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

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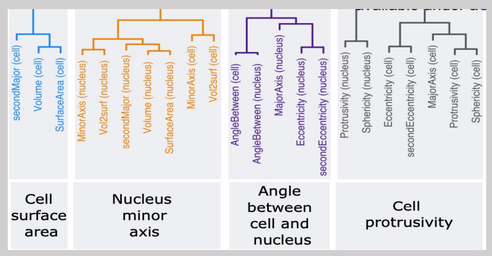
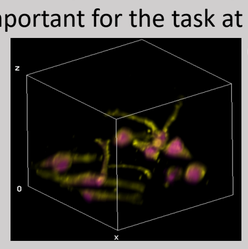
Introduction and background

Shape is connected to function and aberrations in shape can be a cause or sign of disease. Due to the importance of shape, biologists have developed many methods that attempt to measure it. Traditionally, we understand shape using predetermined or ``classical'' features. These are pre-selected, mathematically defined measures of geometry and often require a guessing which features are important for the task at hand.



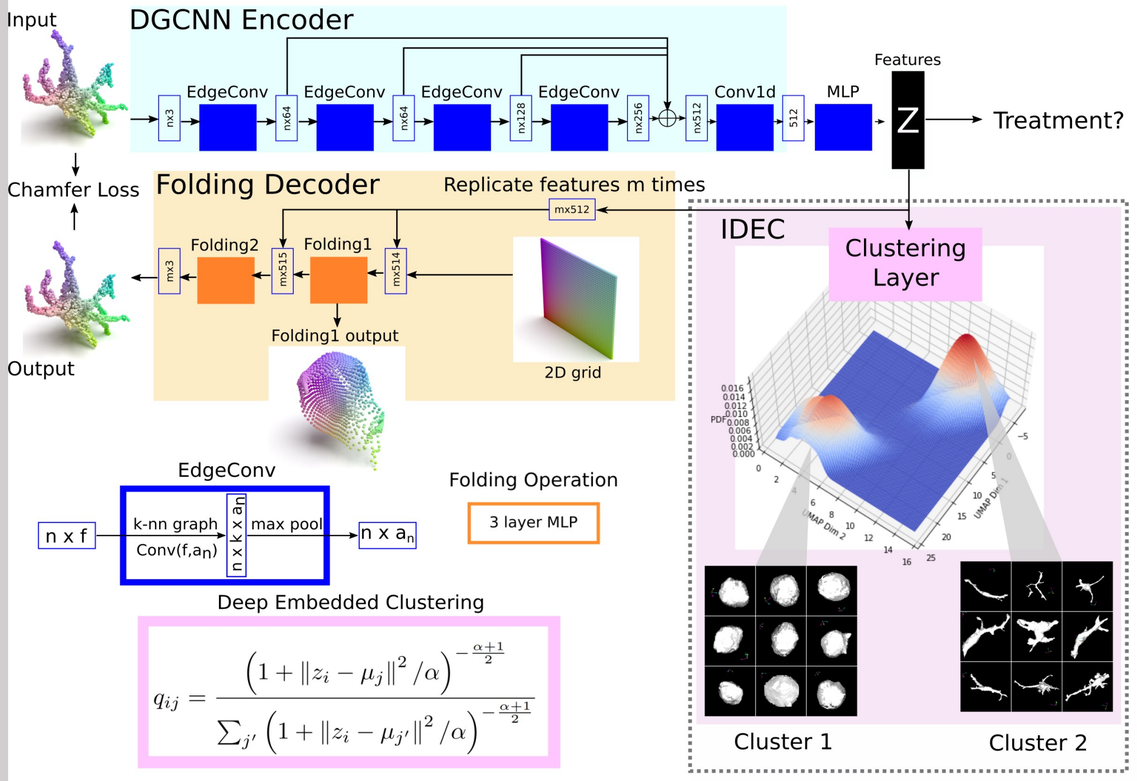


Quantifying shape in 3D is difficult. While measuring shape in 2D images has been illuminating, cells exist in 3D environments, and their 3D geometry is a rich source of information about the inner workings of cells and tissues. Recent imaging technologies have made it possible to image large numbers of cells in 3D with sub-cellular resolution. This development has led to a growing need for accurate 3D shape representations.

Geometric deep learning (GDL) to describe cell shape in 3D. We build on the progress made in 3D computer vision and use graph-based neural networks to automatically learn high-quality shape representations for single cells in 3D microscopy images. After generating high-quality 3D shape representations, we use our GDL features to predict drug treatments, 3D blood cell shape classes and explore and explain the features learned.

