**What:**

A complete understanding of the complex phenomenon of cancer cell migration across several spatial and temporal scales is crucial to derive an adequate quantification for single cell-based analysis. Typically, mesenchymal cell migration can adopt two sub-modes: discontinuous (or random) and continuous, and can also switch between modes depending on their requirements [1]. The use of systems microscopy, from living cell to algorithms, holds a great potential to elucidate the spatiotemporal complexities of cell migration by the quantitative recording of dynamic cellular responses over time.

**Why:**

The spatiotemporal behaviour of dynamic cells such as motion heterogeneity, splitting, and persistence is often complex and overabundance of experimental data makes manual prediction of migration modes challenging. Clinicians often require a large time-lapse image sequence of cells to predict the cell migration sub-modes with a high confidence. However, exposing the cells with higher photon counts for a longer duration resulting in photo-toxicity (or to cell apoptosis), and thereby reducing the number of cells for subsequent analysis. Such consequences can be mitigated using the automatized and integrated algorithms.

**How:**

Here, we demonstrate that a CNN can prospectivelypredict the migration sub-mode from a single image patch of a cell, and thereby overcoming the challenges of high photo-toxicity while minimizing the data acquisition efforts and data storage requirements. Furthermore, it addresses the inter- and intra-observer prediction variability by providing the model uncertainties while yielding high accuracy.

Automation can help to reduce the noise induce by the multiple manual intervention

High resolution images of H1299 (human non-small lung carcinoma) cell is acquired with Nikon A1R confocal microscope using a PlanApo VC 60X/1.4 NA oil-immersion objective (Nikon, Amsterdam, Netherlands). Images are acquired for 8–10 hr at 5 min intervals with a pixel resolution of 0.21 μm.

Table: Data specification

|  |  |  |  |
| --- | --- | --- | --- |
| Fibronectin Concentration (FN) | Experimental repeats | Number of Cells | Overall Cell observations |
| 2.5 μg/ml | 3 | 34 | 2525 |
| 10 μg/ml | 19 | 118 | 6528 |

Training is performed using approx. 4800 cell observation image patches of 80 cells from 11 experimental repeats of 10 μg/ml FN concentration.

Network Training Data:

10 μg/ml FN concentration using 11 experimental repeats covering 71 cells, resulting in approx. 3800 cell observation image patches.

Network Testing data:

10 μg/ml FN concentration using 5 experimental repeats covering 31 cells, resulting in approx. 1600 cell observation image patches.

2.5 μg/ml FN concentration using 1 experimental repeats covering 14 cells, resulting in approx. 734 cell observation image patches.

Data augmentation:

Flipping: Horizontal and verical

For comprehensive and adequate quantitative analysis, we focus on harnessing the discriminative capabilities of deep learning based methods to perform real-time classification of two migration modes, and thereafter, to increase the understanding of underlying phenomenon that influences the cellular organization of each migration mode.

Furthermore, to reveal how and why CNN models can predict future moving direction, we visualized the features of the cell images that were learned by the CNN models and contributed to their prediction: e.g., the protrusions and trailing edge.

**Mesenchymal cell migration is heterogeneous and migrating cell can switch between the modalities of Continuous and Discontinuous cell migration (Shafqat-Abbasi et al. eLife 2015). Manual classifications of migrating cells into the different modalities have previously been performed by analysing long time-lapse movies from migrating cells. These movies are often acquired during several hours, 8 hours or more, generating large amount of data (Shafqat-Abbasi et al. eLife 2015). During live cell acquisitions cells are exposed to laser power, in order to excite and visualize the fluorophores /markers expressed in cells. Exposure to laser power can cause photo toxicity, injure live cells and possibly cause cell death by apoptosis. Photo toxicity can therefore reduce the number of cells to be classified and/or used in downstream experiments. Can affect large scale analysis**

**A migration mode classifier, using only one time frame need less acquired data reducing time efforts and data storage. Live cells will be exposed to less photo toxicity which will increase the number of viable cells available for migration mode classification and downstream applications.**

**Why:  
How:**

Here, we demonstrate that CNNs prospectively predict the future direction of cell movement with high accuracy from a single image patch of a cell at a certain time. Furthermore, to reveal how and why CNN models can predict future moving direction, we visualized the features of the cell images that were learned by the CNN models and contributed to their prediction: e.g., the protrusions and trailing edge. To illustrate that CNNs can predict cell fate based on current cell shape, we set out to construct a CNN model that predicts the future direction of cell movement from a single image patch of a cell at a certain time. Cell migration is central to the development and maintenance of multicellular organisms. Fundamental understanding of cell migration can, for example, direct novel therapeutic strategies to control invasive tumour cells. However, the study of cell migration yields an overabundance of experimental data that require demanding processing and analysis for results extraction. Computational methods and tools have therefore become essential in the quantification and modelling of cell migration data.

