[ECCV 2024] Mew: Multiplexed Immunofluorescence Image Analysis through an Efficient Multiplex Network

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Mew: Multiplexed Immunofluorescence Image Analysis through an Efficient Multiplex Network

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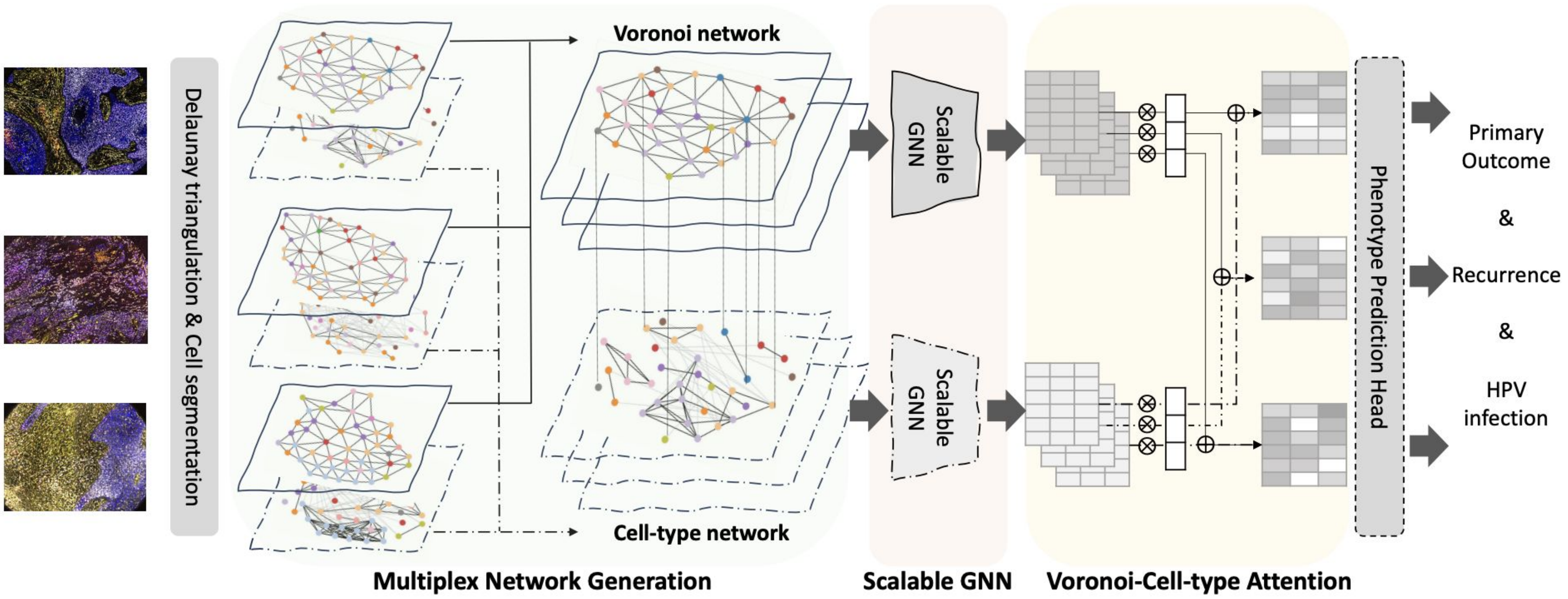
Mew - In a nutshell,

[ECCV 2024] Mew: Multiplexed Immunofluorescence Image Analysis through an Efficient Multiplex Network

