Incorporating morphology via deep learning improves classification performance of MALDI imaging for skin lesions

Wanqiu Zhang; Nathan Heath Patterson; Nico Verbeeck; Jessica Moore; Alice Ly; Richard M. Caprioli; Bart De Moor; Jeremy L. Norris; Marc Claesen

AGENTSCHAP INNOVEREN & ONDERNEMEN

Vlaanderen is ondernemen

KU LEUVEN

Aspect Analytics

FRONTIER DIAGNOSTICS

VANDERBILT UNIVERSITY

Background

- As the 3rd most common form of skin cancer, melanoma causes **most** skin cancer deaths

- Current definitive diagnosis of melanoma is mostly based on *histopathologic evaluation*

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Does combining histopathology data with MALDI IMS improve the unimodal classification results on melanoma diagnosis?
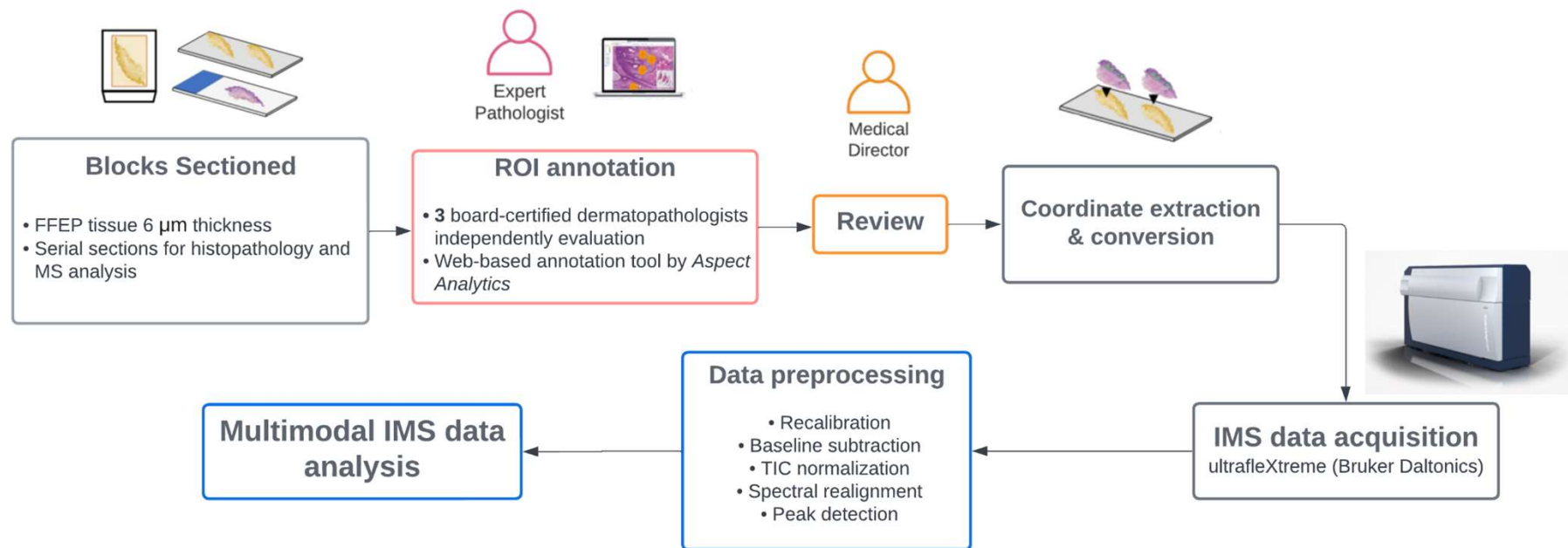
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Malignant melanoma

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Histology-guided IMS sample preparation pipeline