, it will overcome the inter-observer prediction variability, less acquired data, reduced time efforts, and data storage. Also, a large time-lapse image sequence of cells is often required to manually predict the cell migration sub-modes with a high confidence.

This will thus, benefit us with less photo-toxicity, less acquired data, reduced time efforts, and data storage. A migration mode classifier, using only one-time frame need less acquired data reducing time efforts and data storage. Live cells will be exposed to less photo toxicity which will increase the number of viable cells available for migration mode classification and downstream applications. The study of cell migration yields an overabundance of experimental data that require demanding processing for quantitative analysis.

**Challenges:**

However, the spatiotemporal behaviour of dynamic cells such as motion heterogeneity, splitting, and persistence is often complex and challenging for manual classification and analysis.

During the high throughput screening of live cells, high photon exposure can cause photo-toxicity that causes cell apoptosis and thereby potentially reducing the number of cells for subsequent analysis. Also, the spatiotemporal behaviour of dynamic cells such as motion heterogeneity, splitting, and persistence is often complex and overabundance of experimental data makes manual prediction of migration modes challenging.

Mesenchymal cell migration is heterogeneous and migrating cell can switch between the modalities of Continuous and Discontinuous cell migration (Shafqat-Abbasi et al. eLife 2015). Manual classifications of migrating cells into the different modalities have previously been performed by analyzing long time-lapse movies from migrating cells. These movies are often acquired during several hours, 8 hours or more, generating large amount of data (Shafqat-Abbasi et al. eLife 2015). During live cell acquisitions cells are exposed to laser power, in order to excite and visualize the fluorophores /markers expressed in cells. Exposure to laser power can cause photo toxicity, injure live cells and possibly cause cell death by apoptosis. Photo toxicity can therefore reduce the number of cells to be classified and/or used in downstream experiments.

A migration mode classifier, using only one time frame need less acquired data reducing time efforts and data storage. Live cells will be exposed to less photo toxicity which will increase the number of viable cells available for migration mode classification and downstream applications.

**Pros**

Faster

Less imaging hours

Data amount reduced

Less cell death

No need for a CO2 chamber

**Cons**

Accurate classification ?

Automated prediction of mesenchymal cell migration modes in confocal microscopy images using deep learning

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<https://sysmic.ki.se/>

***Abstract:***

The ability of the cancer cell to migrate constitutes a central aspect of cancer metastasis, which causes most cancer lethality. Typically, cells can adopt several substantially diverse migration modalities. During a specific type of movement called mesenchymal migration, the cells adopt two mathematically distinct migration sub-modes: discontinuous (or random) and continuous, and can also switch between modes depending on their requirements [1]. A complete understanding of this complex phenomenon (cell migration) across several spatial and temporal scales is indeed crucial to derive an adequate quantification for single cell-based analysis.

The use of systems microscopy, from living cell to algorithms, holds a great potential to elucidate and understand the spatiotemporal complexities of cell migration, and thereby can allow detailed analysis of systematic cell arrays and perturbations by the quantitative recording of multiple dynamic cellular responses over time. However, the spatiotemporal behavior of dynamic cells such as motion heterogeneity, splitting, and persistence is often complex and challenging for manual classification and analysis.

Automatized and integrated algorithms are thus highly desired to facilitate mesenchymal migration sub-modalities classification. For comprehensive and adequate quantitative analysis, this work focuses on harnessing the discriminative capabilities of deep learning based methods to perform real-time classification of two migration modes, and thereafter, to increase the understanding of underlying phenomenon that influences the cellular organization of each migration mode.

***Introduction***

Mesenchymal cell migration can adopt two sub-modes: discontinuous and continuous, and can also switch between modes [1].