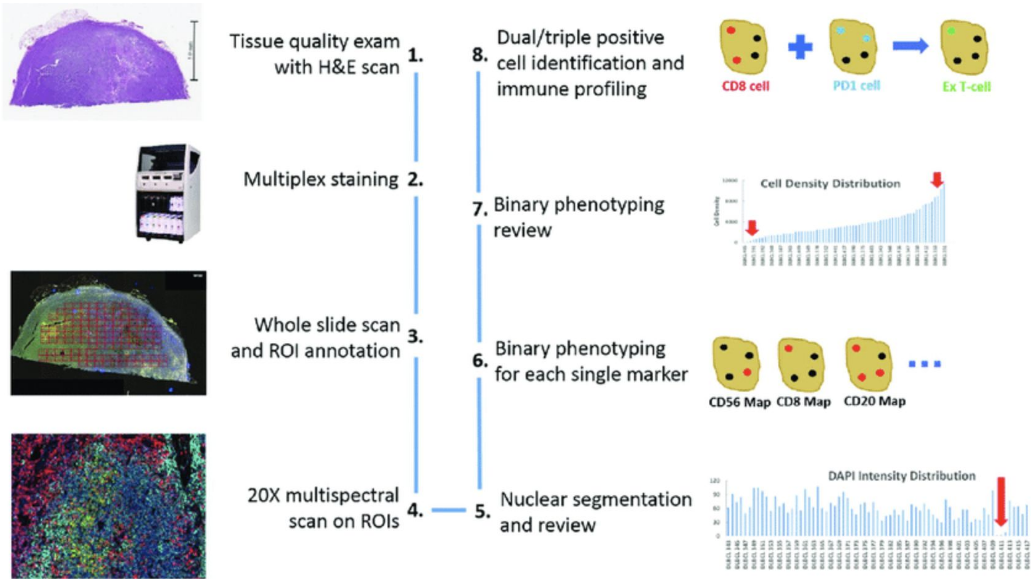
- **Motivation:** Can we alleviate 1) Cellular Heterogeneity 2) Scalability in mIF image analysis?
- **Idea: Mew - Multiplex Network + Efficient Graph Neural Networks**

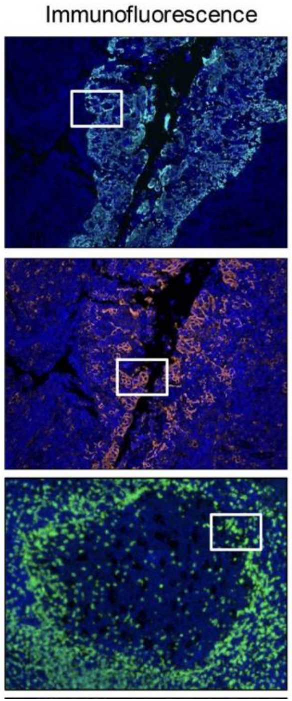


Mew - *Background & Motivation*

mIF image

- **Multiplex immunofluorescence (mIF)**
  - Technique uses <u>multiple fluorescent dyes</u> to label and visualize several target molecules <u>simultaneously</u> in a <u>single tissue</u> sample.
  - Allows for the detailed study of complex cellular interactions and the spatial relationships between different molecules