Developed by Aspect Analytics
Booth 324

Histology-guided IMS sample preparation pipeline
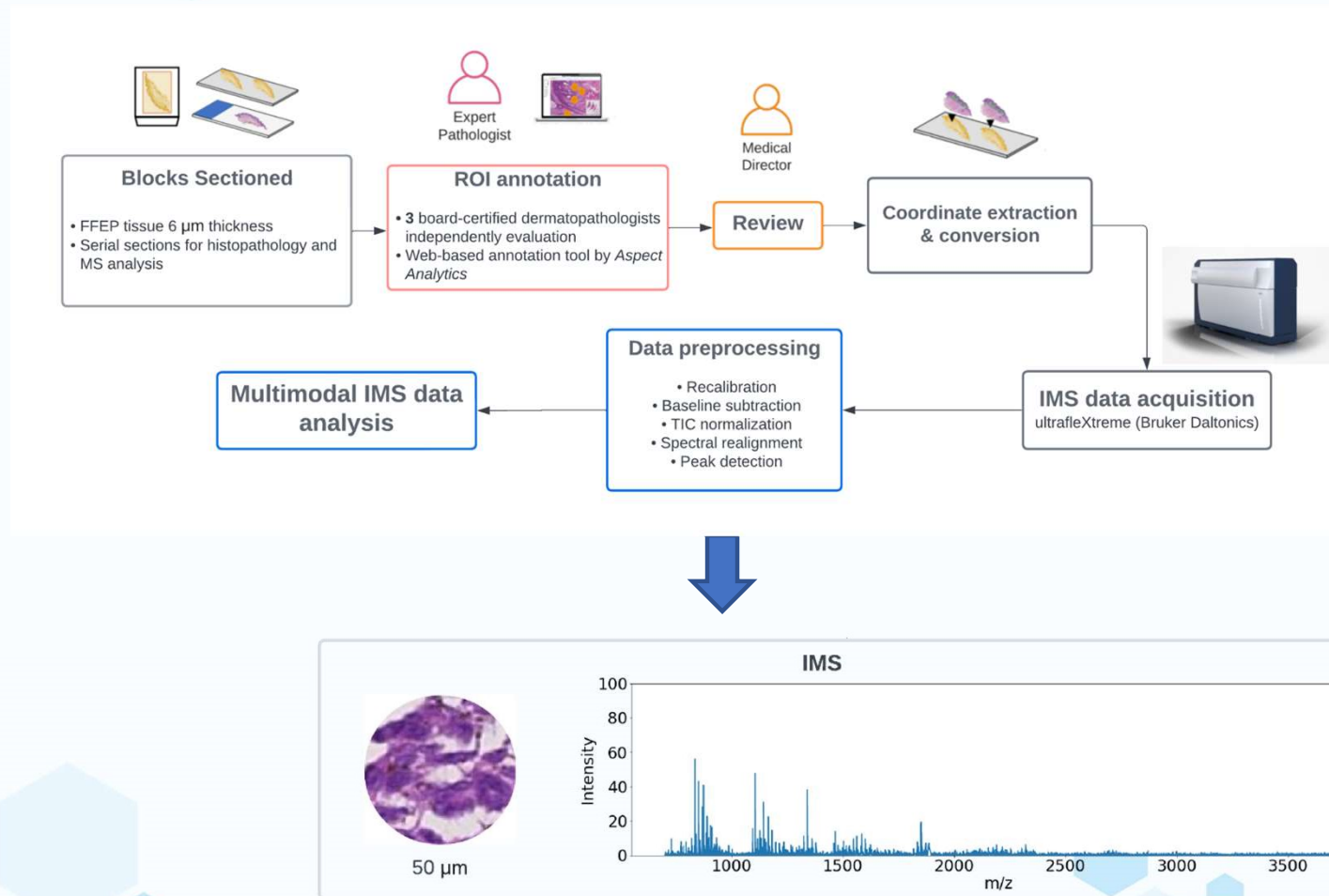
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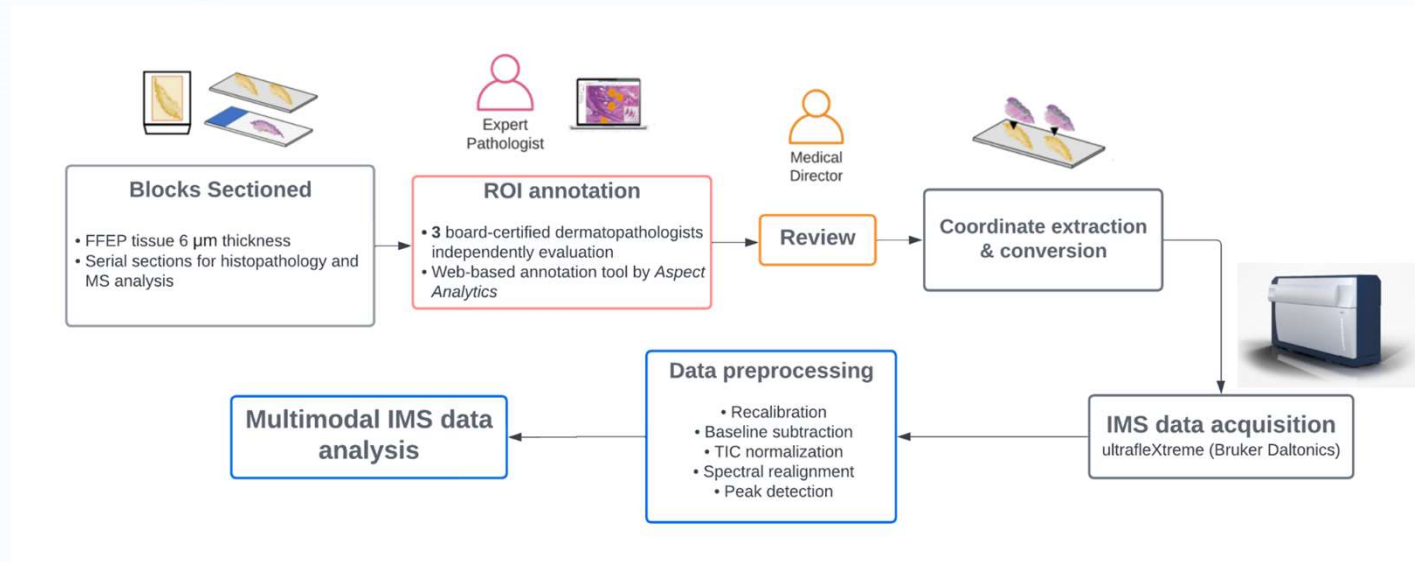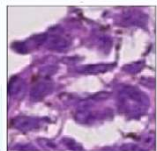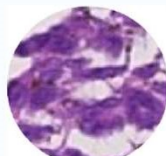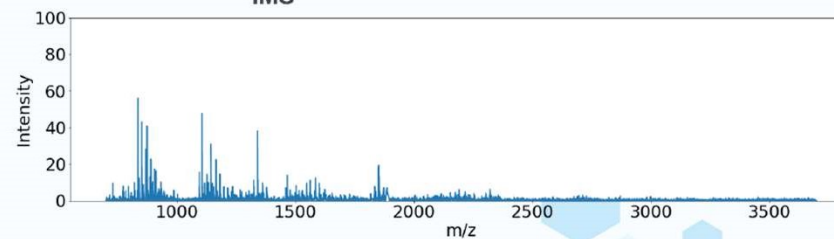
IMS data sample selection
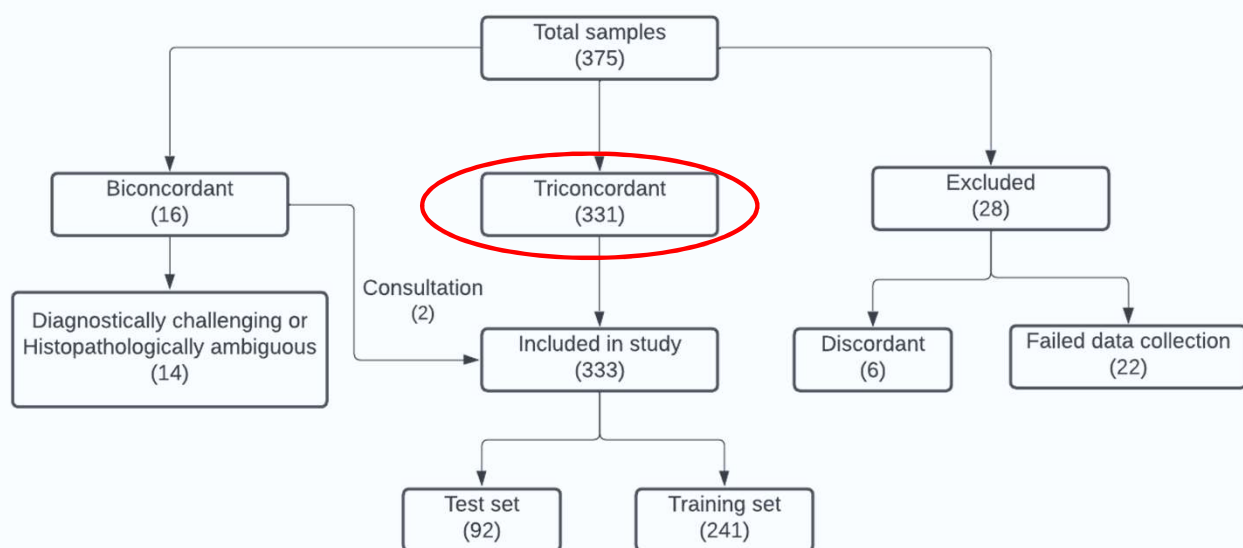
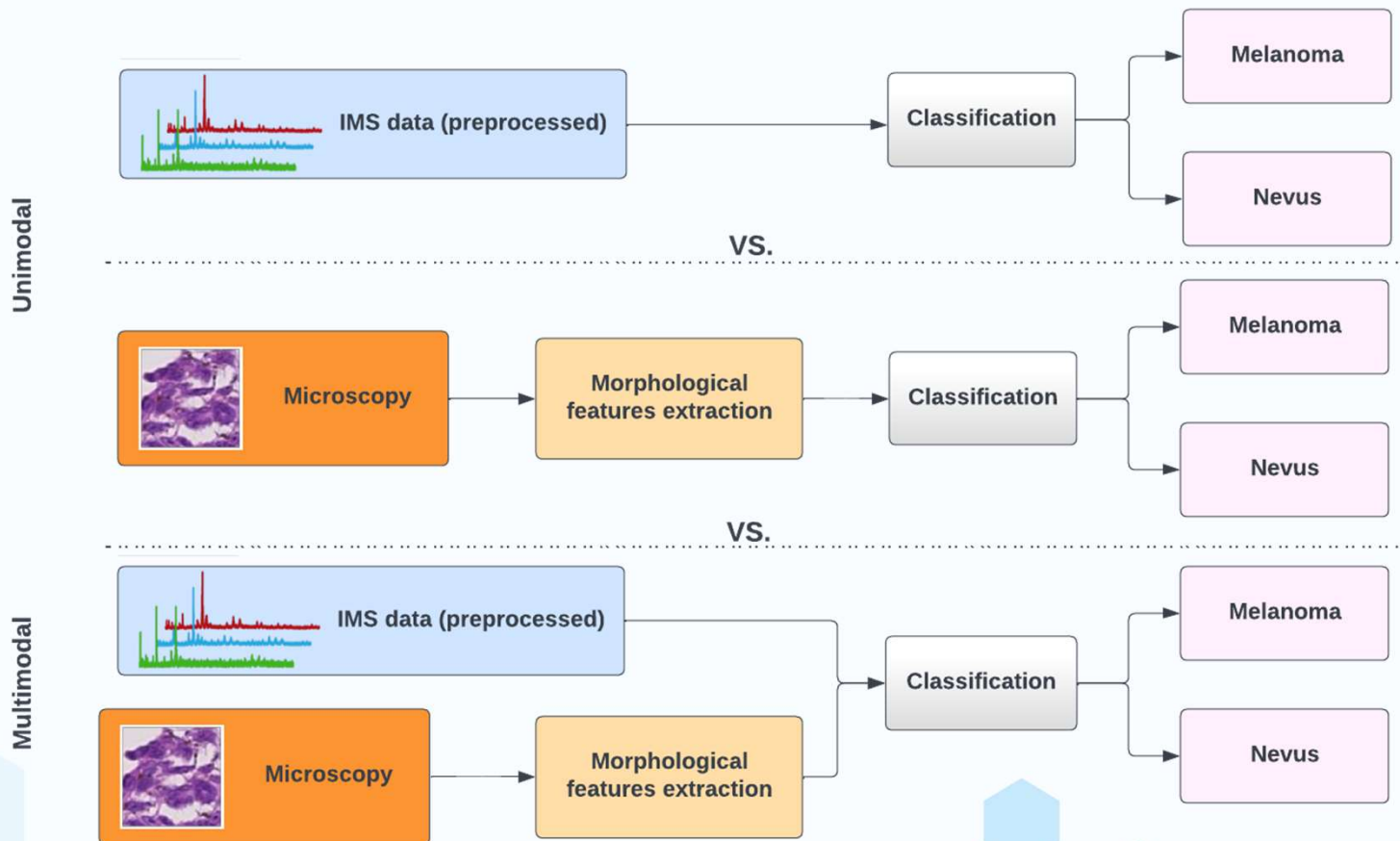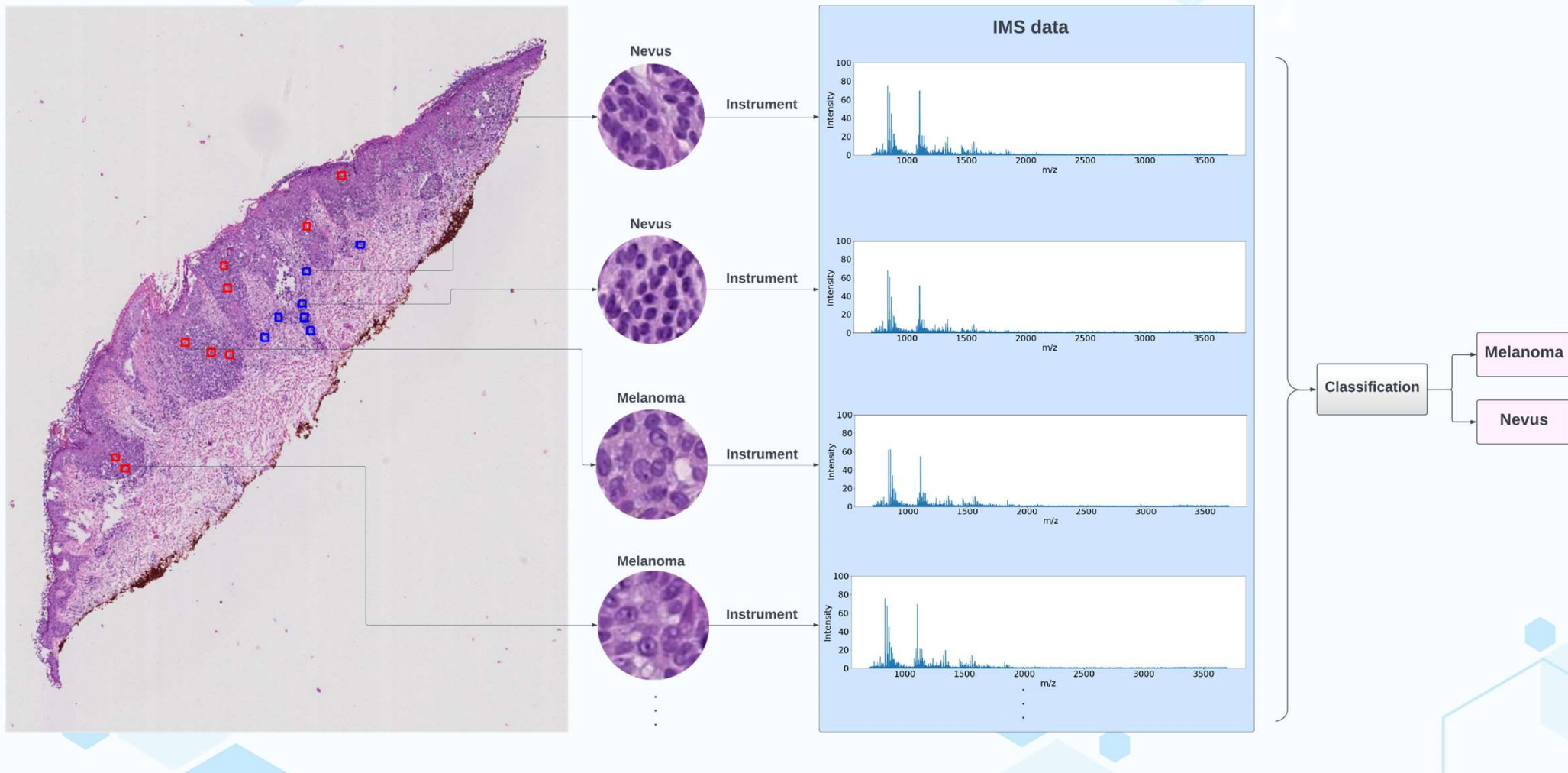
Note: Each sample has 21 annotation spots on average

TABLE 1 Patient demographics for training and test sets

	Training set	Test set
Benign subtype		
Intradermal nevus	75	25
Compound nevus	65	24
Blue nevus	1	0
Total benign	141	49
Melanoma subtype		
Superficial spreading	47	23
Lentigo maligna	26	11
Mel-NOS	9	5
Nodular	8	2
Spitzoid	3	1
Desmoplastic	3	0
Spindle cell	2	1
Nevoid	1	0
Acral	1	0
Total melanoma	100	43
Other clinical parameters		
Mean patient age		
Benign	44.4	39.9
Melanoma	61.3	63.9
Patient sex		
Benign		
Male	52	18
Female	89	31
Melanoma		
Male	55	28
Female	45	15
Mean Breslow depth		
Benign	–	–
Melanoma	1.42 mm	1.12 mm

Al-Rohil, Rami N., Jessica L. Moore, Nathan Heath Patterson, Sarah Nicholson, Nico Verbeeck, Marc Claesen, Jameelah Z. Muhammad et al. "Diagnosis of melanoma by imaging mass spectrometry: Development and validation of a melanoma prediction model." Journal of cutaneous pathology 48, no. 12 (2021): 1455-1462.

Data visualization
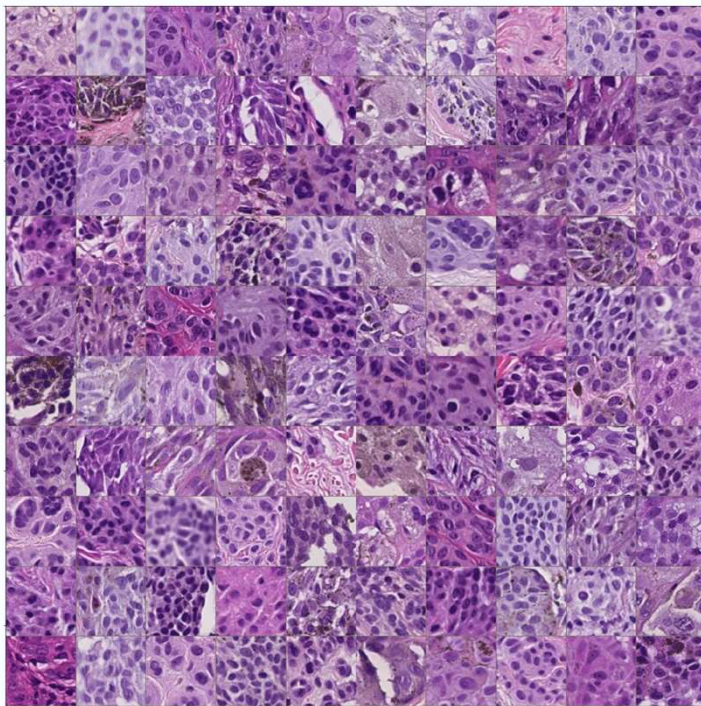
Randomly sampled microscopy data