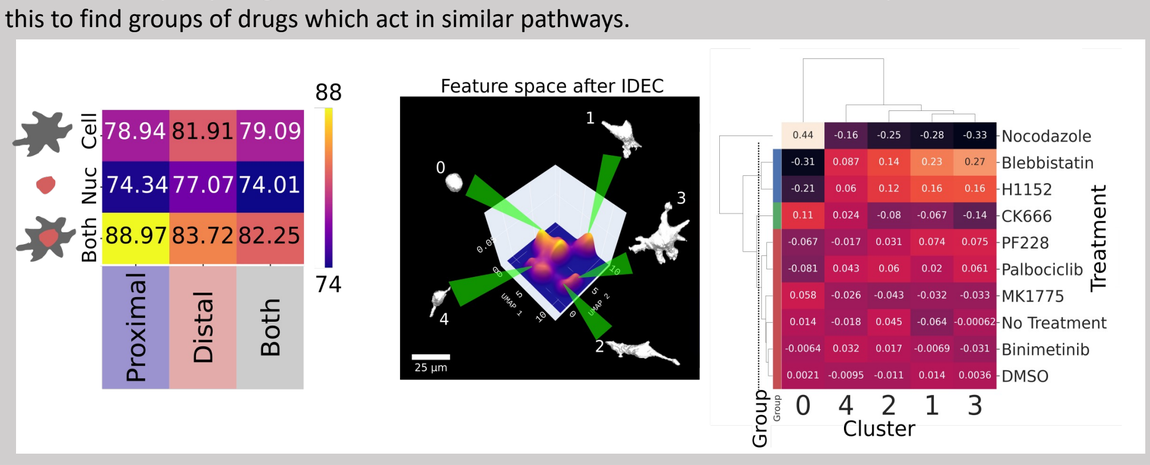
State-of-the-art computer vision

A dynamic graph convolutional foldingnet autoencoder was used to learn a lower-dimensional representation of the input cell shape. This consisted of a Dynamic Graph CNN as an encoder (light blue) and a FoldingNet decoder (light orange). In order to learn representations and shape classes simultaneously, improved deep embedded clustering adds a clustering layer to the feature representations (light purple). This maps the representations of each cell to a specific shape class and gives a morphological signature for each cell in terms of the different shape classes that exist in the dataset. We show a dotted box around this component of the model as it is not always used and is an addition to the autoencoder.



Predicting small molecule treatment through 3D quantitative morphological signatures

We used our learned features to predict small molecule treatment with up to 89% accuracy. We describe a shape by a signature of how similar it is to a number of different exemplar classes and use this to find groups of drugs which act in similar pathways.



Python package for ease-of-use be scientific community

Our software is freely available online as a Python package.

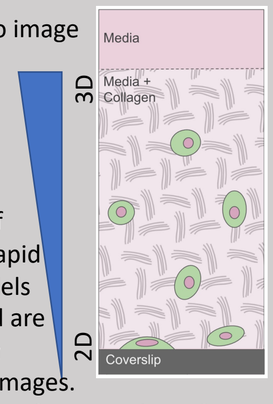
cellshape

GitHub

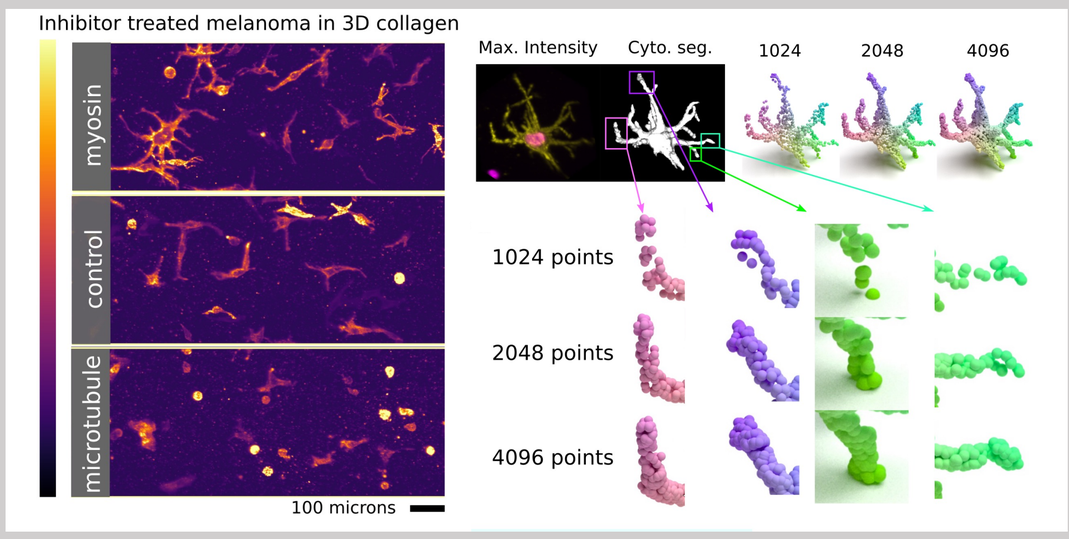
Paper

Data and pre-processing

High-throughput 3D light-sheet microscopy. We used light-sheet microscopy to image more than 70 000 WM266.4 metastatic melanoma cells embedded in tissue-like collagen matrices. The cells spanned an environment from a rigid surface to soft and 3D. The cells were treated with several different drugs including myosin inhibitors and microtubule polymerisation inhibitors.

