The Institute of Cancer Research

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3D single-cell shape analysis of cancer cells using geometric deep learning

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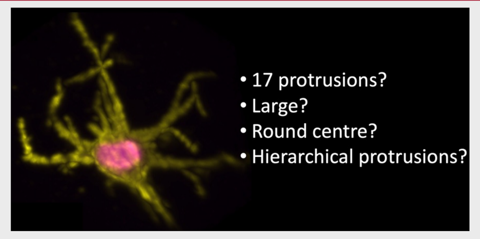
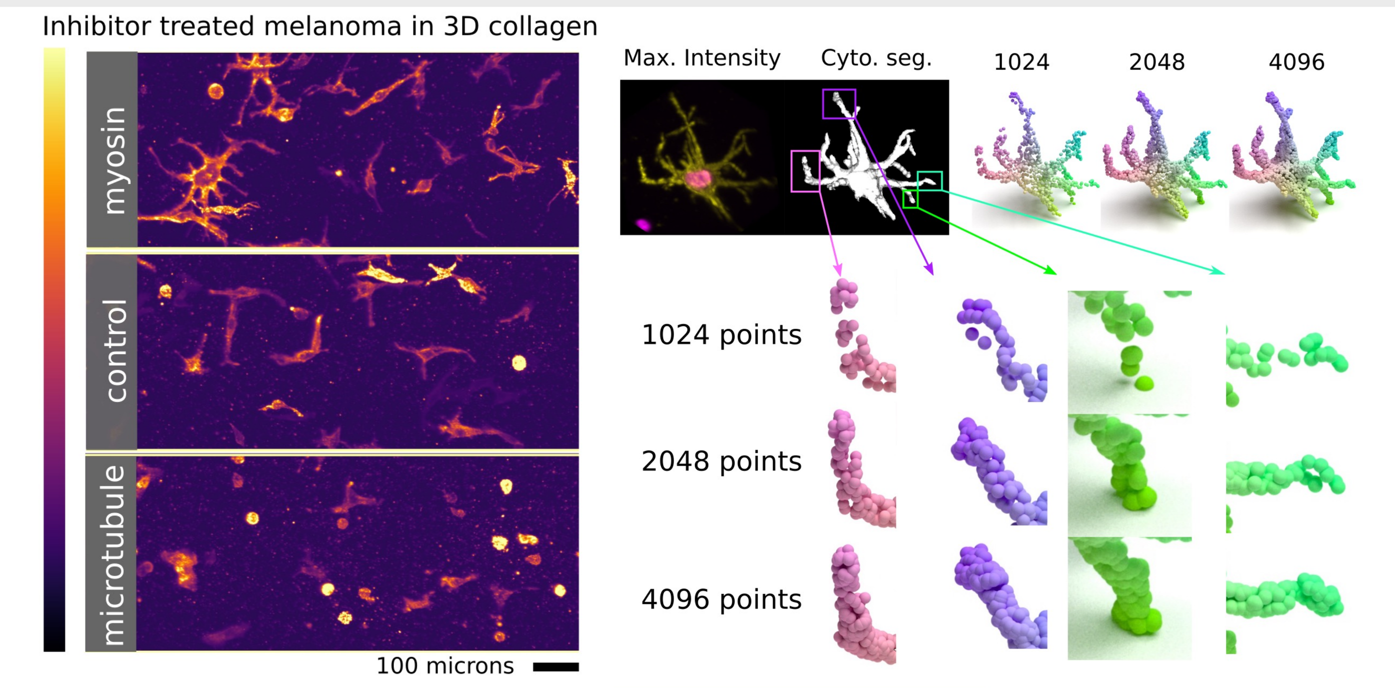
Cell shape is a sign for disease

Shape is connected to function and aberrations in shape can be a cause or sign of disease.
Quantifying shape in 3D is difficult. Cells exist naturally in 3D.
Instead of hand-crafter features, we learn features using geometric deep learning