IMS data
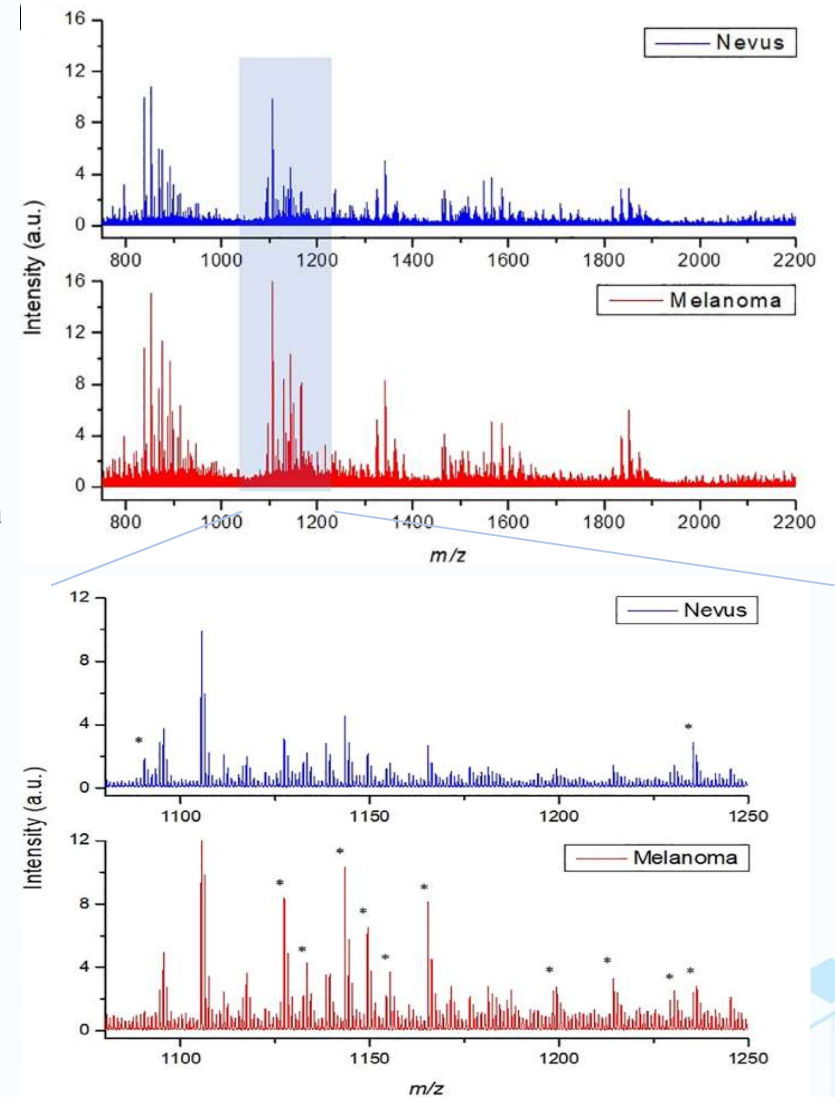
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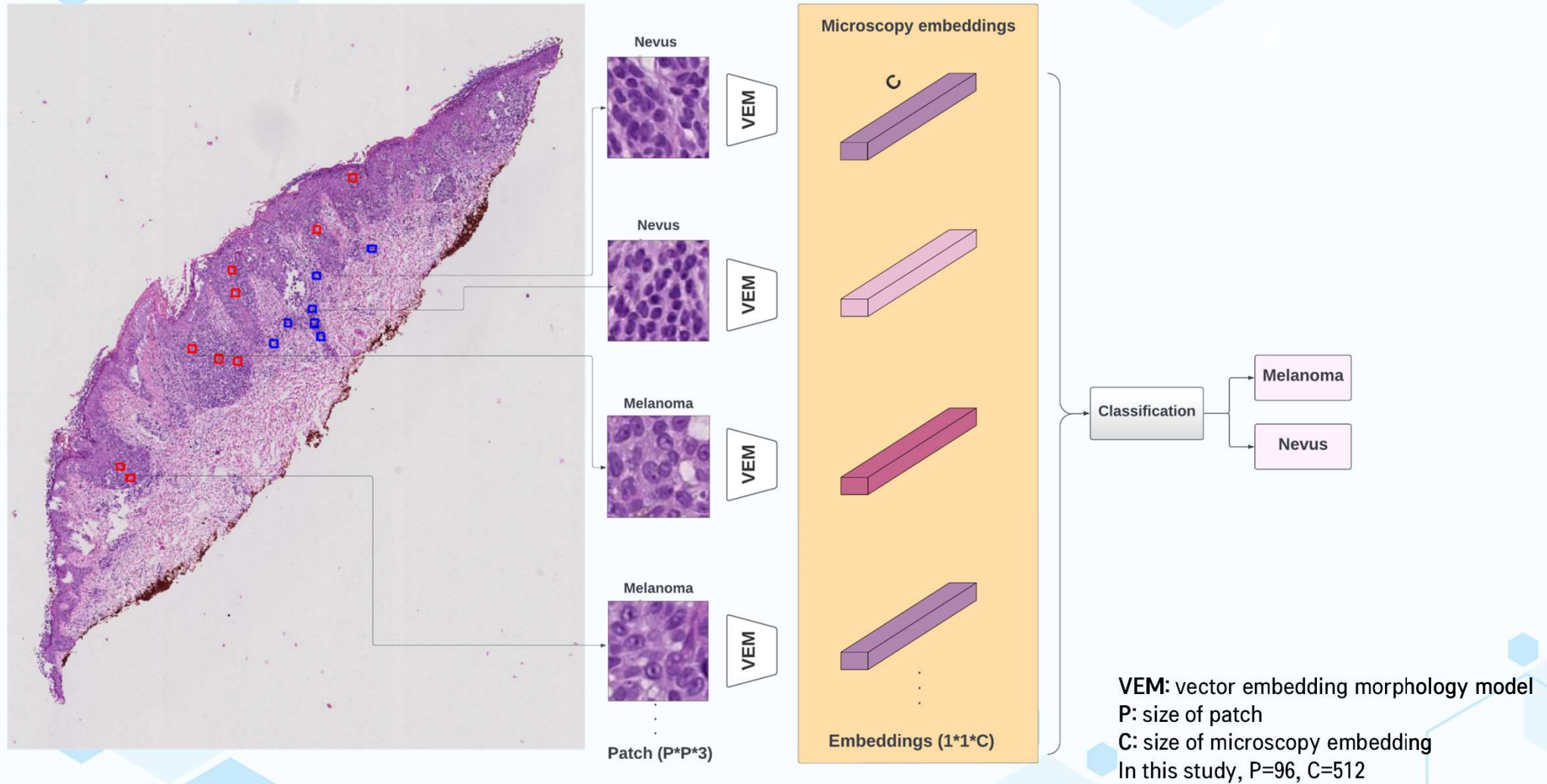
Data analysis pipeline (Study design)
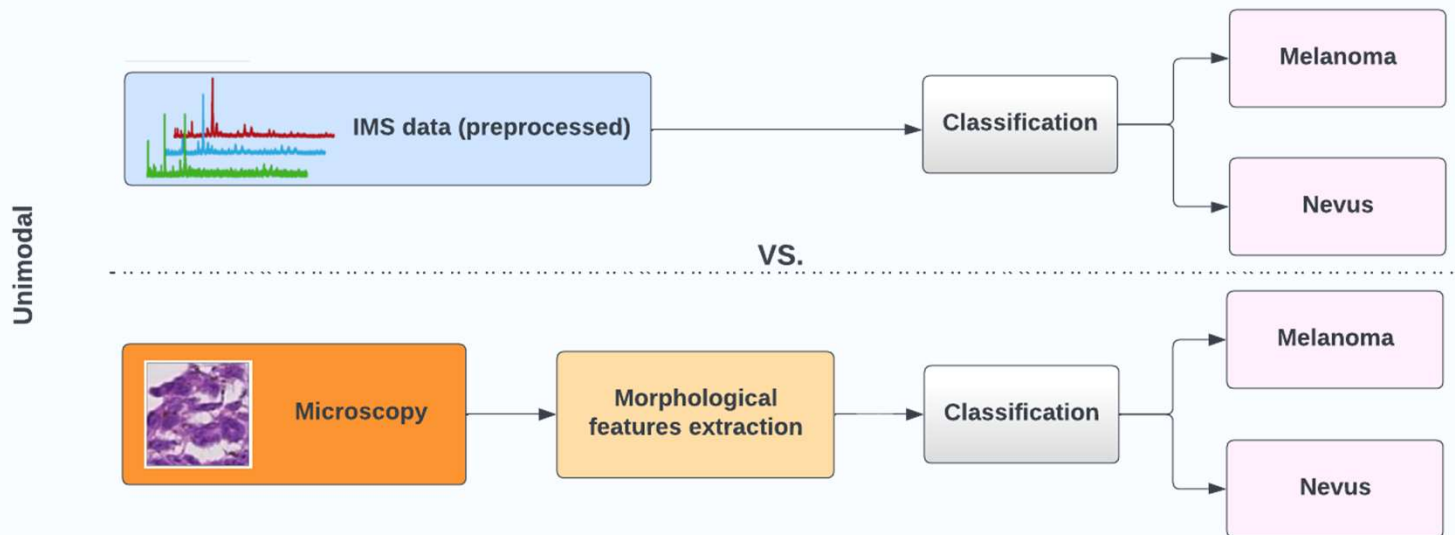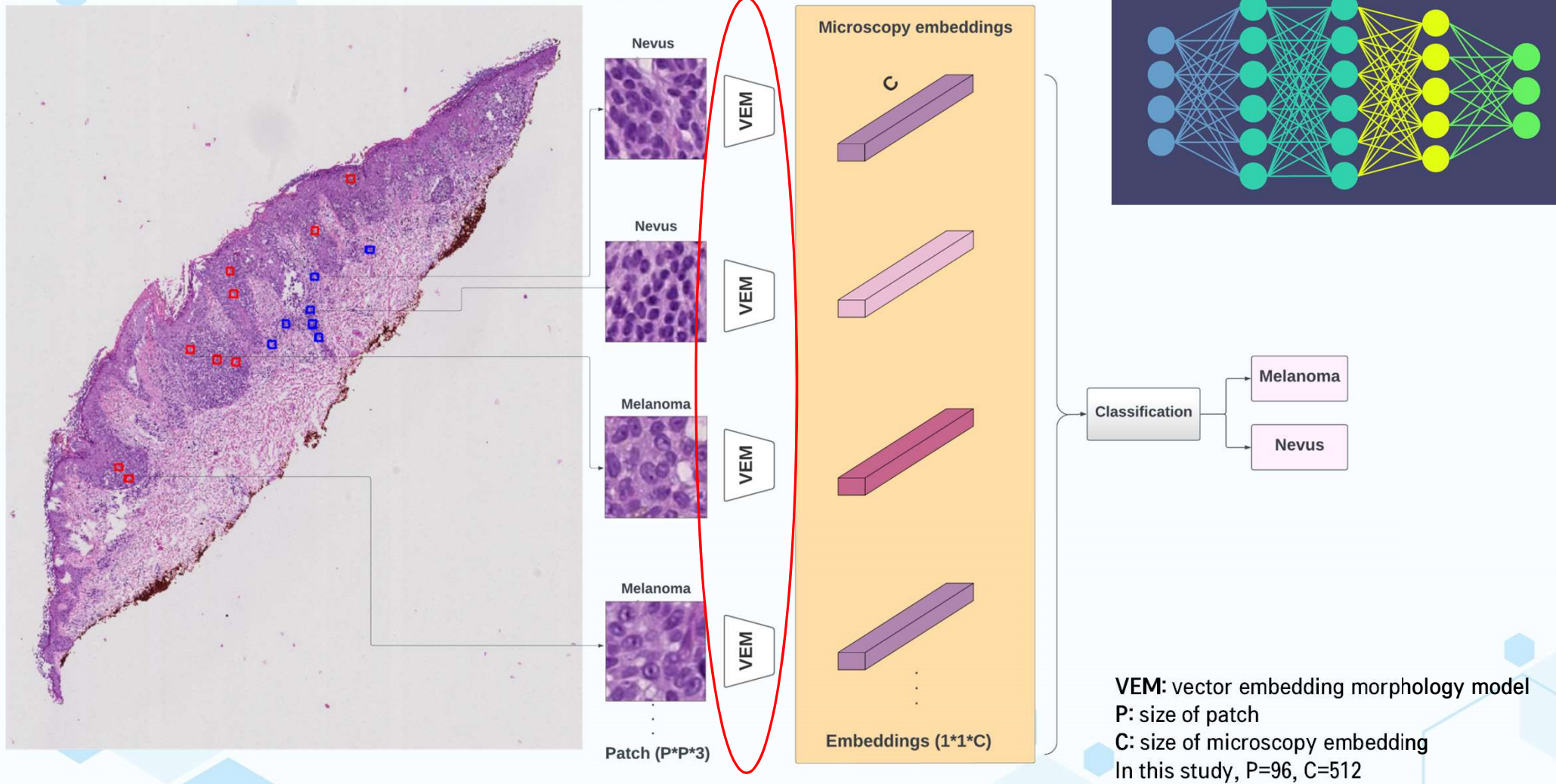
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Unimodal IMS pipeline