Different fibronectin (FN) concentration level: From a clinical perspective, multiple experiments repeats are performed with both low and high FN concentration level to quantify the behavior of cell migration modes. When the cells are treated with low (2.5 μg/ml) FN level, the discontinuous migration mode tends to be more dominant and when cells are treated with (10 μg/ml) FN level, the continuous migration mode is more dominant.

From the automatization perspective, we aim to develop a single (DenseNet-based CNN) classifier which can classify different mesenchymal cell migration modes (i.e., continuous, discontinuous, and switching) in the time-lapse movies (nd2 format) of cells created using different FN concentration level. The spatiotemporal behavior of dynamic cells such as motion heterogeneity, splitting, and persistence is often complex and the overabundance of experimental data makes a manual prediction of migration modes challenging. During the high throughput screening of live cells, an automated classifier can thus, minimize the time efforts required for manual classification and provide us with the consistent prediction (inter- or intraobserver variability).

The migration modes are:

1. Unknown (clinicians are uncertain about the migration mode)
2. Discontinuous mode grade 1
3. Discontinuous mode grade 2
4. Continuous mode grade 1
5. Continuous mode grade 2

Severely wrong classification case: when the classifier predicts the different mode for a completely different migration mode

Wrong classification case: when the classifier predicts the different grade of the same migration mode.

Conclusion:

1. A CNN network model can potentially be trained to predict the mesenchymal cell migration modes from an image of a single cell observation.
2. The proposed model yields a substantial performance on the image dataset with different fibronectin concentration levels and thereby showing a great potential to be used as an automated method for large-scale live cells screening. However, whether the inclusion of temporal information improves the prediction performance or not is remained to be shown.
3. Next, to reveal how and why CNN models can predict the migration modes, we will visualize the features of the cell images that were learned by the CNN models and contributed to their prediction: e.g., the protrusions and trailing edge.

The motivation for classifying migration mode from a single cell observation (patch):

1. The overabundance of experimental data makes a manual prediction of migration modes challenging (time-consuming and tedious) and eventually often leads to erroneous prediction.
2. Clinicians often require a large time-lapse image sequence of cells to predict the cell migration sub-modes with high confidence.
3. Exposing the cells with higher photon counts resulting in photo-toxicity (or to cell apoptosis), and thereby reducing the number of cells for subsequent analysis.

Contributions:

1. We present an empirical study of different CNN architectures for predicting cell migration sub-modalities per frame.
2. We present a multi-channel ROI based densenet for predicting cell migration sub-modalities per frame.
3. We present a recurrent multi-roi densenet for predicting cell migration sub-modalities to exploit temporal information. (May not be included in the experiments)

*First Veronica will provide some motivation for single frame classification. Second, the prediction using single frame is motivated by the fact that cells from one migration mode can switch to other mode and if the CNN can classify per frame then cnn can capture the spatial morphological changes per frame to understand which morphological changes influence the migration mode of cells. Here, we demonstrate that CNNs prospectively predict the future direction of cell movement with high accuracy from a single image patch of a cell at a certain time. Furthermore, to reveal how and why CNN models can predict future moving direction, we visualized the features of the cell images that were learned by the CNN models and contributed to their prediction: e.g., the protrusions and trailing edge. To illustrate that CNNs can predict cell fate based on current cell shape, we set out to construct a CNN model that predicts the future direction of cell movement from a single image patch of a cell at a certain time. Cell migration is central to the development and maintenance of multicellular organisms. Fundamental understanding of cell migration can, for example, direct novel therapeutic strategies to control invasive tumour cells. However, the study of cell migration yields an overabundance of experimental data that require demanding processing and analysis for results extraction. Computational methods and tools have therefore become essential in the quantification and modelling of cell migration data.*

***Data:***

We have high resolution confocal images of cells from two different fibronectin concentrations, i.e., 10 FN and 2.5 FN. For 10 FN, we used images from 11 experiments for training and remaining 5 for independent testing and 5 image dataset from 2.5 FN experiments for testing. For ablation we performed other way around as well. ***Write details of experiments and microscope and clinical samples***. ***Also, mention the total number of patches in both training and test datasets.***

***Method:***

***Experiments:***

*For single frame networks:* Train three popular DCNN methods i.e., VGGNet, DensNet, ResNet on 10 FN training data and test on the data mentioned in the **Section Data**. ***Perform transfer learning to show generalization.***

*For multi-channel network:* The best network will be used and train on different channels. The motivation is to show the actin can influence the prediction performance. And, if this will not be done then the motivation is that the network will be enforced to learn the ***attention mechanism*** and use motivation from the ***corresponding reference***.