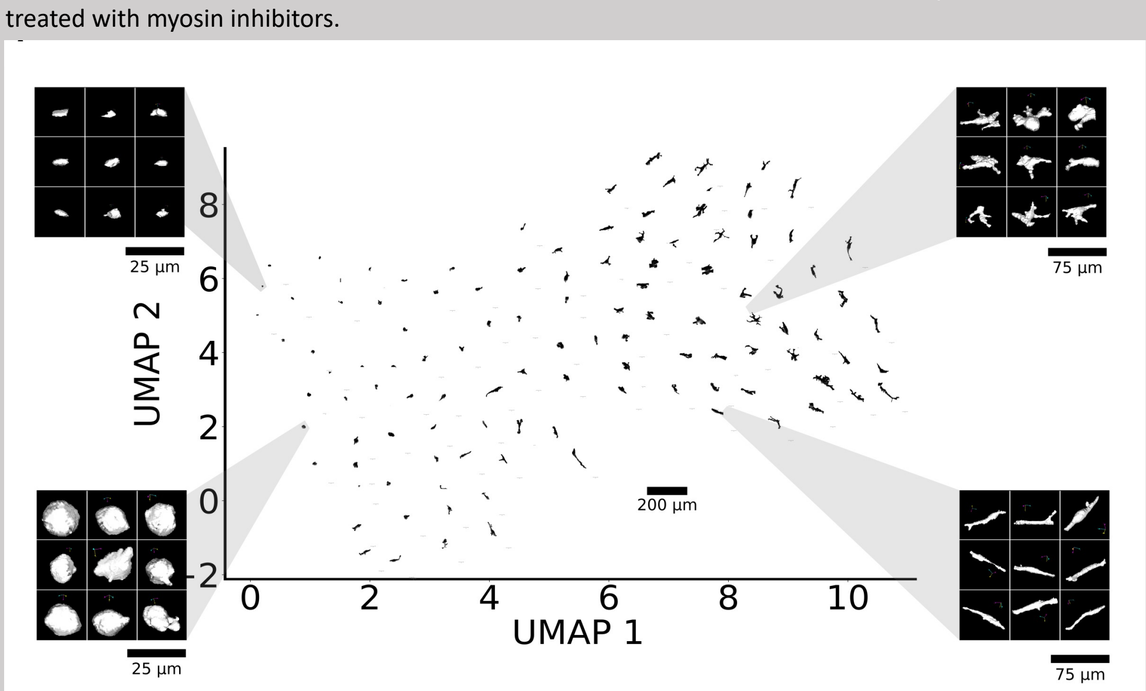


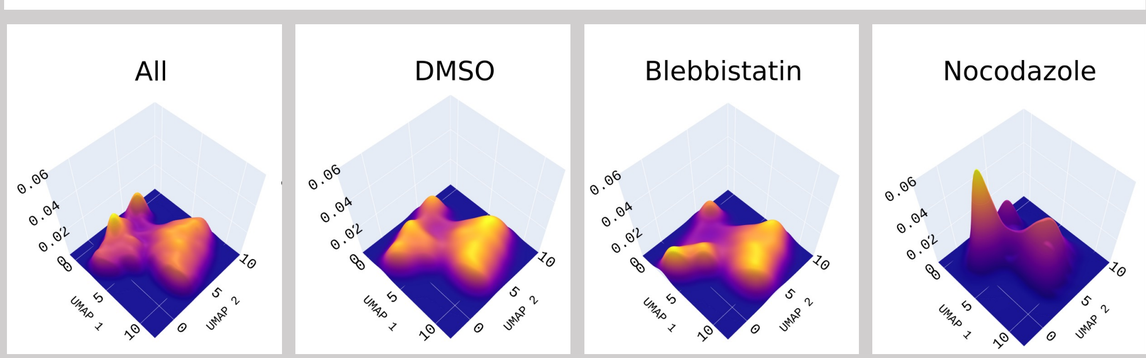
Point cloud representation of 3D shape. Robust representation of the shape of 3D objects is a major goal in the field of computer vision, and there has been rapid progress in this domain. State-of-the-art methods have analysed these 3D models as point clouds. Point clouds are scattered collections of points in 3D space and are arguably the simplest shape representation. These are easily obtainable once a segmented mask has been created and are memory-efficient compared to 3D images. We have segmented cell and nuclei shapes in 3D and sampled points from the surfaces meshes of these shape at different sampling densities.



Geometric deep learning reveals the cell shape landscape

Our trained DFN model without the clustering layer was first used to extract 3D shape features from all cells in our dataset. We show how microtubule inhibited cells take on different shapes than cells treated with myosin inhibitors.





Predicting red blood cell shape better than classical methods

We used our learned features to predict 3D red blood cell shapes from a recently published library. We achieved an accuracy of up to 99% which was better than classical methods (87%) and spherical harmonics (97%).