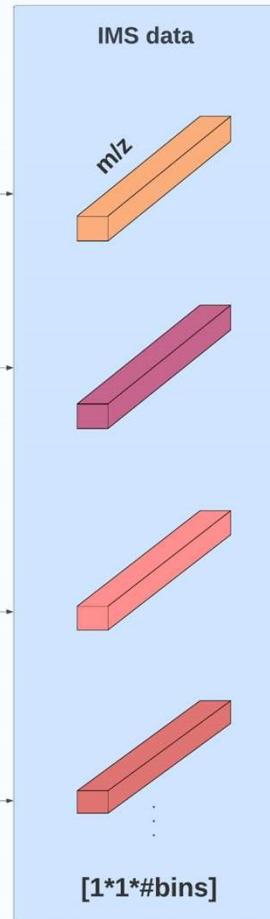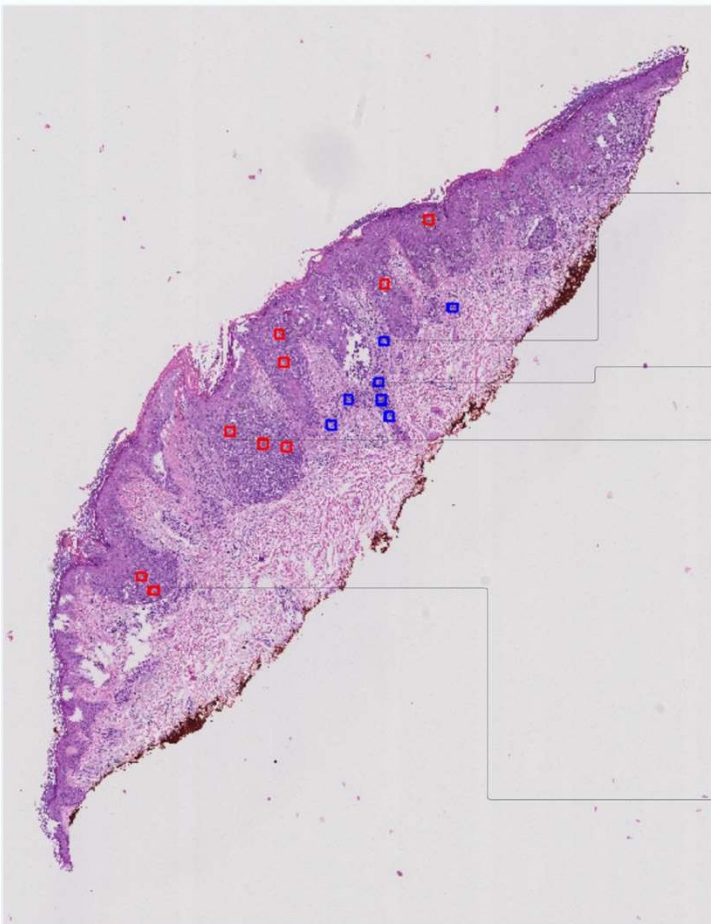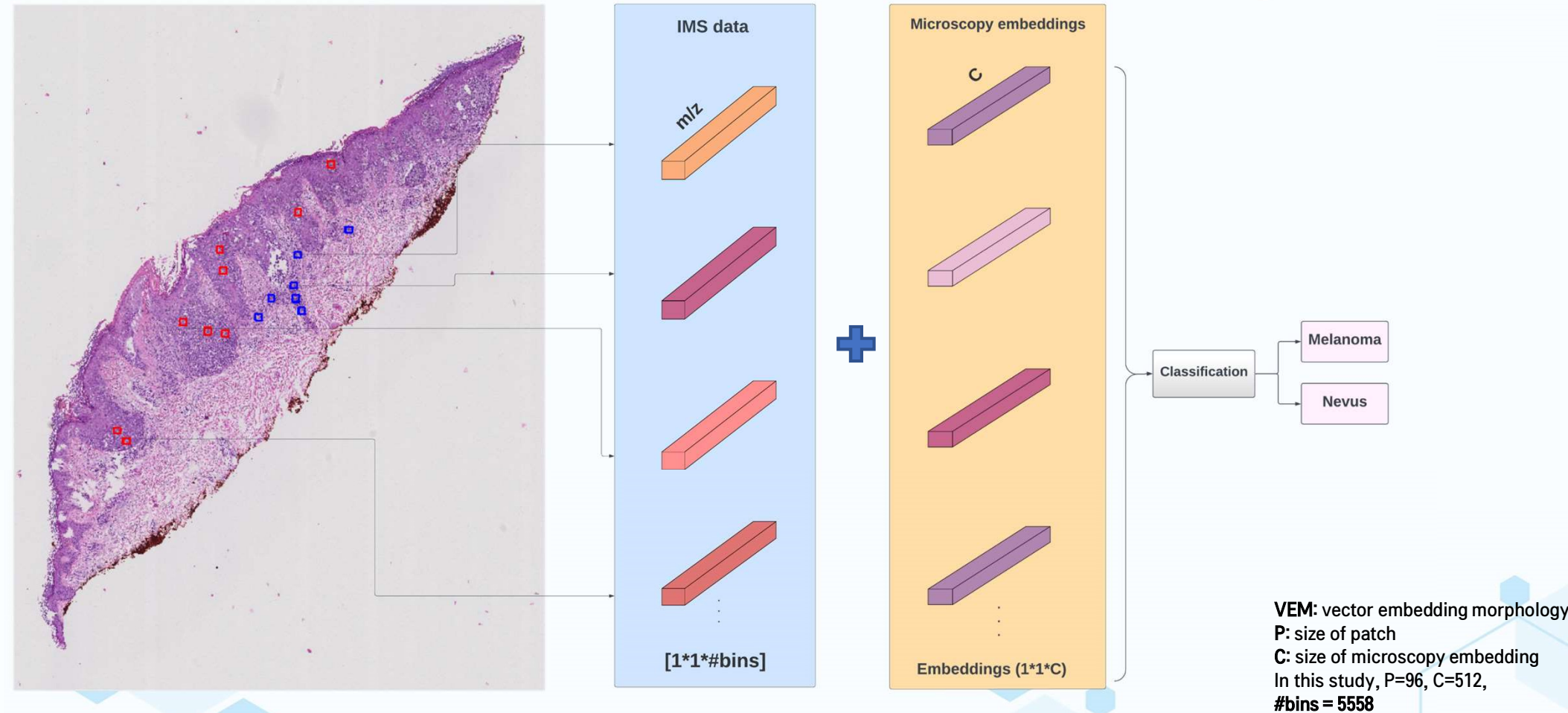# Unimodal Microscopy pipeline

Unimodal Microscopy pipeline

VEM: vector embedding morphology model
P: size of patch
C: size of microscopy embedding
In this study, P=96, C=512

Pre-trained neural networks

Before training

[1]Ciga, Ozan, Tony Xu, and Anne Louise Martel. "Self supervised contrastive learning for digital histopathology." *Machine Learning with Applications* 7 (2022): 100198.

Pre-trained neural networks

57 histopathology multi-organ datasets[1]:
- 206,000 patches in 23 datasets;
- 25,000 giga-resolution images in 35 datasets