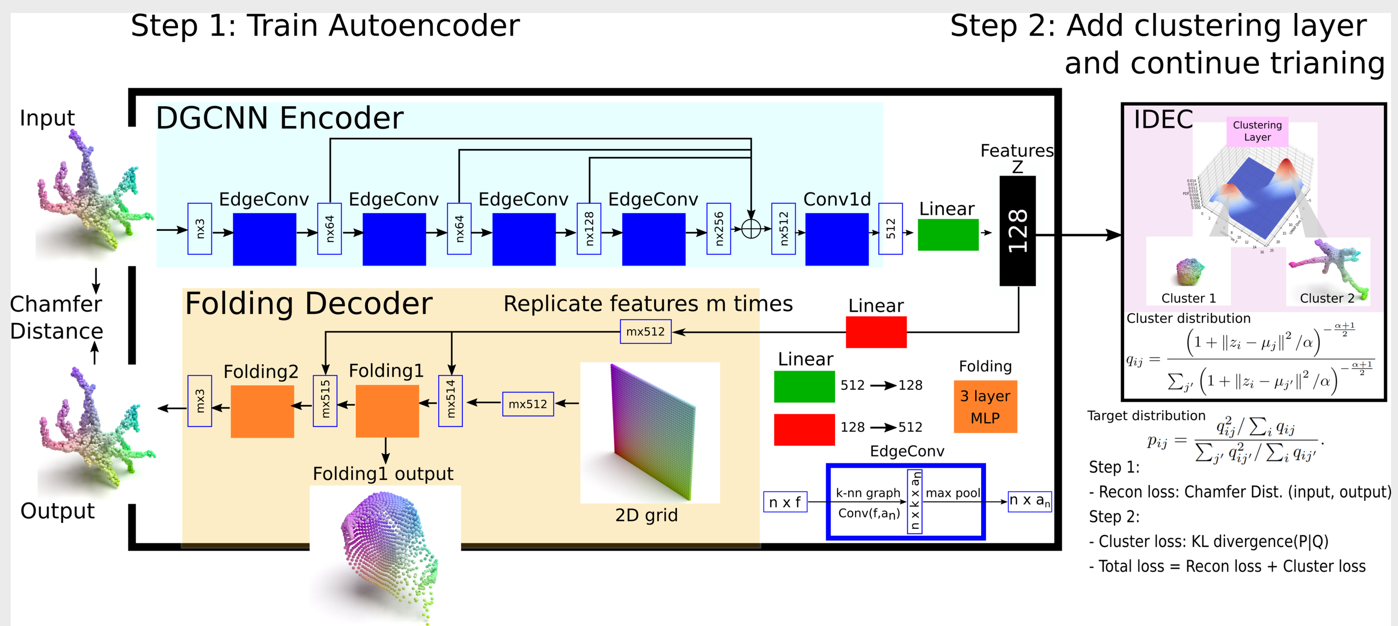
Data and pre-processing

High-throughput 3D light-sheet microscopy. 70 000 drug-treated WM266.4 metastatic melanoma cells embedded in tissue-like collagen matrices were.
Point cloud representation of 3D shape. Point clouds are scattered collections of points in 3D space and are arguably the simplest shape representation. We tested a range of sampling densities to trade off between efficiency and representation.



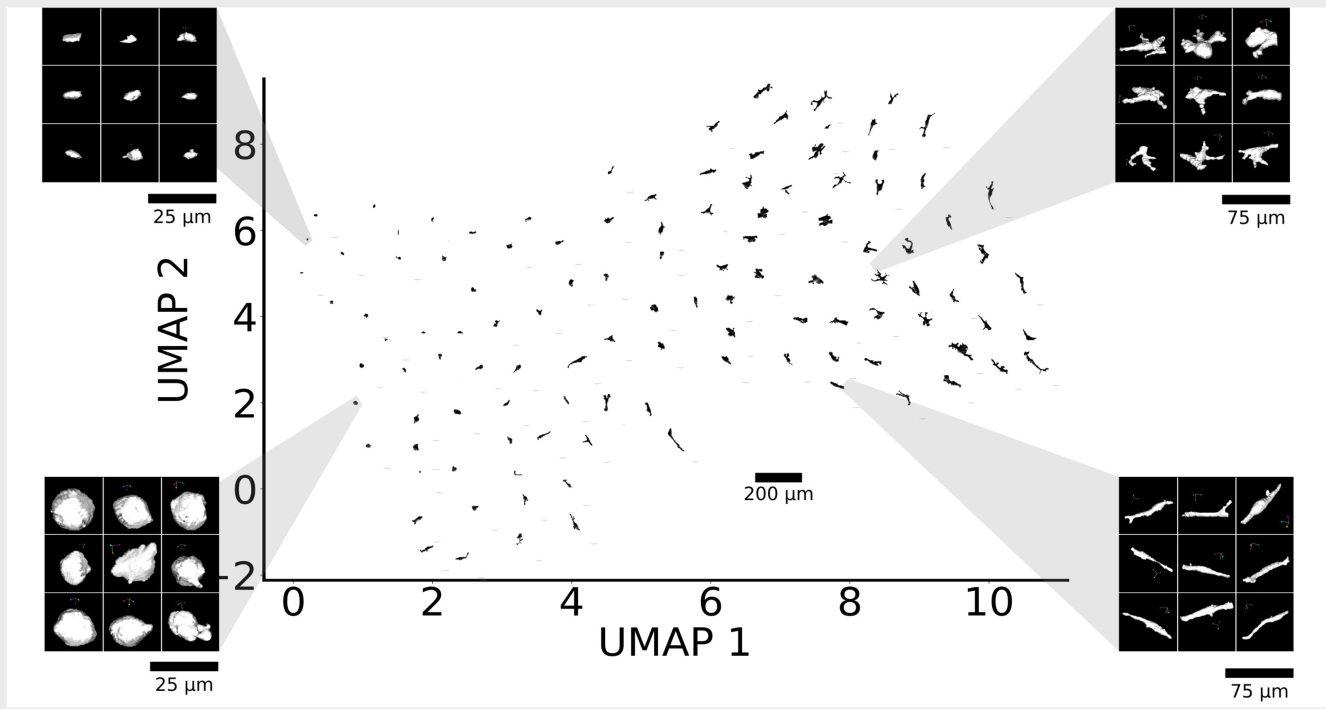
Geometric deep learning to learn 3D cell shape

