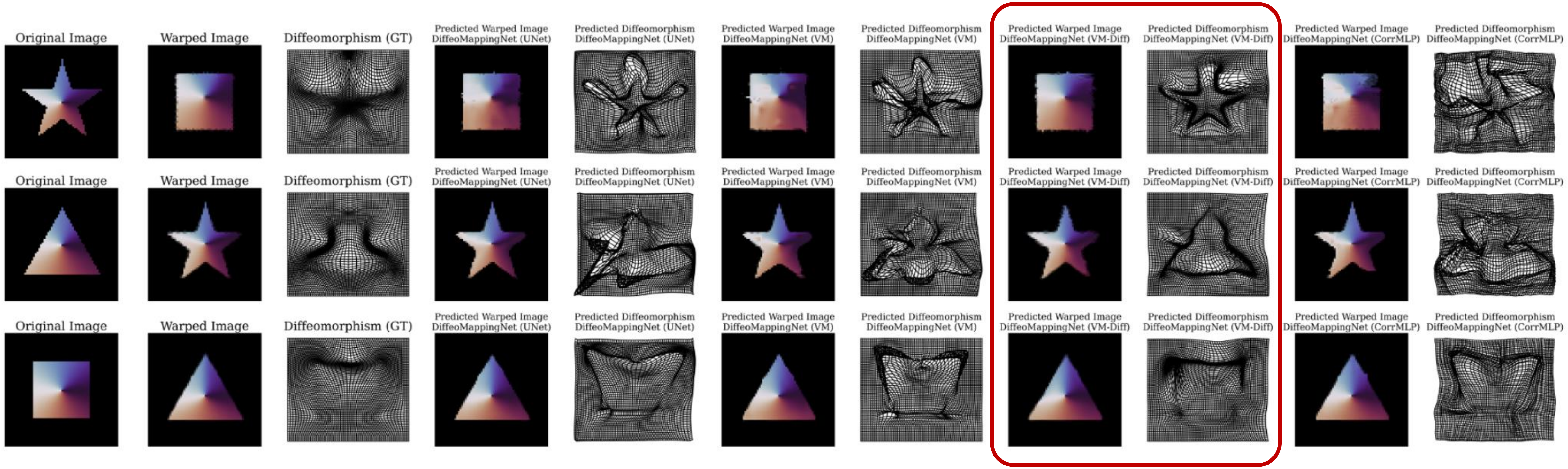

Fig. 2. Mapping diffeomorphisms of synthetic shapes with DiffeoMappingNet.

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Sanity Checks for DiffeoMappingNet

→ Ablating DiffeoMappingNet architecture on Synthetic Shape Registration

TABLE II

DIFFEOMORPHISM PREDICTION ON SYNTHETIC SHAPES.

	UNet [13]	VM [25]	VM-Diff [26]	CorrMLP [27]
NCC ($\mathcal{W}$) ↑	$\underline{-0.096}$ ± 0.961	−0.310 ± 0.899	**0.668** ± 5.397	−0.609 ± 0.527
D_{L1} ($\mathcal{W}$) ↓	1.758 ± 0.443	1.386 ± 0.232	**1.298** ± 0.258	$\underline{1.356}$ ± 0.087
D_{L1} (image) ↓	28.367 ± 2.937	27.180 ± 5.559	**26.621** ± 3.712	$\underline{26.701}$ ± 3.675
DSC (mask) ↑	0.964 ± 0.014	0.957 ± 0.020	$\underline{0.966}$ ± 0.012	**0.972** ± 0.012
IoU (mask) ↑	0.931 ± 0.025	0.918 ± 0.036	$\underline{0.935}$ ± 0.023	**0.946** ± 0.022
Runtime ↓	19.067 ± 1.424	**2.243** ± 0.130	$\underline{3.220}$ ± 0.153	53.281 ± 1.602

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Application 1: Cell Counting

TABLE III

CELL COUNTING PERFORMANCE ON HISTOLOGY IMAGES [30].

		Precision ↑	Recall ↑	F1 ↑
Breast Cancer	Blob Detection	0.488 ± 0.001	0.269 ± 0.020	0.347 ± 0.019
	DiffKillR **(ours)**, 10%	$\mathbf{0.500} \pm 0.076$	$\mathbf{0.719} \pm 0.003$	$\mathbf{0.585} \pm 0.054$
Colon Cancer	Blob Detection	0.323 ± 0.070	0.260 ± 0.044	0.288 ± 0.055
	DiffKillR **(ours)**, 10%	$\mathbf{0.410} \pm 0.051$	$\mathbf{0.500} \pm 0.053$	$\mathbf{0.450} \pm 0.051$
Prostate Cancer	Blob Detection	0.343 ± 0.038	0.264 ± 0.053	0.298 ± 0.048
	DiffKillR **(ours)**, 10%	$\mathbf{0.464} \pm 0.077$	$\mathbf{0.640} \pm 0.046$	$\mathbf{0.531} \pm 0.034$

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Application 2: Cell Orientation Prediction

TABLE IV
CELL ORIENTATION PREDICTION ON EPITHELIAL CELLS.