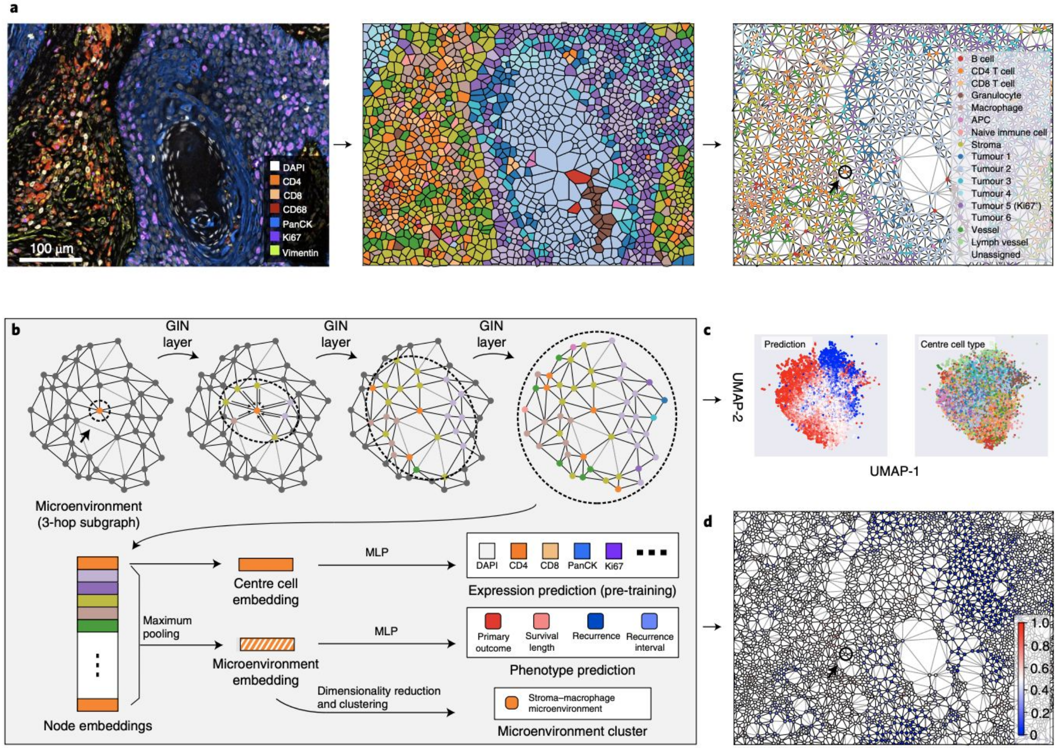
Mew - *Background & Motivation*

Graph ML in mIF image

- Recent advancements of Graph ML
  - [Nature BME 2023] SPACE-GM

Table 1 | Prediction performance on UPMC-HNC and DFCI-HNC tasks

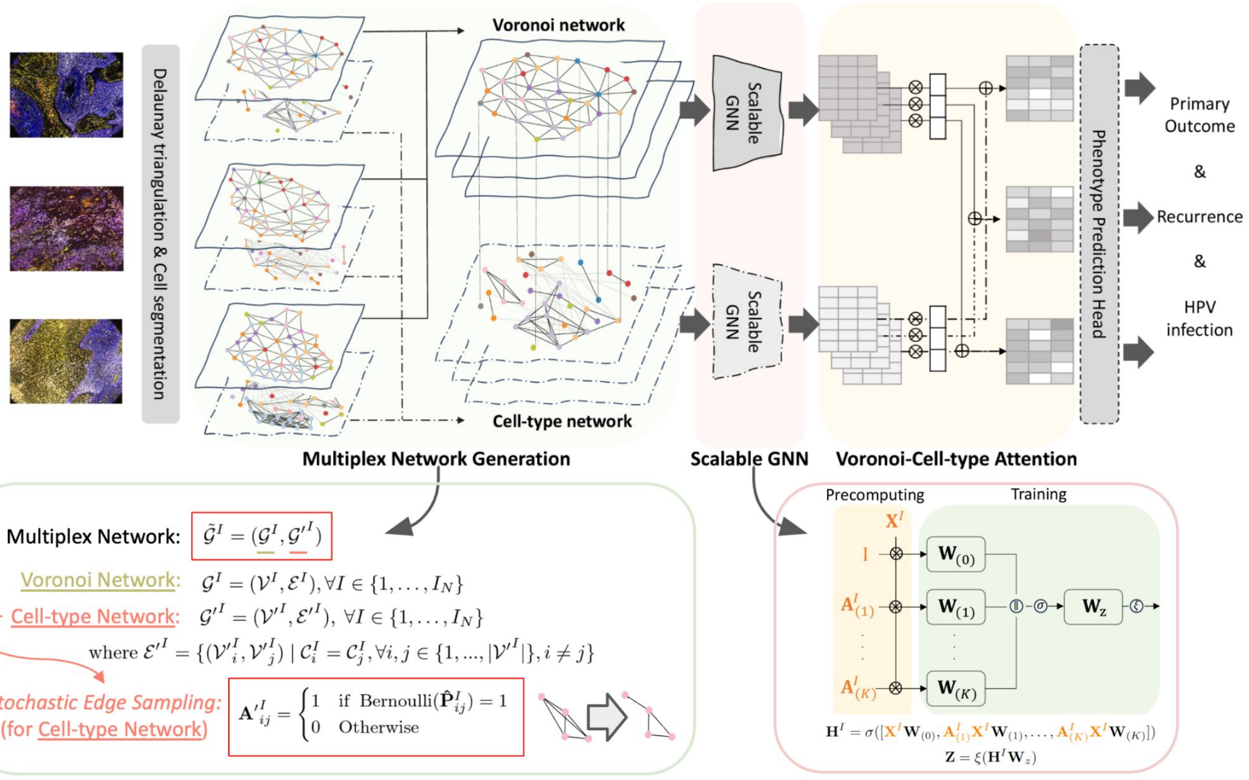
Model	Binary classification (ROC-AUC)			Hazards model (C-index)	Generalization (ROC-AUC)
	Primary outcome	Recurrence	Human papillomavirus (HPV) infection	Survival length	Primary outcome[a]
Linear on composition (sample)	0.783	0.852	0.870	0.696	0.731
MLP on composition (sample)	0.771	0.869	0.879	0.721	0.754
Linear on composition (microenvironment)	0.774	0.823	0.864	0.700	0.799
MLP on composition (microenvironment)	0.814	0.832	0.891	0.751	0.806
SPACE-GM, no-pretraining	0.854	0.882	0.918	0.778	0.853
SPACE-GM	0.867	0.883	0.926	0.799	0.873