Before training

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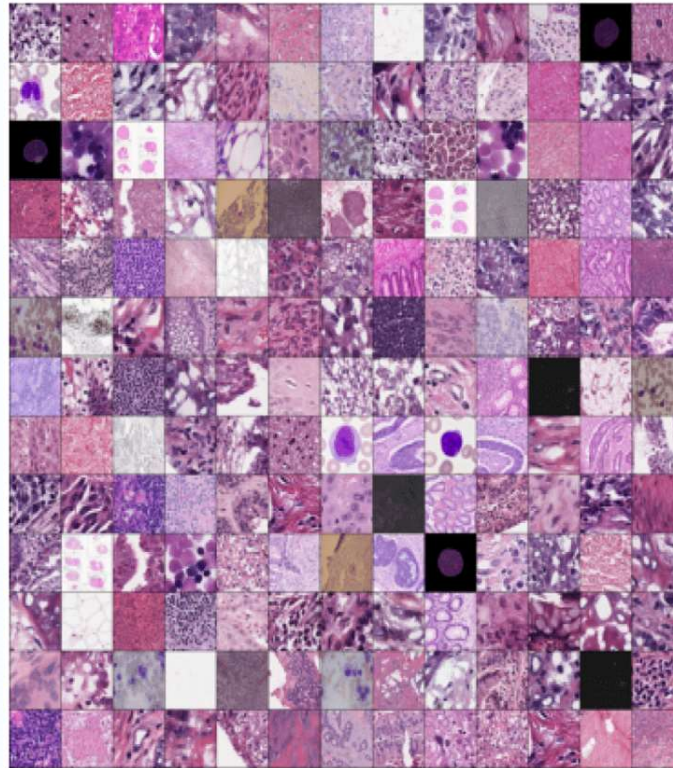
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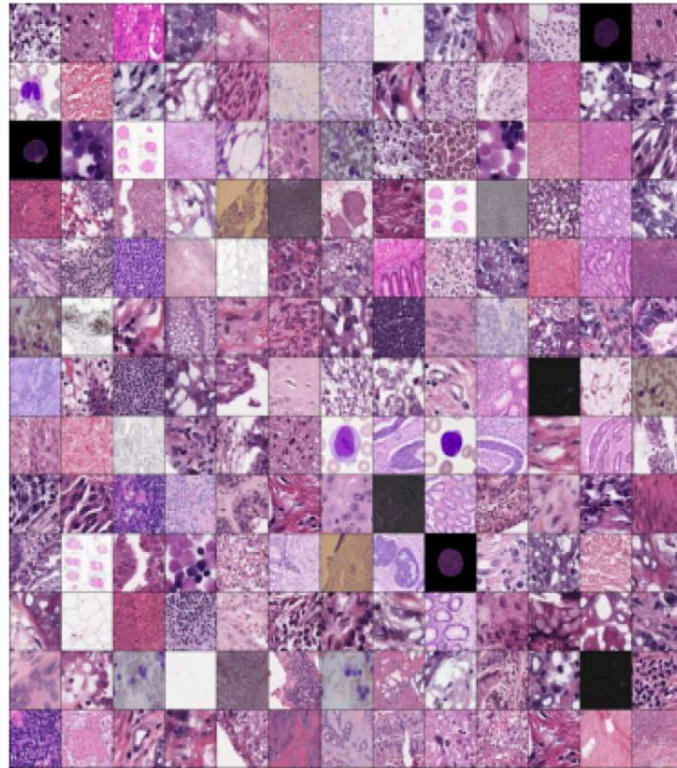
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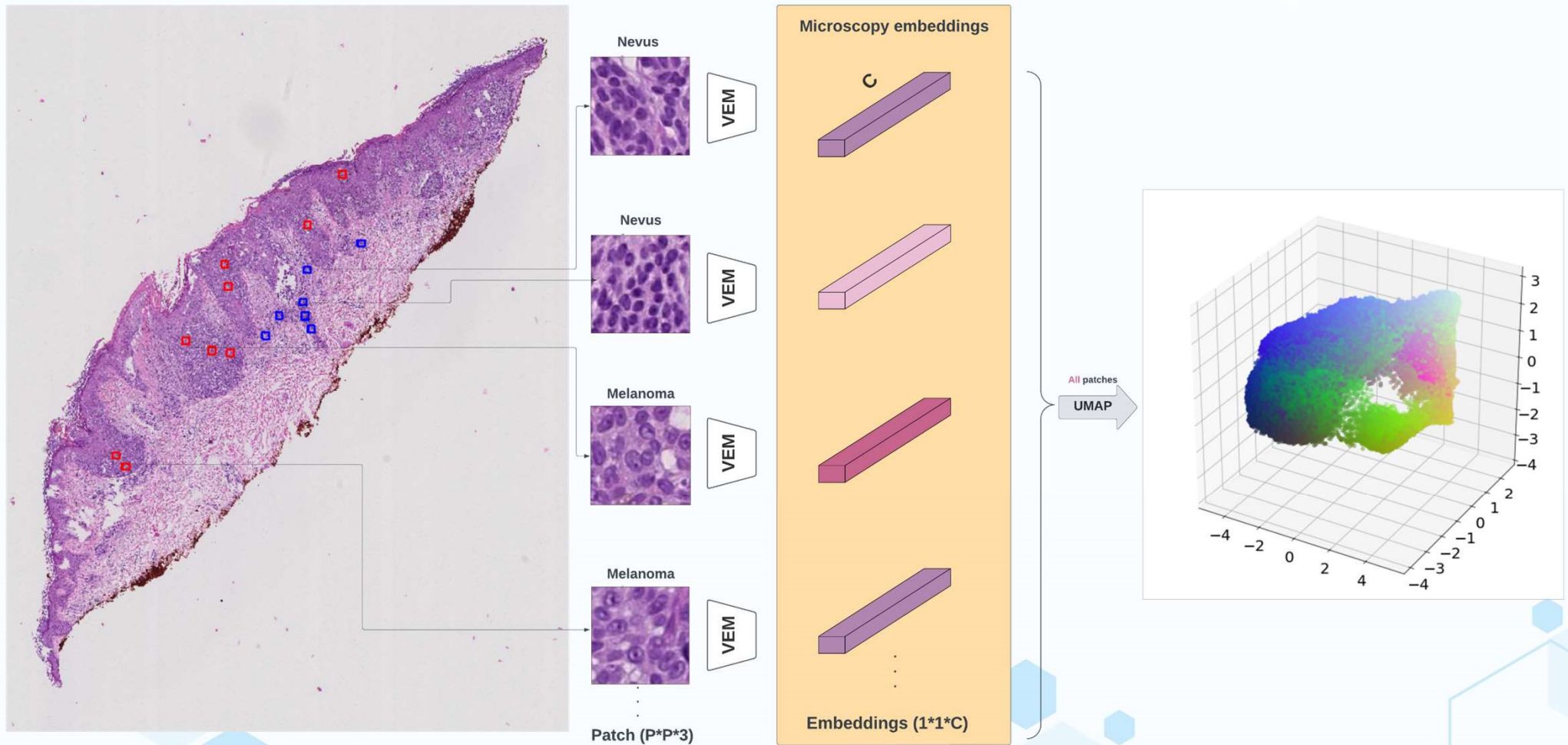
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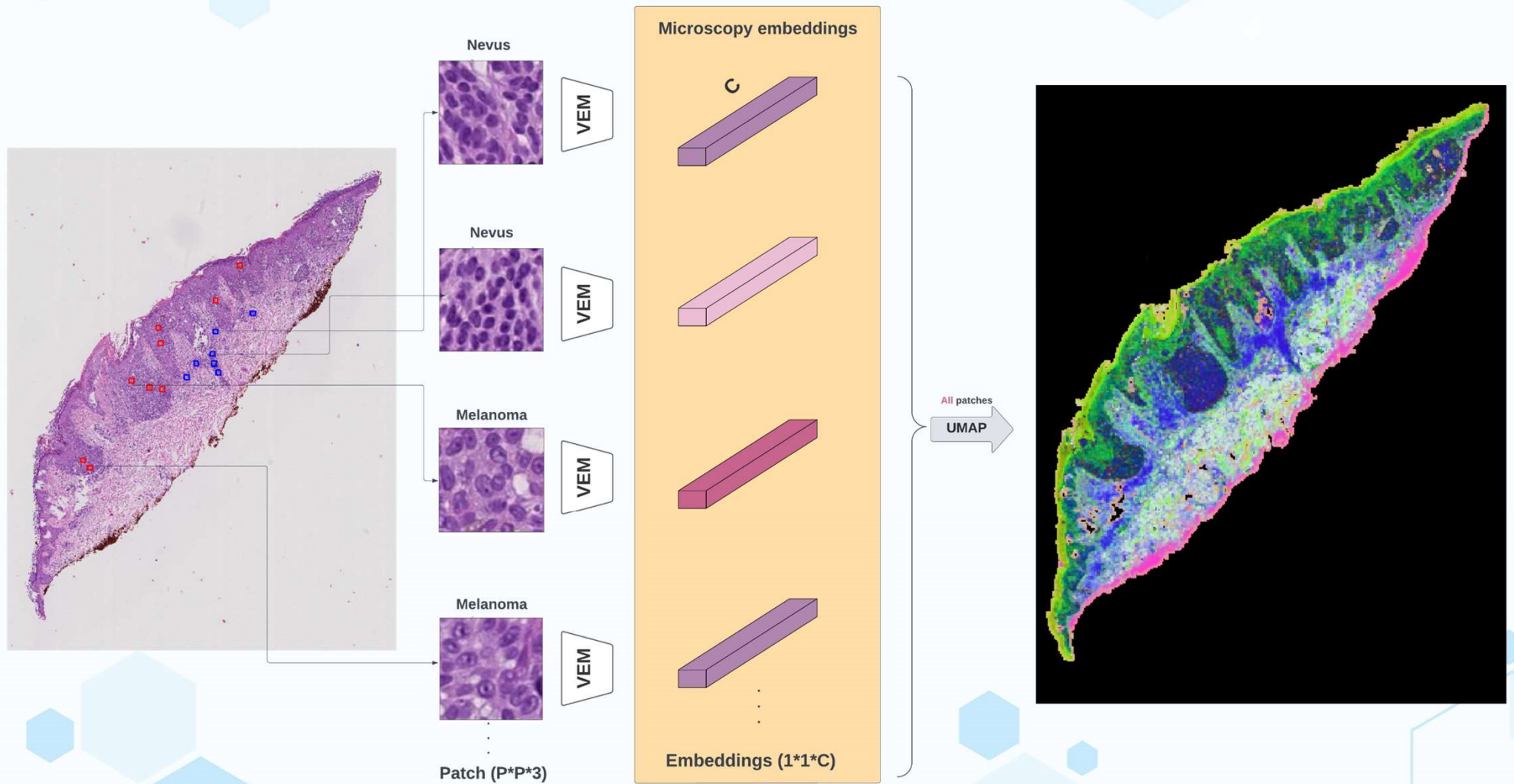
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Multimodal pipeline

IMS data

m/z

[1*1*#bins]

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In this study, P=96, C=512,
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Multimodal pipeline

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Microscopy embeddings

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Embeddings (1*1*C)

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Classification

Melanoma

Nevus

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Results

UMAP on training data

Microscopy embeddings only   IMS data only   Microscopy embeddings + IMS
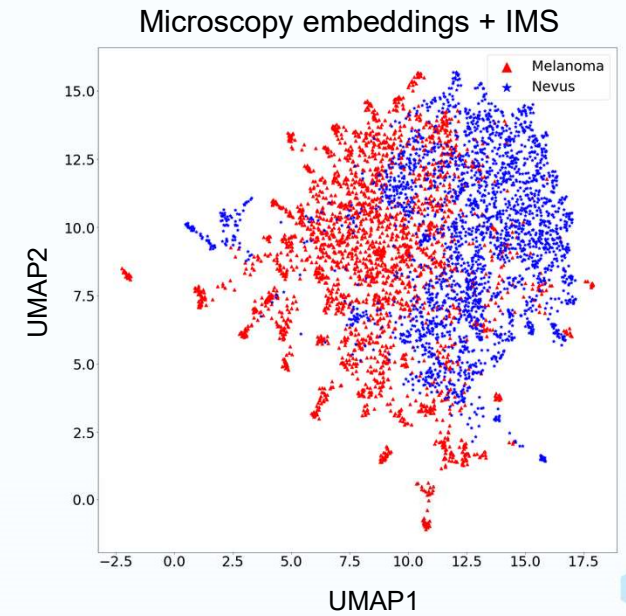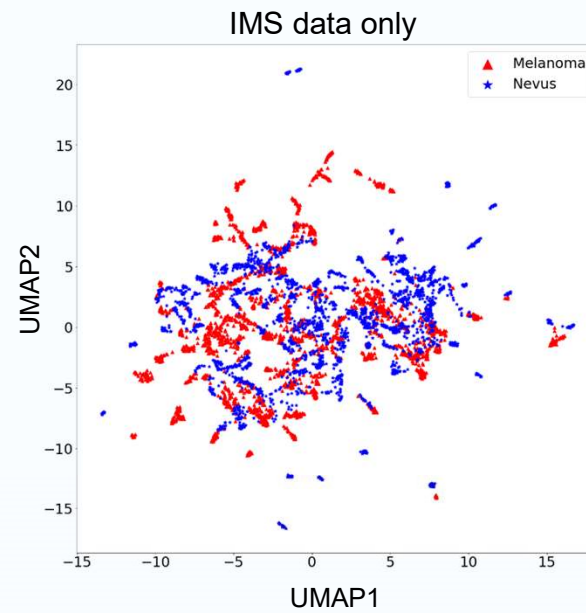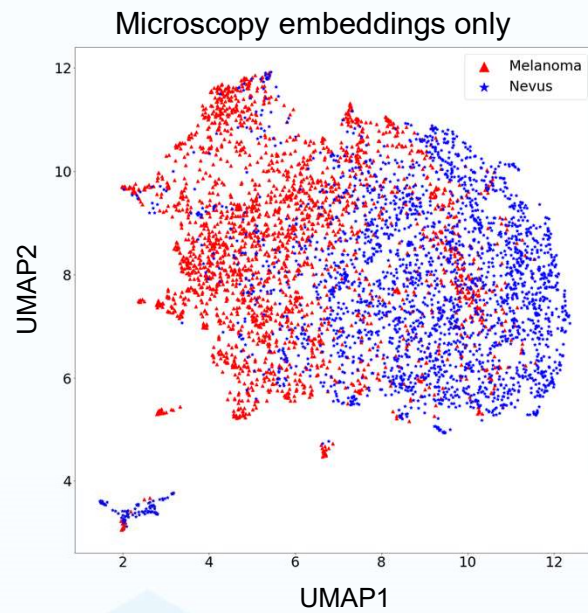
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UMAP on test data
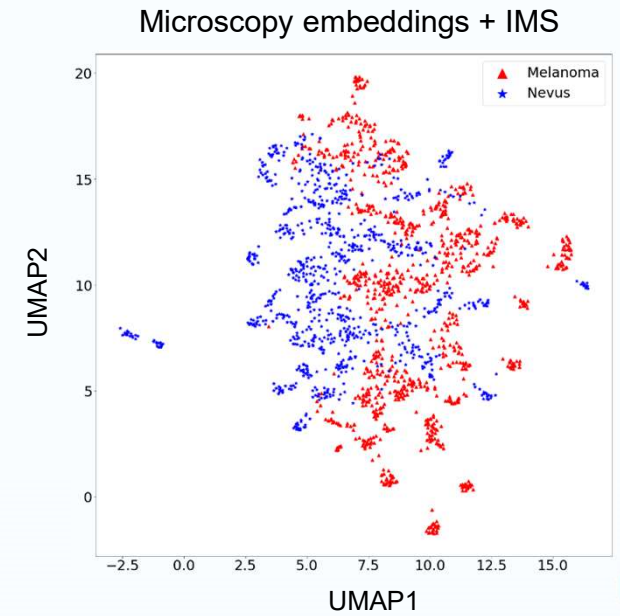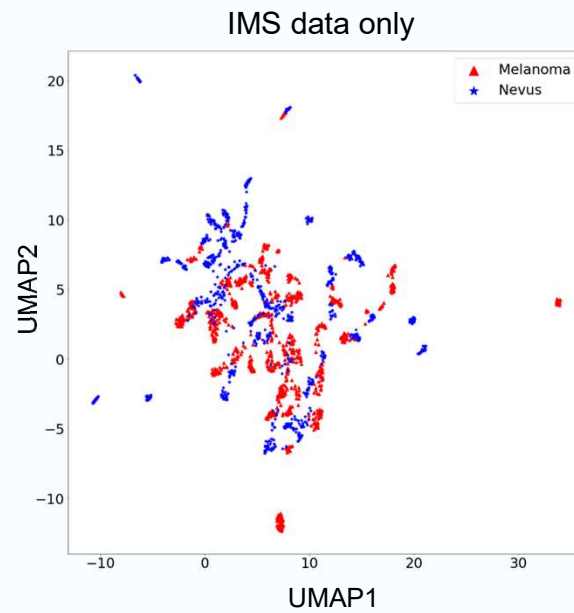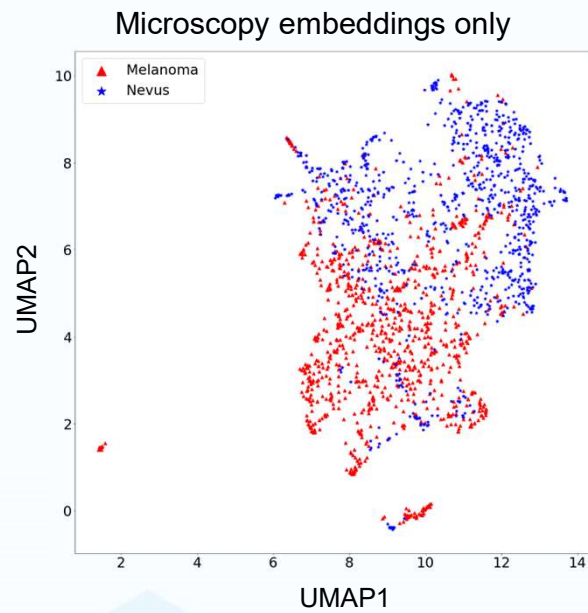
Microscopy embeddings only