Combined three techniques to learn 128 shape features and classes simultaneously.



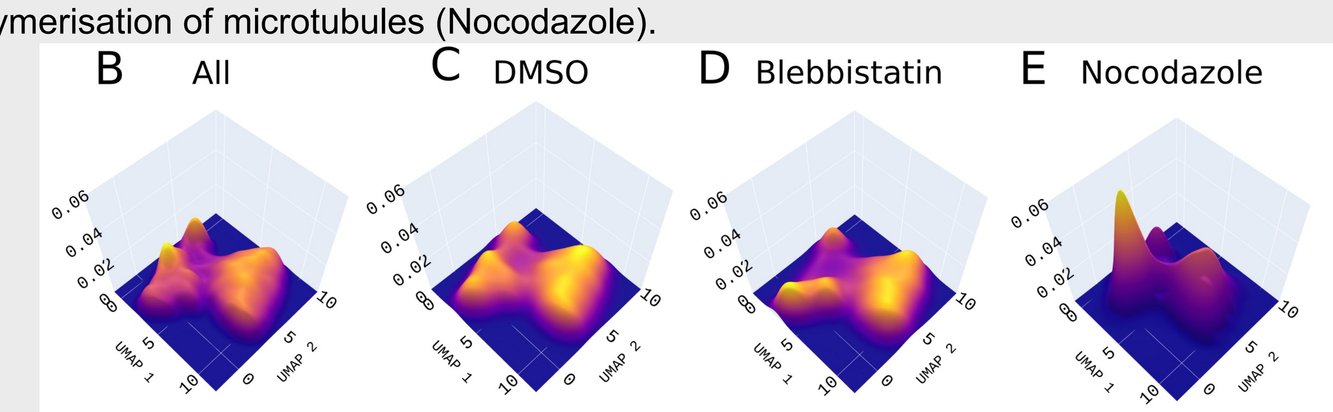
Cell shape landscape of metastatic melanoma

Projecting 128 shape features with UMAP shows the cell shape landscape. These features separate out the small, round, eccentric, and protrusive shaped cells.