Mew - *Methodology*

Mew

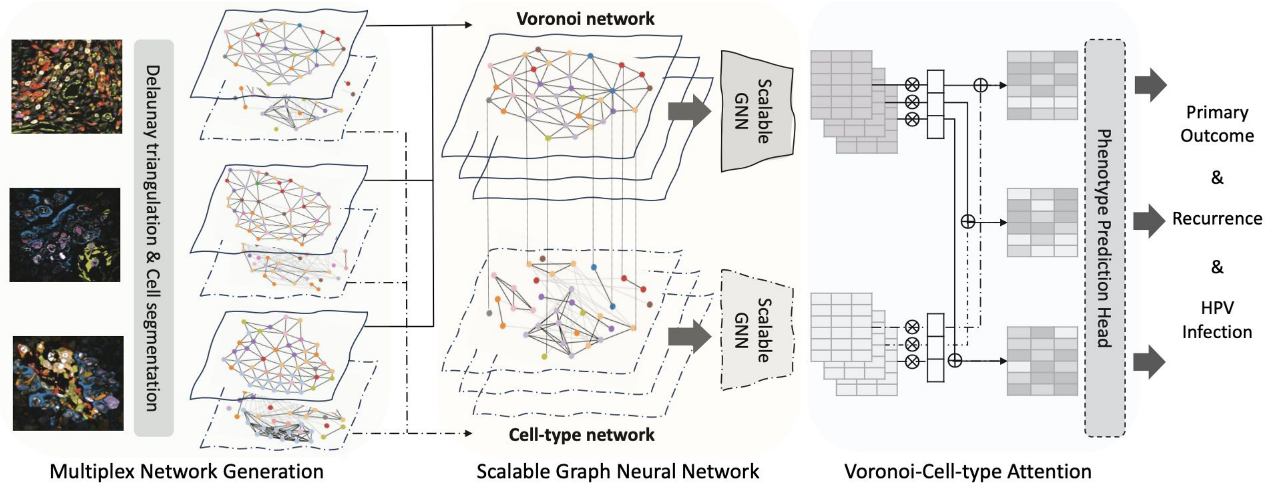
Mew: mIF image through the lens of multiplex network



Mew - *Methodology*

Mew

- (1) Multiplex Network Generation
- (2) Scalable Graph Neural Network
- (3) Voronoi-Cell-type Attention



Algorithm 1 Pseudocode of the proposed algorithm

Input: mpIF image I with its corresponding phenotype $\mathcal{Y}^I$
Output: Pooled Prediction Matrix $\mathbf{P}^I$