*For time-based networks:* If this will be performed then we will use the multi-channel network to perform the LSTM based performance. Also then we will show the ensemble methods for single frame to predict the

***Results and Discussion:***

***Conclusion***

**Introduction**

1. Problem- Understanding of mesenchymal cell migration to derive an adequate quantification for single cell-based analysis
2. Task- Automated tracking of cells so that annotation process can be easily performed on a large scale.
3. Task- mesenchymal cell migration modes prediction to improve the automated detection of mode in confocal microscopy images.
4. Hypothesis- generic dynamic variables (such as displacement and orientation, and etc.) that can be able to classify the two modes and increase the understanding of underlying phenomenon that influences the cellular organization of each migration mode including switching mode too.
5. Hypothesis- to minimize the number of frames and time frequency while increasing the detection accuracy which eventually speed up the image acquisition.
6. Tools- classical ML classifier using generic features defined in 4 and then employ RNN and CNN to classify.

**Data**

1. Samples from two different set of experiments (i.e., fibronectin level).
2. Unlabeled data for further evaluation which should be verified by Veronica.

**Experiments (check notes saved in the notes on macbook)**

1. Generic dynamic feature design and apply feature selection on them for classification using whole cell track and subsets (i.e., divide the cell tracks in multiple set of samples). Aim is to minimize the length of cell track as much as possible. Tools will be tested are Random forest, boosted tree, recurrent networks, SVM, and decision tree. Problem with using whole track is that the displacement and orientation based variables could be biased due to variable length. It has been observed that the std. dev. of displacement is often much higher for discontinuous mode in comparison to the continuous cell mode. Similar observations are observed for the difference of change in the orientation per frame and difference of change in the orientation per two frames. One hypothesis to verify is also to check for difference of change up to five frames. However, this limits us to minimum number of five frames. This task also includes the empirical study for the motivation of using certain dynamic variables. Also, the experiments for feature selection. This will be shown through plots such as curves for std. dev. displacement over time, std. dev. of difference of change in orientations for each up to five frames, and scatter plots for different features how much they are separable. Performance will be compared using F-score, Sensitivity, ROC curve, and confusion matrix. One possible future work is to employ UMAP/ TSNE/PCA clustering algorithms to verify how separable are the clusters based on the selected features. Curves for the performance will include number of frames on the x-axis and performance on the y-axis. Another flaw of using subset is that the cell tracks will be correlated since they are cut out from a single individual cell track. Also, this process is still to be explored for switching modes meaning how it can be used to predict the switching mode. Also, MSD and other direction persistence observation can’t be used due to high homogeneity in the trajectories of both modes. Although, the displacement of discontinuous cells is higher, it is still oddly distributed throughout the trajectories and if subset of cell tracks are used then it would not be enough strong measure. This will be shown by a curve with several trajectories of both modes.
2. Train Convolution recurrent networks using subsets (i.e., divide the cell tracks in multiple set of samples) so as to reduce the need of more frames. The motivation is to exploit both spatial and temporal contexts at the same time. Compare the performance of each RNN network for selected subsets of tracks. The curve should be a plot which will show the accurate number of frames. The empirical study in this task includes predication of modes for all, last and middle frames. This will also help to predict the switch mode. Different strategies are still open to explore here.
3. Train convolution using single frame since RNN can be used but not so optimal for such case. This will show how we can minimize and still predict the motion modes quite substantially.
4. If unsupervised clustering part is performed, then we should go for deep embedding based methods using CNN and RNN where encoder and decoder based network will be implemented to reconstruct the same input patch. The purpose is to constrain the network to learn the underlying discriminative features using pseudorandom labels. Then, the performance of the network will be evaluated using original labels.
5. Performance measures will be same for each experiments.

***Results and discussion part is mentioned in the experiment section. Future work will include the experiments for low res data and have the similar style. Evaluate on the large scale or in real-time imaging sessions.***

***Another approach would be to develop centroid tracker which classifies the cell as well***

***Reference***

1. Shafqat-Abbasi, Hamdah, et al. “An analysis toolbox to explore mesenchymal migration heterogeneity reveals adaptive switching between distinct modes.” *Elife 5* (2016): e11384.