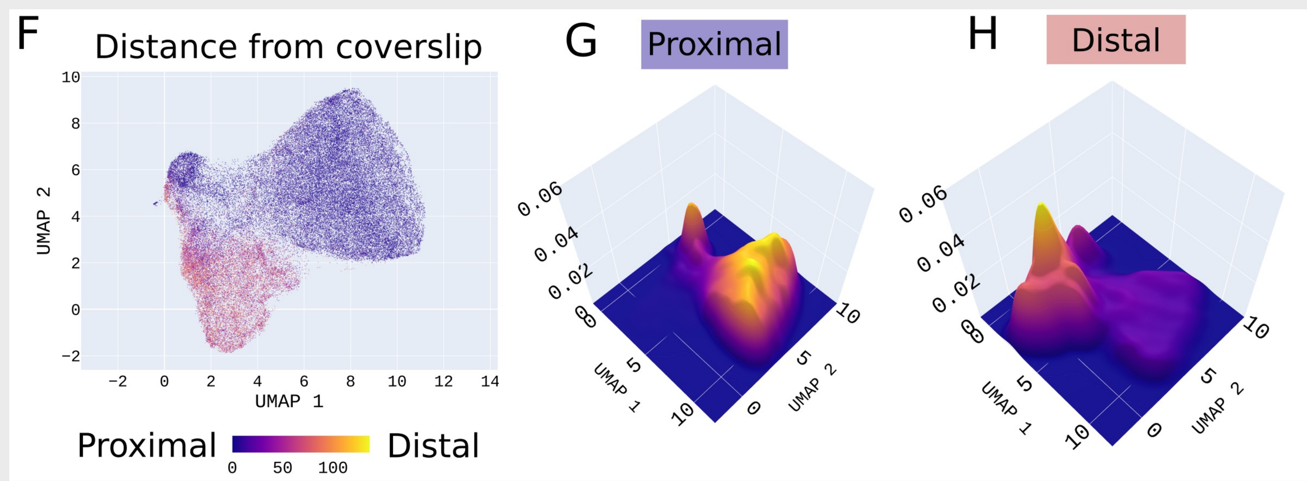


Drugs and environment effect cell shape landscape

Approximating the distribution using kernel density approximation of the UMAP shows how myosin inhibitors (Blebbistatin) have different shape distributions than inhibitors of the polymerisation of microtubules (Nocodazole).

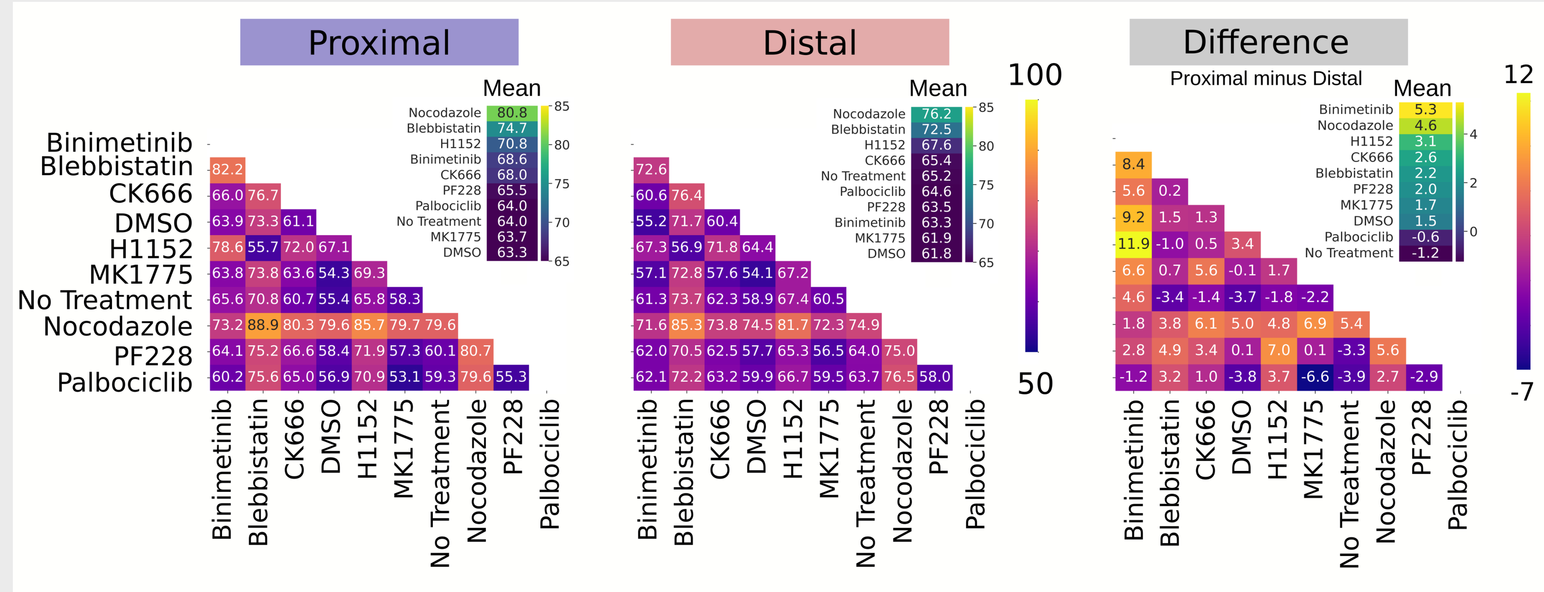


Cell shape is dependent of environment. Cells closer (proximal) to the coverslip are unable to take on shapes dominated by cells further away from the coverslip (distal).