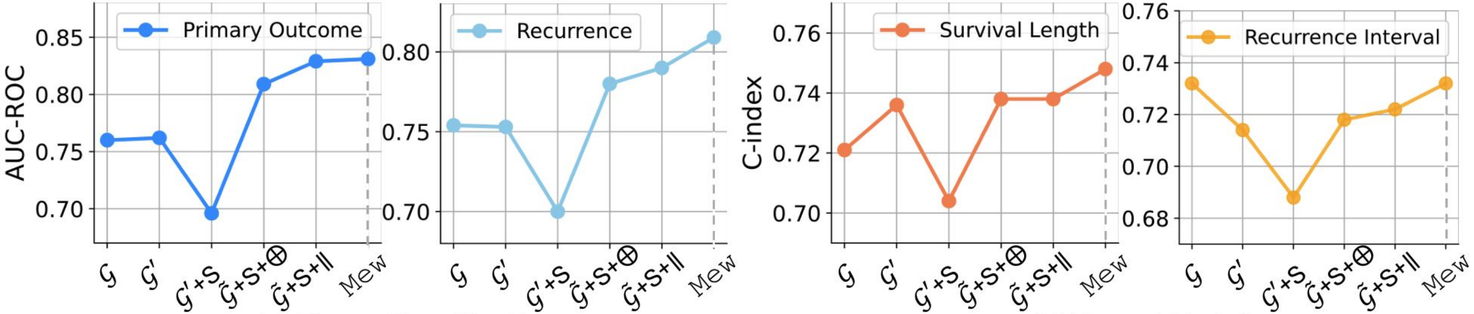
$\mathcal{G}^I \leftarrow (\mathcal{V}^I, \mathcal{E}^I)$ ▷ Voronoi network via preprocessing image I
$\mathcal{E}'^I \leftarrow$ Cell-type Edge Generater$(\mathcal{C}^I, \mathcal{V}^I)$
$\mathcal{G}'^I \leftarrow (\mathcal{V}^I, \mathcal{E}'^I)$ ▷ Cell-type network
$\tilde{\mathcal{G}}^I \leftarrow (\mathcal{G}^I, \mathcal{G}'^I)$ ▷ *Multiplex Network: Voronoi + Cell-type*
$L \leftarrow$ Precomputer$(\mathbf{A}^I, \mathbf{X}^I, K, \text{stochastic}=False)$
$L' \leftarrow$ Precomputer$(\mathbf{A}'^I, \mathbf{X}^I, K, \text{stochastic}=True)$
while not converged **do**
  $\mathbf{H}^I = \sigma([L[0]\mathbf{W}_{(0)}, L[1]\mathbf{W}_{(1)} \dots, L[K]\mathbf{W}_{(K)})$
  $\mathbf{Z}^I = \xi(\mathbf{H}^I \mathbf{W}_z)$
  $\mathbf{H}'^I = \sigma([L'[0]\mathbf{W}_{(0)}, L'[1]\mathbf{W}_{(1)} \dots, L'[K]\mathbf{W}_{(K)})$
  $\mathbf{Z}'^I = \xi(\mathbf{H}'^I \mathbf{W}_z)$
  $\tilde{\mathbf{Z}}^I \leftarrow$ Voronoi-Cell-type Attention$(\mathbf{Z}^I, \mathbf{Z}'^I)$
  $\mathbf{P}^l \leftarrow MLP(\tilde{\mathbf{Z}}^l)$
  $\mathcal{L}_{\text{ce}} \leftarrow CE(\text{Pool}(\mathbf{P}^I), \mathcal{Y}^I)$
end while
function Cell-type Edge Generater$(\mathcal{C}^I, \mathcal{V}^I)$
  $\mathcal{E}'^I = \{(\mathcal{V}'^I_i, \mathcal{V}'^I_j) \mid \mathcal{C}^I_i = \mathcal{C}^I_j, \forall i, j \in \{1, ..., |\mathcal{V}'^I|\}, i \neq j\}$
  return $\mathcal{E}'^I$
end function
function Precomputer$(\mathbf{A}^I, \mathbf{X}^I, K, \text{stochastic}=False)$
  Initialize empty list $L = []$
  Append $\mathbf{X}^I$ to L
  for $k \leftarrow 1$ to $K+1$ **do**
    if stochastic **then**
      $\mathbf{A}^I_{ij} = \begin{cases} 1 & \text{if Bernoulli}(\hat{\mathbf{P}}^I_{ij}) = 1 \\ 0 & \text{Otherwise} \end{cases}$
    end if
    $\mathbf{X}^I \leftarrow \mathbf{A}^I \mathbf{X}^I$
    Append $\mathbf{X}^I$ to L
  end for
  return L
end function
function Voronoi-Cell-type Attention$(\mathbf{Z}^I, \mathbf{Z}'^I)$
  for $\ell \leftarrow 0$ to $|\mathcal{V}^I|$ **do**
    $\alpha_{\ell,\text{Voronoi}} = \frac{\exp(\text{LeakyReLU}(\mathbf{a}^\top \mathbf{z}^I_\ell))}{\exp(\text{LeakyReLU}(\mathbf{a}^\top \mathbf{z}^I_\ell)) + \exp(\text{LeakyReLU}(\mathbf{a}^\top \mathbf{z}'^I_\ell))}$
    $\alpha_{\ell,\text{Cell-type}} = \frac{\exp(\text{LeakyReLU}(\mathbf{a}^\top \mathbf{z}'^I_\ell))}{\exp(\text{LeakyReLU}(\mathbf{a}^\top \mathbf{z}^I_\ell)) + \exp(\text{LeakyReLU}(\mathbf{a}^\top \mathbf{z}'^I_\ell))}$
    $\tilde{\mathbf{z}}^I_\ell = \alpha_{\ell,\text{Voronoi}} \mathbf{z}^I_\ell + \alpha_{\ell,\text{Cell-type}} \mathbf{z}'^I_\ell$
  end for
  return $\tilde{\mathbf{Z}}^I$
end function