**Comment from Carolina on poster:**

**Background:**

1. Understanding of cancer cell migration in relation to environmental factors and drug treatment may give us clues on how of reduce the risk of metastasis
2. With an automated and quantitative approach for understanding cell migration modes, we open up for large scale systems microscopy and drug screening.

**Challenges:**

1. Exposing the cells to high photon counts results in photo-toxicity, which many in itself influence behavior of the cells.

**Conclusion:**

1. **The proposed model yields the probability with an uncertainty that describes the confidence regarding predictions.**

**If we manage to predict the migration behavior with just single frame then the phototoxity and staining can be overcome which is good (read thesis as an example to get the content)**

cell over the time. While

Indeed, such deluge of heterogeneous image data poses a direct requisite for automatized and integrated algorithms that facilitate migration mode classification.

and thereafter, the comprehensive analysis of underlying cellular organization of each mode. enable the detection of discrete mesenchymal migration sub-modalities, and thereafter, the comprehensive analysis of underlying cellular organization of each mode.

The use of this key enabling technology platform, , will be a cornerstone for next-generation systems biology to complex and dynamic molecular, sub-cellular and cellular networks.

However, the mechanism by which cancer cells control directional persistence during migration is a major question. During a type of movement called mesenchymal migration, the front end of a cell grows outwards and attaches to a different section of the matrix. The rear of the cell is pulled forward and it detaches from the matrix and retracts, which allows the entire cell to move forward. They can also switch between modes depending on their requirements. Indeed, cells can adopt several substantially different migration modalities, including multicellular, amoeboid, and mesenchymal (also termed lamellipodial or lamellipodial-driven) migration, which can all be utilized by a broad range of cell types, as well as lobopodial migration, which has been observed specifically in fibroblasts. These migration modes represent ’prespecified’ cellular configurations (i.e. cell states) that are favoured under particular conditions. Switch-like conversion between these distinct modes is therefore part of the plastic, adaptive/compensatory response of cells to either environmental modulation. The experiments reveal that the cells adopt two distinct migration modes, which Shafqat-Abbasi et al. termed ’Discontinuous’ and ’Continuous’. The majority of cells migrated in the Discontinuous mode, in which cells moved in many different directions. This was caused by a lack of coordination between the outgrowth of the front end of the cell, and the retraction of the back from the matrix. In contrast, in the cells that migrated using the Continuous mode, an outgrowth consistently led to a retraction, which enabled cells to move in one direction. H1299 (non-small cell lung carcinoma) cells stably expressing EGFP-paxillin (marker for CMACs) and RubyRed-LifeAct (marker for F-actin) (H1299 P/L cells) were imaged via confocal microscopy on glass coated with 2.5 mg/ml fibronectin (FN). H1299 P/L cells moved individually and exclusively via mesenchymal (lamellipodial) migration. Nonetheless, we observed and classified two qualitatively different migration modes emerging within the clonally derived H1299 P/L cell population. We termed these migration modes ’Discontinuous’ and ’Continuous’, reflecting their contrasting stepwise and smooth motion, respectively. Specifically, cells migrating in the Discontinuous mode cycle in sequence through at least three recognizable stages of movement, which we term ’lateral protrusion’, ’polarization’, and ’tail retraction’. These stages produce dramatic changes in cell morphology and frequent changes in migratory direction. Such directional changes occur at least in part because lateral protrusions typically develop at approximately 90° to the axis of the preceding tail retraction. Automated cell tracking revealed that cells in the Discontinuous mode migrate significantly faster than during Continuous migration. By applying mean squared displacement analysis of cell trajectories to assess measures related to cell speed (migration coefficient) and directionality (persistence time), we found that Discontinuous migration is less directionally stable at any given speed.