	Hard Example Mining Ratio	Metric to Identify Best Flip & Rotation	D_{L1} (label) $\downarrow$	D_{θ} (label) $\downarrow$
Matching Archetype's Label	–	–	0.246 ± 0.036	30.29 ± 4.57
Flipping & 90-degree rotations	–	NCC	0.207 ± 0.025	19.67 ± 7.22
DiffKillR **(ours)**	0.00	NCC	$\underline{0.175} \pm 0.030$	$\underline{18.29} \pm 6.90$
	0.25	NCC	$\mathbf{0.168} \pm 0.025$	$\mathbf{17.68} \pm 6.43$
	0.50	NCC	0.189 ± 0.028	19.01 ± 7.25
	0.75	NCC	0.191 ± 0.029	19.06 ± 6.79
	1.00	NCC	0.187 ± 0.076	19.54 ± 7.21
Flipping & 90-degree rotations	–	MI	0.186 ± 0.021	11.34 ± 7.29
DiffKillR **(ours)**	0.00	MI	$\underline{0.152} \pm 0.024$	$\underline{10.25} \pm 6.31$
	0.25	MI	$\mathbf{0.151} \pm 0.039$	$\mathbf{9.74} \pm 5.81$
	0.50	MI	0.178 ± 0.020	10.40 ± 6.70
	0.75	MI	0.180 ± 0.027	10.48 ± 6.53
	1.00	MI	0.196 ± 0.031	11.21 ± 6.83

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Application 3: Few-Shot Cell Segmentation

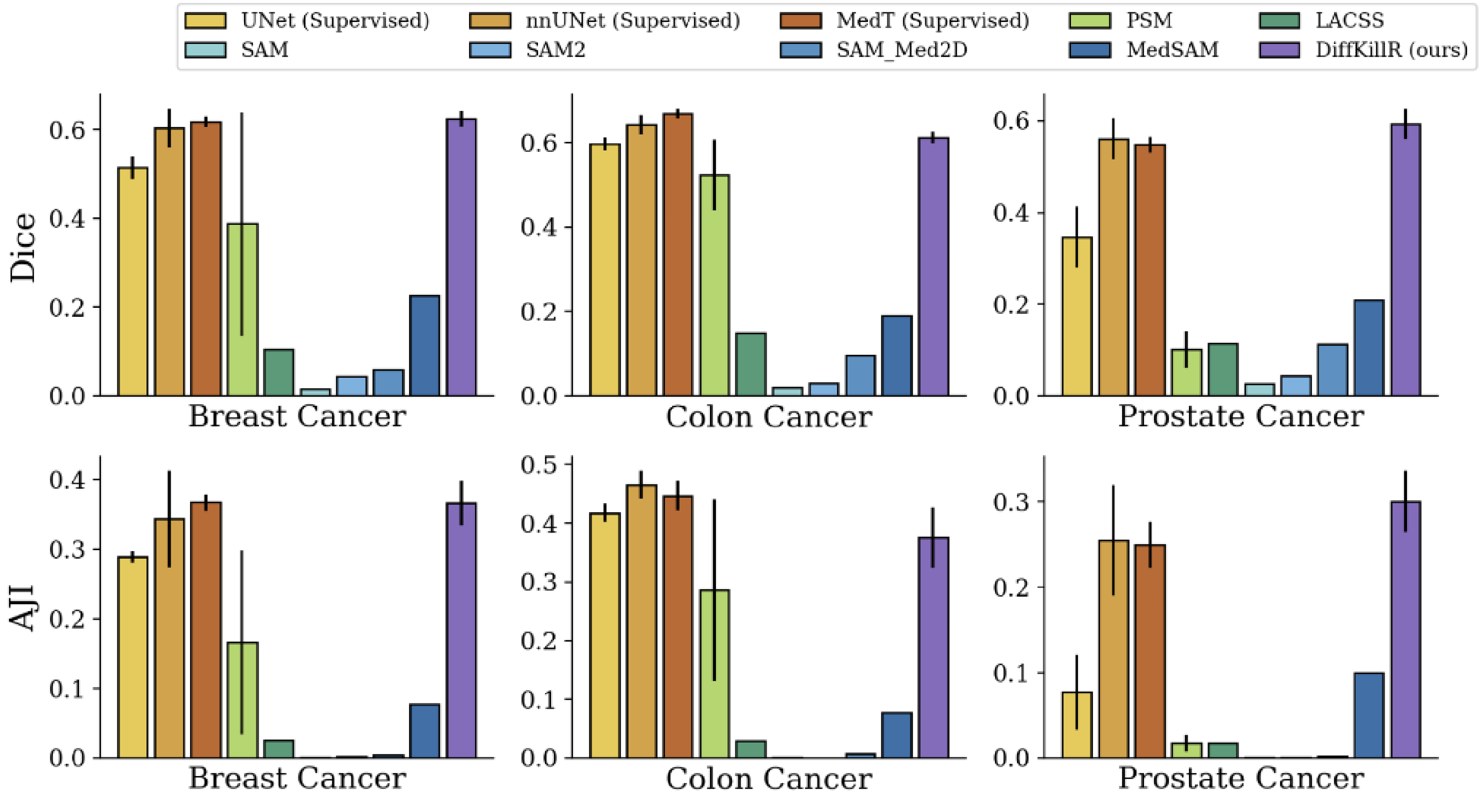

Fig. 3. Few-shot cell segmentation performance on histology images [30].