Mew - *Experiments*

Patient-level Phenotype Prediction & Ablation Study

	Binary Classification (BC)				Hazard Modeling	Generalization
	Primary Outcome	Recurrence	HPV infection	**Average (BC)**	Survival Length	Primary Outcome
GCN [27]	0.687±0.052	0.751±0.035	0.748±0.064	0.729	0.693±0.045	0.480
GAT [58]	0.690±0.072	0.745±0.009	0.761±0.072	0.732	0.705±0.066	0.531
GraphSAGE [22]	0.708±0.063	0.743±0.034	0.767±0.085	0.739	0.708±0.061	0.430
SIGN [13]	0.715±0.030	0.729±0.030	0.808±0.035	0.751	0.701±0.040	0.467
ClusterGCN [7]	0.714±0.042	0.678±0.044	0.800±0.023	0.731	0.707±0.016	0.676
FAGCN [3]	0.712±0.024	0.785±0.054	0.773±0.031	0.757	0.562±0.056	0.524
HDMI [26]	0.705±0.050	0.807±0.055	0.797±0.062	0.770	0.702±0.041	0.585
SPACE-GM [59]	0.716±0.059	0.767±0.036	0.778±0.052	0.754	0.600±0.129	0.685
Mew	**0.737**±0.060	**0.832**±0.065	**0.813**±0.067	**0.794**	**0.728**±0.044	**0.743**

	Binary Classification (BC)			Hazard Modeling (HM)		
	Primary Outcome	Recurrence	**Average (BC)**	Survival Length	Recurrence Interval	**Average (HM)**
GCN [27]	0.579±0.036	0.630±0.098	0.605	0.571±0.079	0.568±0.087	0.570
GAT [58]	0.539±0.022	0.524±0.043	0.532	0.603±0.012	0.567±0.037	0.585
GraphSAGE [22]	0.540±0.110	0.572±0.093	0.556	0.578±0.068	0.507±0.055	0.543
SIGN [13]	0.522±0.008	0.466±0.076	0.494	0.541±0.096	0.553±0.082	0.547
ClusterGCN [7]	0.545±0.059	0.531±0.060	0.538	0.473±0.136	0.484±0.047	0.479
FAGCN [3]	0.584±0.092	0.498±0.081	0.541	0.567±0.037	0.502±0.021	0.535
HDMI [26]	0.499±0.026	0.483±0.028	0.491	0.565±0.076	0.572±0.033	0.569
SPACE-GM [59]	0.563±0.035	0.524±0.041	0.544	0.492±0.059	0.577±0.043	0.535
Mew	**0.658**±0.030	**0.660**±0.047	**0.659**	**0.631**±0.048	**0.597**±0.083	**0.614**