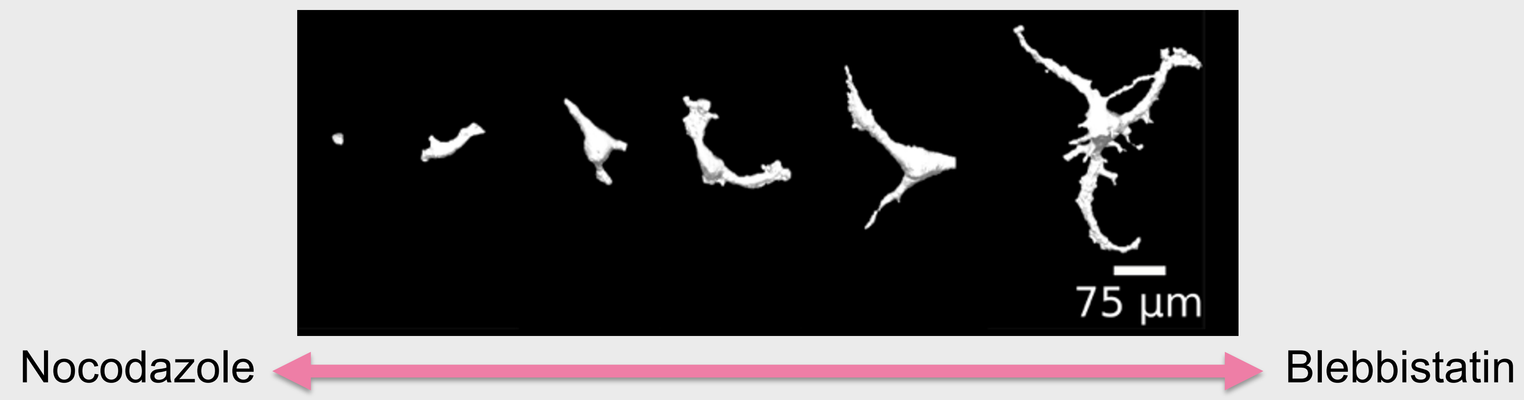
Predicting treatment from 3D cell shape

Trained linear SVM to classify treatments using 128 shape features. One-vs-one classification shows a highest accuracy of 89%. Accuracy was dependent on environment.



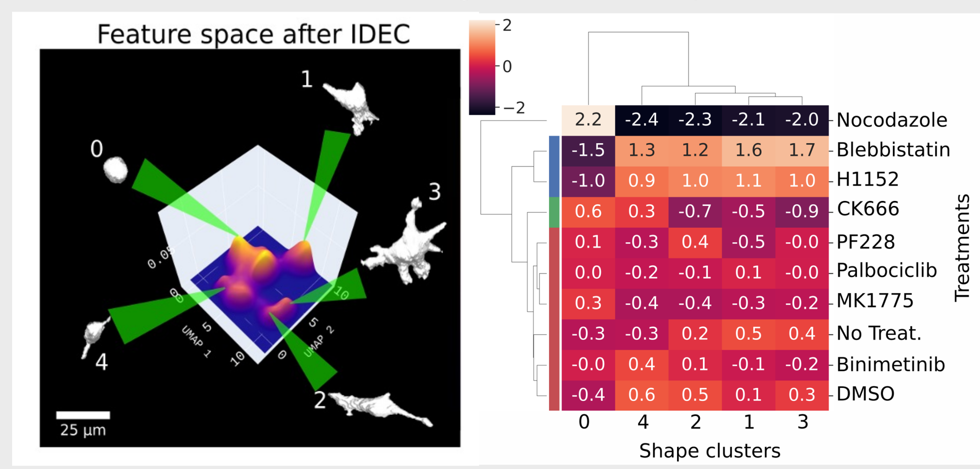
Interpolating between treatment exemplar shapes

Explainable AI. We varied the most important feature in classifying between Nocodazole and Blebbistatin to interpolate between treatment classes.



Deep embedded clustering learns shape signatures

Defined 3D quantitative morphological signature (3DQMS) which represents how similar each treatment is on average to the 5 shape clusters that exist in the dataset.



3DQMS groups treatments with similar mechanisms of action. This shows potential for use in phenotypic drug screening pipeline.

Preprint Code

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