IMS data only

Microscopy embeddings + IMS

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Experiments details:

- Classification model: linear support vector machine (SVM)

- Nested cross validation with grid search parameter tuning (on training data)

  - Inner cross validation: 10 folds

  - Outer cross validation: 10 folds

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Spots that measured in the same tissue were grouped in the same fold, during each iteration

Final Multimodal IMS and Microscopy data		
Number	**Training set**	**Test set**
Samples/Patients	239	92
Spots	5080	1924
Diagnosis Melanoma	2476	999
Diagnosis Nevus	2604	925

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Nested cross validation results on training data:

Model	Mean ROC-AUC		Mean F1 score		Mean Precision		Mean Recall	
Unimodal IMS	0.915	0.049	0.823	0.067	0.846	0.085	0.815	0.11
Unimodal Microscopy	0.937	0.03	0.82	0.056	0.857	0.104	0.805	0.111
Multimodal	**0.968**	0.023	**0.866**	0.056	**0.920**	0.051	**0.83**	0.112

Note: Melanoma is negative; all results are based on spots-level; Standard deviation are in grey, ROC-AUC = 1 means the classifier can distinguish between all Positive and Negative class points perfectly correctly.

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Results on independent test data (with optimized parameters):

Model	ROC-AUC	F1 score	Precision	Recall	Specificity
Unimodal IMS	0.931	0.856	0.828	0.886	0.83
Unimodal Microscopy	0.938	0.861	0.871	0.851	0.883
Multimodal	**0.968**	**0.91**	**0.924**	**0.90**	**0.932**
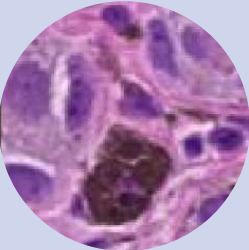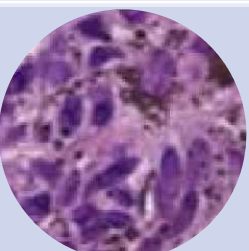