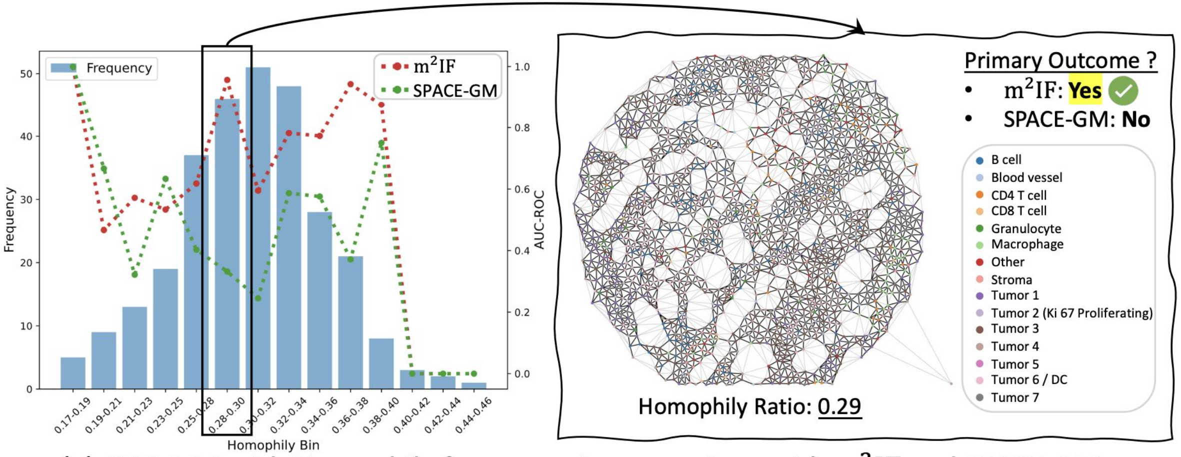


(a) Binary Classification (b) Hazard Modeling

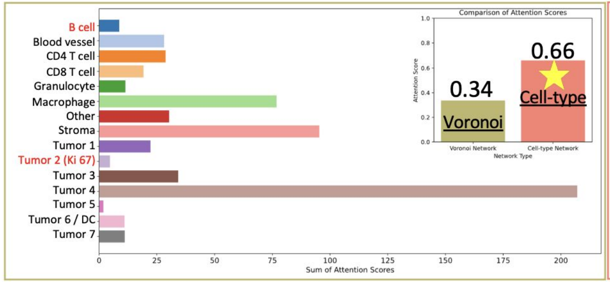
Mew - *Experiments*

In-depth Analysis & Scalability

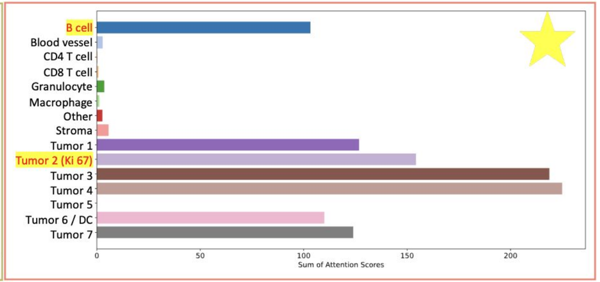
	SPACE-GM (chunk-save)	SPACE-GM (on-the-fly)	Mew
Preprocessing ($\lvert\mathcal{G}\rvert = 308$)	5345.12s	-	75.60s
Training ($\lvert\mathcal{G}\rvert = 16$)	7.03s ($\lvert\bar{\mathcal{V}}\rvert = 1,071$)	20.45s ($\lvert\bar{\mathcal{V}}\rvert = 1,071$)	36.01s ($\lvert\bar{\mathcal{V}}\rvert = 117,974$)
Evaluation ($\lvert\mathcal{G}\rvert = 53$)	60.28s	156.18s	0.53s



(a) AUC-ROC with Homophily frequency in comparison with m^2IF and SPACE-GM



Attention scores for each cell-type in Voronoi Network



Attention Scores for each cell-type in Cell-type Network