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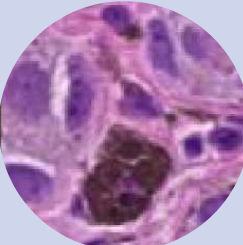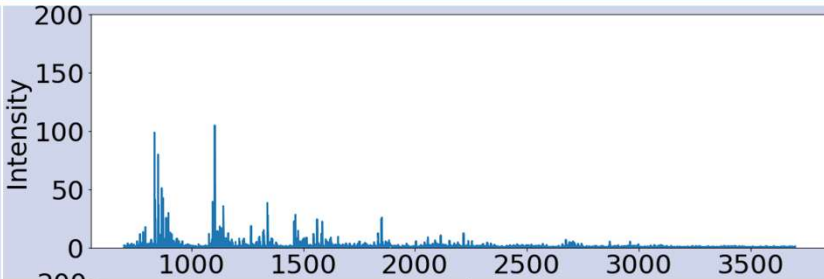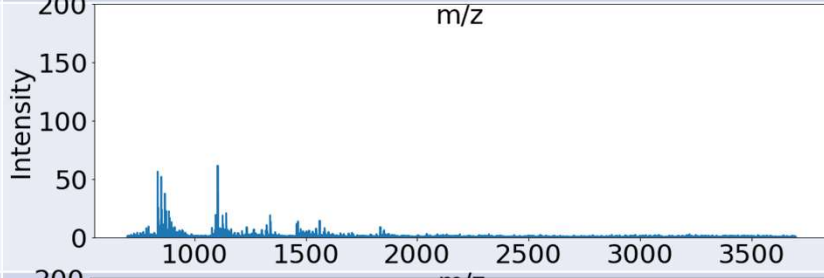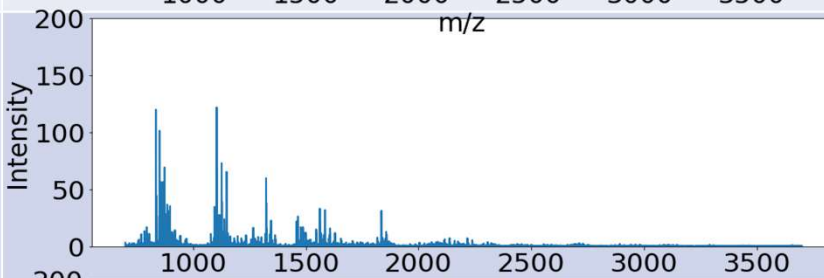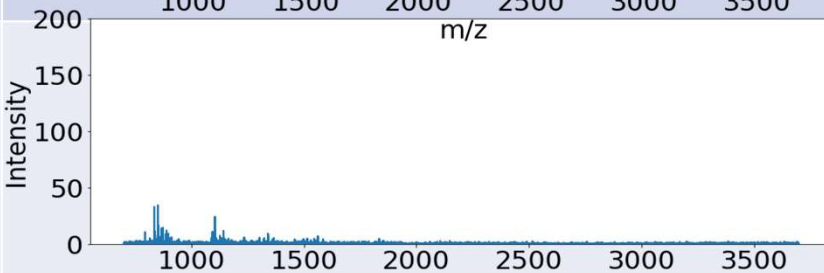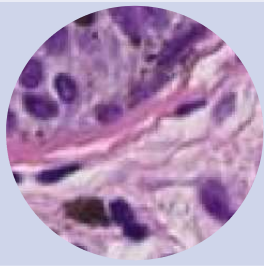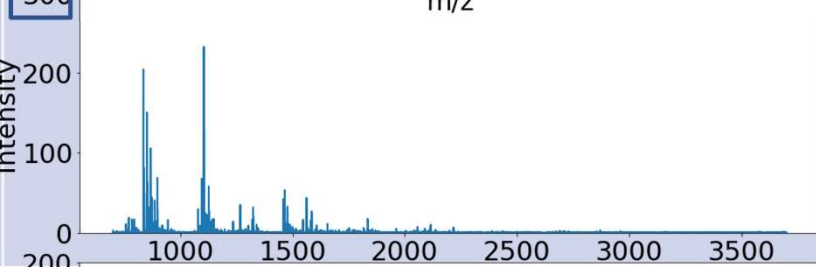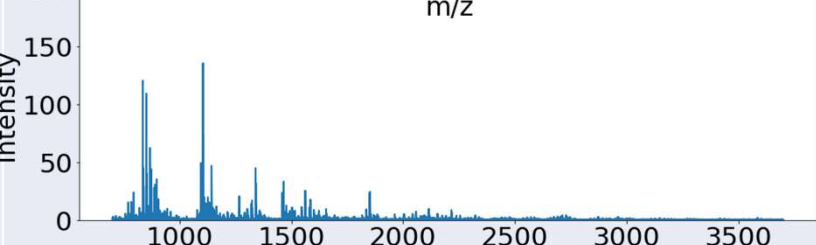
Results on independent test set
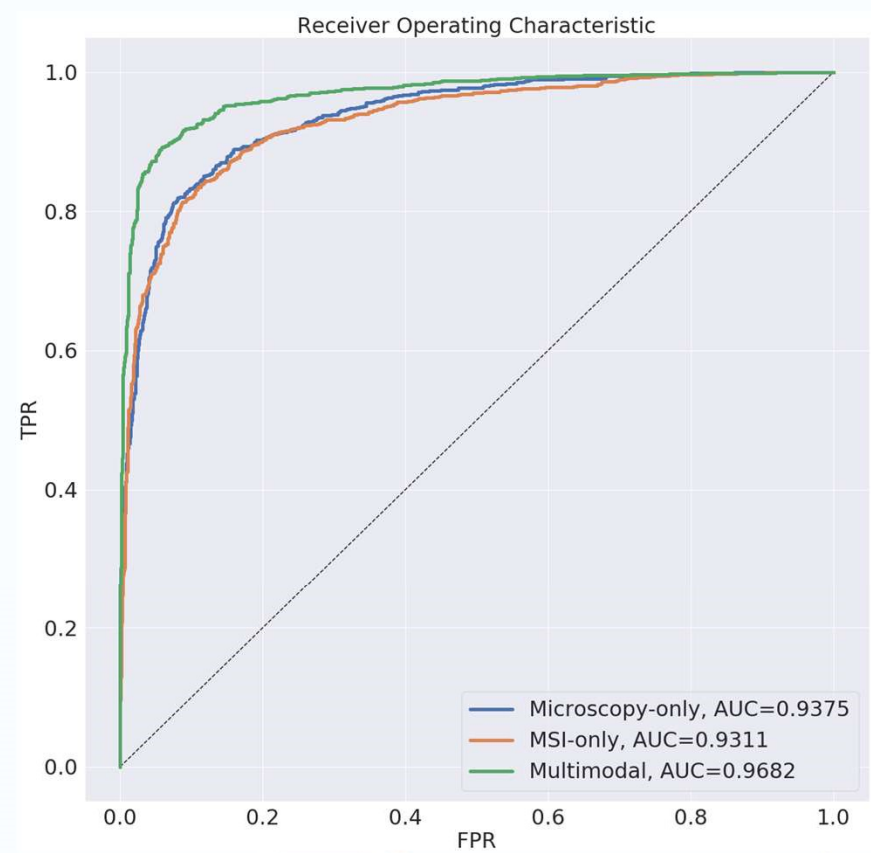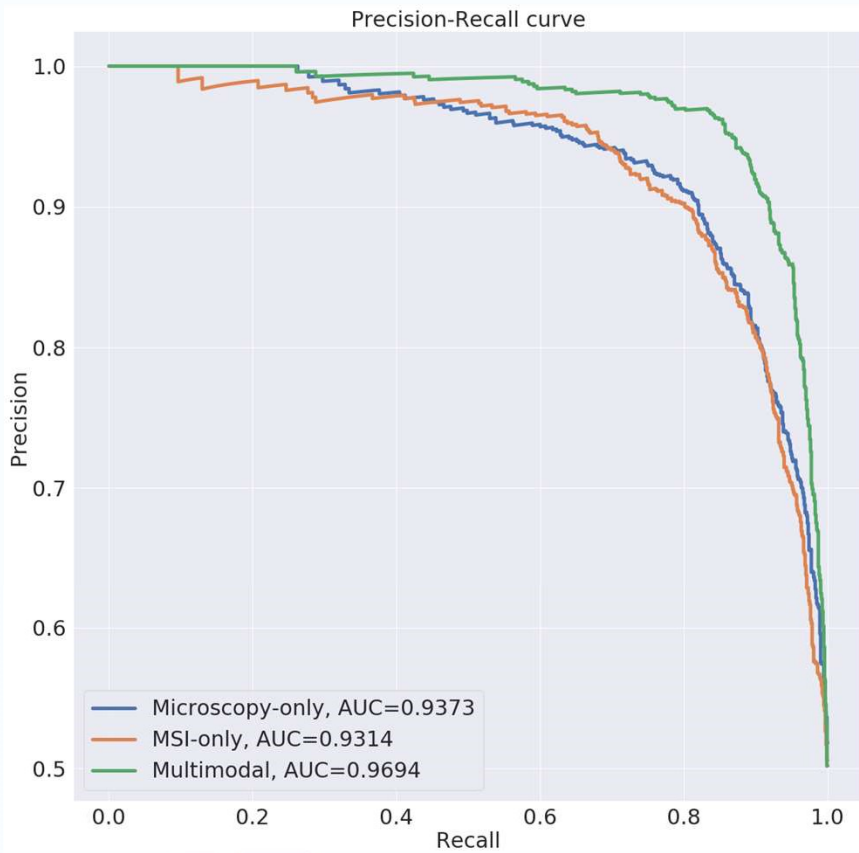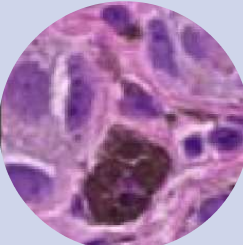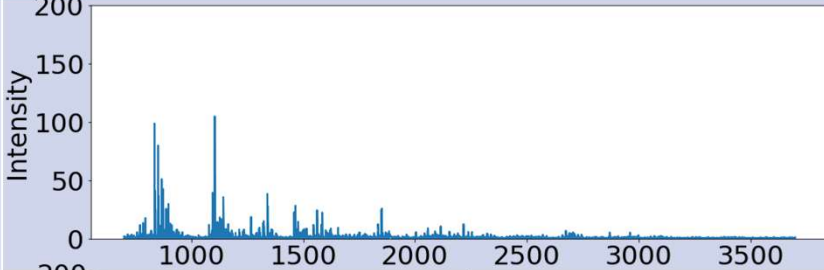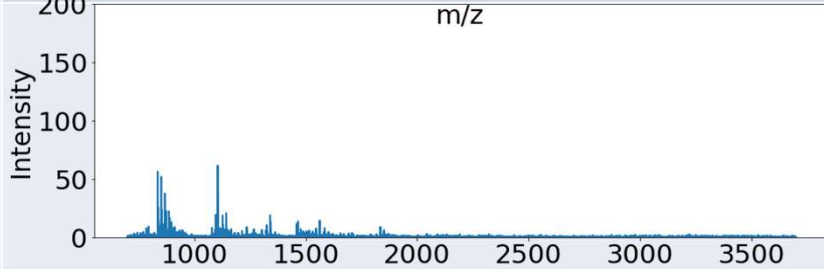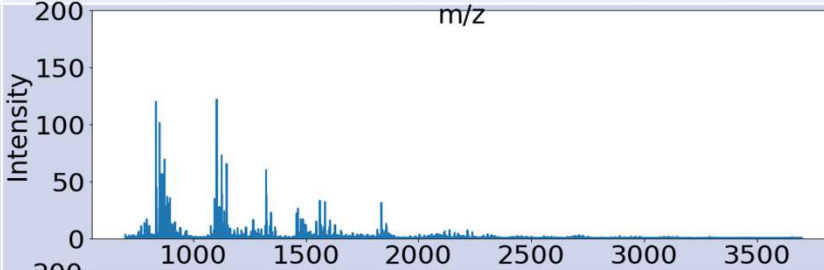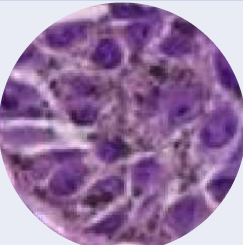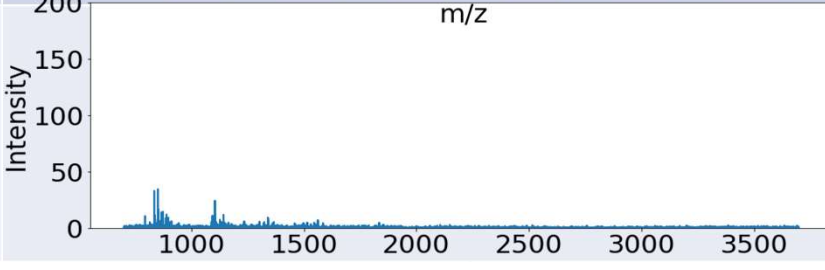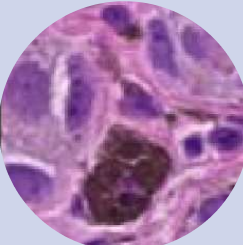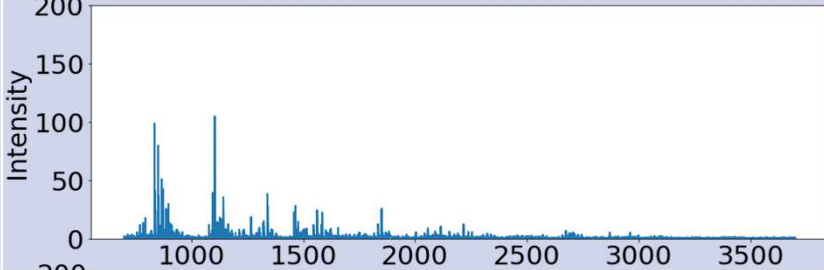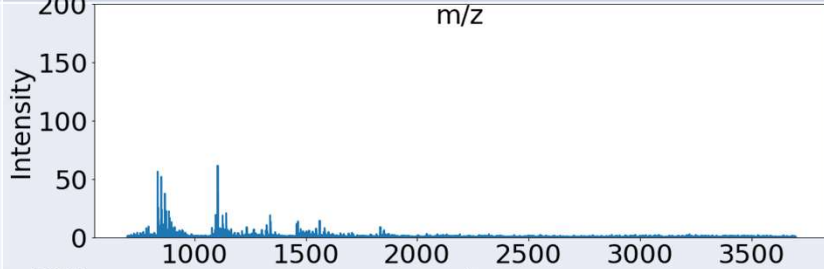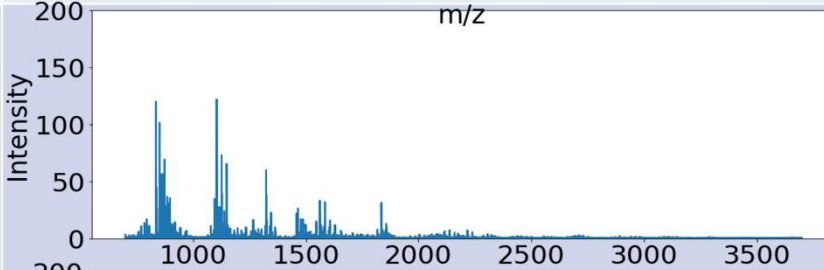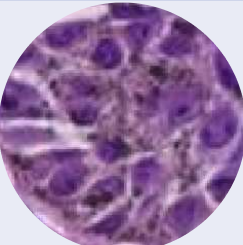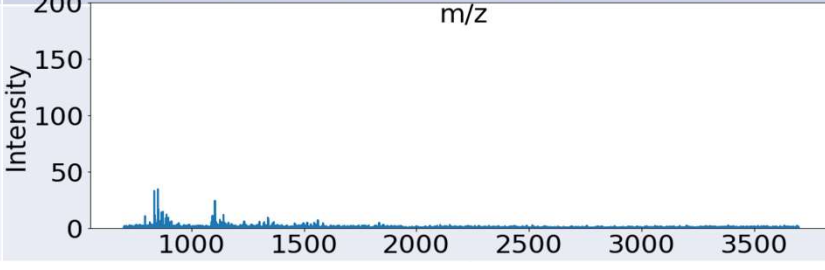
Interesting cases
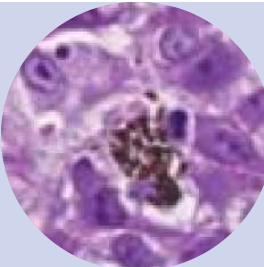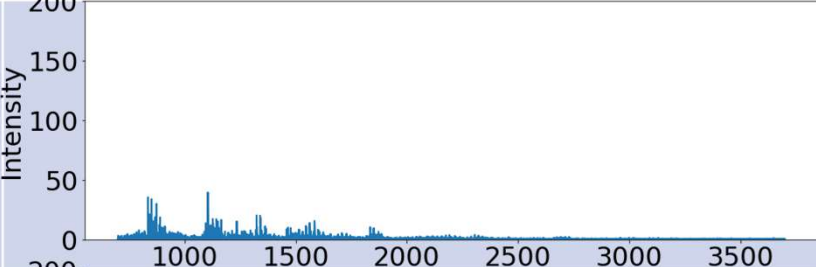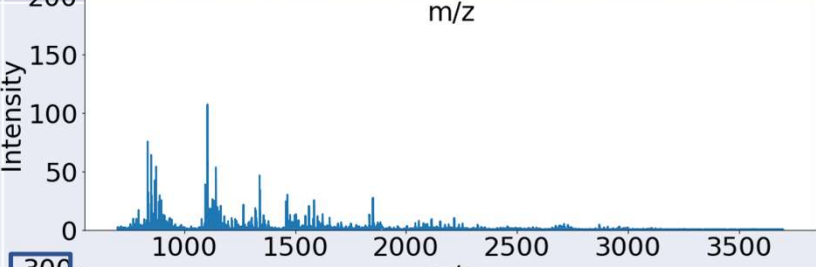
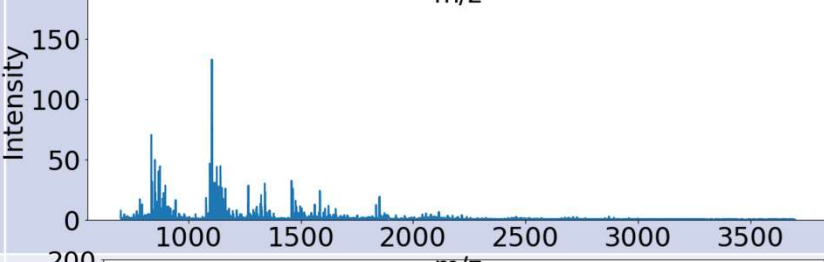Misclassified cases from unimodal pipelines

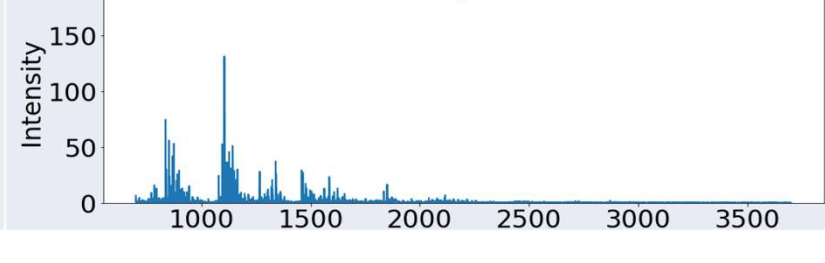| Microscopy data	IMS data	Unimodal Microscopy prediction	Unimodal IMS prediction	Multimodal prediction	Experts evaluation
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					Nevus

Microscopy data	IMS data	Unimodal Microscopy prediction	Unimodal IMS prediction	Multimodal prediction	Experts evaluation
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					Nevus
					Nevus

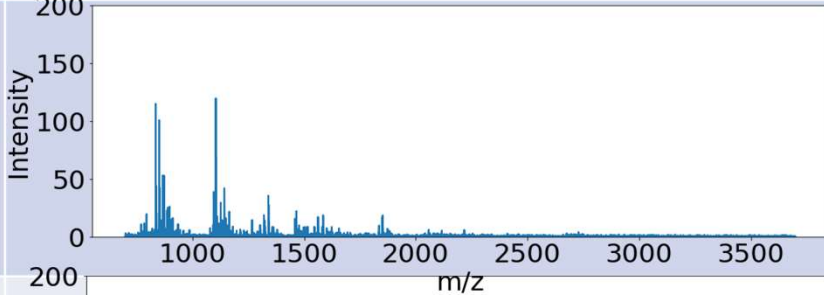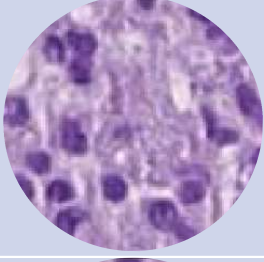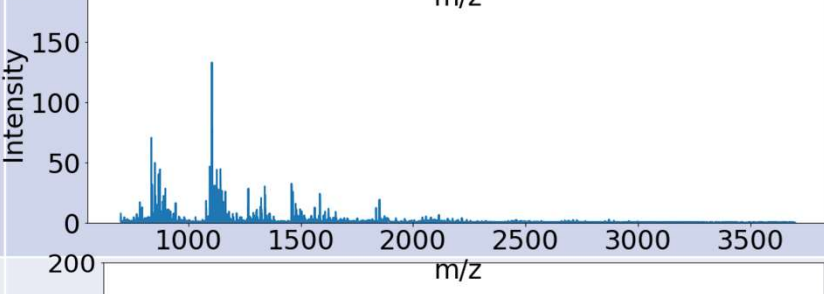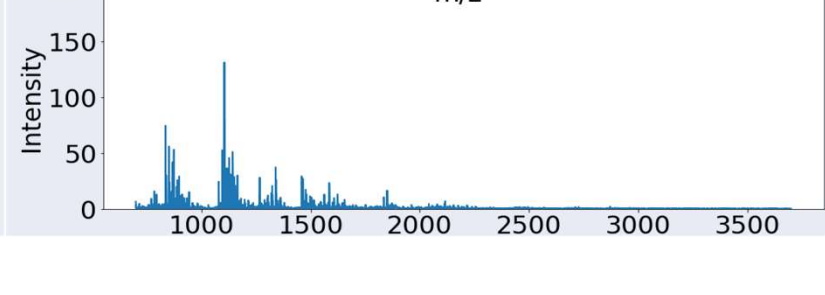| Microscopy data	IMS data	Unimodal Microscopy prediction	Unimodal IMS prediction	Multimodal prediction	Experts evaluation
		Nevus	Melanoma		Melanoma
		Nevus	Melanoma		Melanoma
		Melanoma	Nevus		Nevus
		Melanoma	Nevus		Nevus

Microscopy data	IMS data	Unimodal Microscopy prediction	Unimodal IMS prediction	Multimodal prediction	Experts evaluation
		Nevus	Melanoma	Melanoma	Melanoma
		Nevus	Melanoma	Melanoma	Melanoma
		Melanoma	Nevus	Nevus	Nevus
		Melanoma	Nevus	Nevus	Nevus

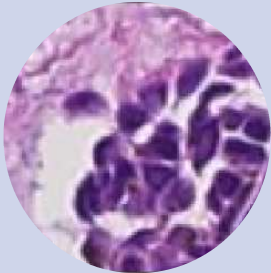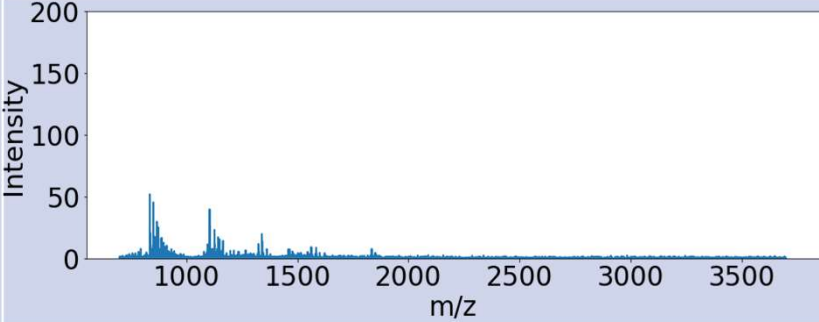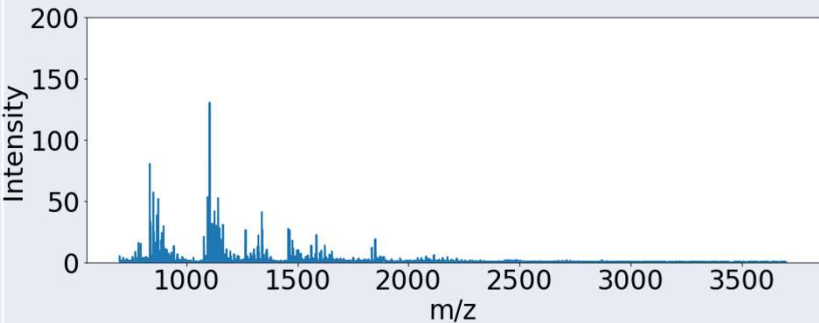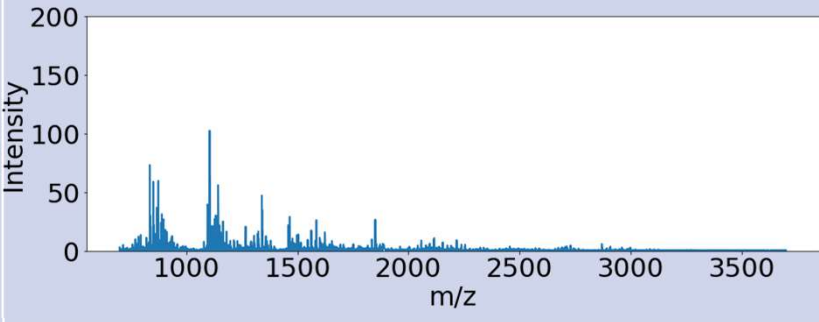| Microscopy data	IMS data	Unimodal Microscopy prediction	Unimodal IMS prediction	Multimodal prediction	Experts evaluation
		Melanoma	Nevus	Melanoma	Melanoma
		Melanoma	Nevus	Melanoma	Melanoma
		Nevus	Melanoma	Nevus	Nevus
		Nevus	Melanoma	Nevus	Nevus

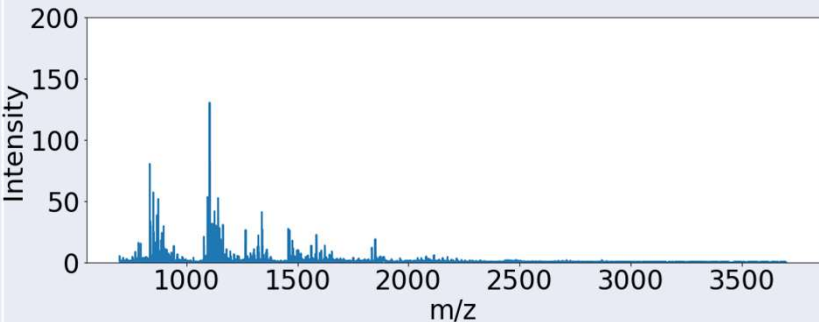| Microscopy data	IMS data	Unimodal Microscopy prediction	Unimodal IMS prediction	Multimodal prediction	Experts evaluation
		Melanoma	Melanoma		Nevus
		Nevus	Nevus		Melanoma
		Nevus	Nevus		Melanoma
		Nevus	Nevus		Melanoma

Microscopy data	IMS data	Unimodal Microscopy prediction	Unimodal IMS prediction	Multimodal prediction	Experts evaluation
		Melanoma	Melanoma	Nevus	Nevus
		Nevus	Nevus	Melanoma	Melanoma
		Nevus	Nevus	Melanoma	Melanoma
		Nevus	Nevus	Melanoma	Melanoma

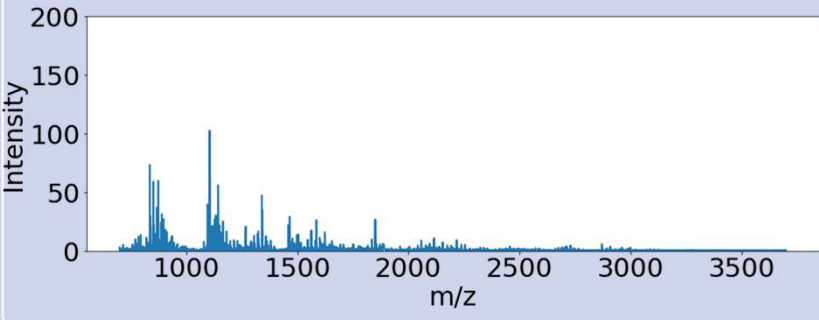| Microscopy data	IMS data	Unimodal Microscopy prediction	Unimodal IMS prediction	Multimodal prediction	Experts evaluation
		Nevus	Nevus		Melanoma
		Nevus	Nevus		Melanoma
		Nevus	Nevus		Melanoma

Microscopy data	IMS data	Unimodal Microscopy prediction	Unimodal IMS prediction	Multimodal prediction	Experts evaluation
		Nevus	Nevus	Melanoma	Melanoma
		Nevus	Nevus	Melanoma	Melanoma
		Nevus	Nevus	Melanoma	Melanoma

Conclusion

- Multimodal is great!
- Do not throw your microscopy data away ☺
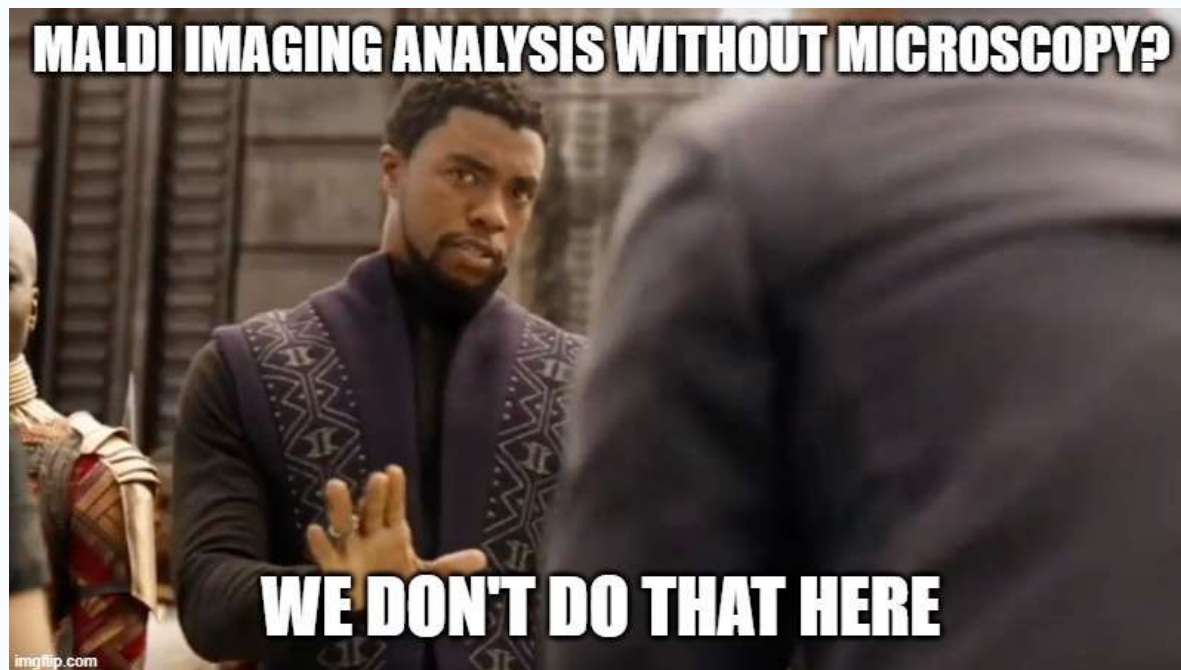
Want to know more?

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Want to know more?

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Nico Verbeeck; Alice Ly; Bart De Moor; Marc Claesen

Conflict of Interest

[1] Al-Rohil, Rami N., Jessica L. Moore, Nathan Heath Patterson, Sarah Nicholson, Nico Verbeeck, Marc Claesen, Jameelah Z. Muhammad et al. "Diagnosis of melanoma by imaging mass spectrometry: Development and validation of a melanoma prediction model." Journal of cutaneous pathology 48, no. 12 (2021): 1455-1462.