Mesenchymal (lamellipodial) migration is heterogeneous, although whether this reflects progressive variability or discrete, ’switchable’ migration modalities, remains unclear. Yet, partly due to a lack of adequate quantification, it remains unclear to what extent variation within modes occurs either progressively along a continuum or in a switch-like manner between as yet undefined intra-modal subpopulations. Indeed, cells can adopt several substantially different migration modalities, including multicellular, amoeboid, and mesenchymal (also termed lamellipodial or lamellipodial-driven) migration, which can all be utilized by a broad range of cell types, as well as lobopodial migration, which has been observed specifically in fibroblasts. These migration modes represent ’prespecified’ cellular configurations (i.e. cell states) that are favoured under particular conditions. Switch-like conversion between these distinct modes is therefore part of the plastic, adaptive/compensatory response of cells to either environmental modulation. During a type of movement called mesenchymal migration, the front end of a cell grows outwards and attaches to a different section of the matrix. The rear of the cell is pulled forward and it detaches from the matrix and retracts, which allows the entire cell to move forward. There are large variations in how cells move and they can adopt modes that lie between the two extremes of mesenchymal and amoeboid migration. They can also switch between modes depending on their requirements. The aim of this work is to developed a method to analyse how individual human lung cancer cells move. The experiments reveal that the cells adopt two distinct migration modes, which Shafqat-Abbasi et al. termed ’Discontinuous’ and ’Continuous’. The majority of cells migrated in the Discontinuous mode, in which cells moved in many different directions. This was caused by a lack of coordination between the outgrowth of the front end of the cell, and the retraction of the back from the matrix. In contrast, in the cells that migrated using the Continuous mode, an outgrowth consistently led to a retraction, which enabled cells to move in one direction. Such an approach, generally based on quantitative imaging, is especially effective when multiscale data capturing both cell behavior (migration) and organization (e.g. CMAC and F-actin status) is derived simultaneously on a per cell basis. This facilitates the leveraging of natural or induced heterogeneity to define: i) the statistical structure of variation (e.g. progressive or discrete) within and between cell populations, as well as; ii) key trends, dependencies and relationships within the cell migration system. To enable the detection of discrete mesenchymal migration sub-modalities, and thereafter, the comprehensive analysis of cellular organization, regulation, and adaptation underlying each mode, we have integrated a unique combination of analytical tools. H1299 (non-small cell lung carcinoma) cells stably expressing EGFP-paxillin (marker for CMACs) and RubyRed-LifeAct (marker for F-actin) (H1299 P/L cells) were imaged via confocal microscopy on glass coated with 2.5 mg/ml fibronectin (FN). H1299 P/L cells moved individually and exclusively via mesenchymal (lamellipodial) migration. Nonetheless, we observed and classified two qualitatively different migration modes emerging within the clonally derived H1299 P/L cell population. We termed these migration modes ’Discontinuous’ and ’Continuous’, reflecting their contrasting stepwise and smooth motion, respectively. Specifically, cells migrating in the Discontinuous mode cycle in sequence through at least three recognizable stages of movement, which we term ’lateral protrusion’, ’polarization’, and ’tail retraction’. These stages produce dramatic changes in cell morphology and frequent changes in migratory direction. Such directional changes occur at least in part because lateral protrusions typically develop at approximately 90° to the axis of the preceding tail retraction. Overall, the stepwise nature of Discontinuous migration is highly reminiscent of previous descriptions of fibroblast-like migration. By contrast, cell migrating in the Continuous mode move progressively, with less frequent changes in cell morphology and motile direction, in a manner analogous to classical keratocyte-like migration. Automated cell tracking revealed that cells in the Discontinuous mode migrate significantly faster than during Continuous migration. By applying mean squared displacement analysis of cell trajectories to assess measures related to cell speed (migration coefficient) and directionality (persistence time), we found that Discontinuous migration is less directionally stable at any given speed. Importantly, an extensive comparison of migratory behaviors in several additional cell lines and during H1299 cell migration on alternative extracellular matrix ligands indicated that Discontinuous and Continuous migration modes are consistently recurring phenomena. We quantitatively compared the spatial and temporal dynamics of membrane protrusions and retractions between and within each migration mode based on defining membrane dynamics over the minimal imaging interval of 5 min. This revealed that protrusions share similar size (area) distributions in both modes, while retraction events are more extreme in size during Discontinuous migration, that is, more frequently very small or very large. When compared within each mode, membrane retractions have a broader size distribution than protrusions in the Continuous mode, although this is far more striking in the Discontinuous mode. This revealed a relatively unstructured pattern of dynamics in Continuous cells, although retractions tended to be smaller and protrusions larger. In contrast, Discontinuous migration consistently displayed a wide distribution of retraction sizes (very small and very large), with protrusion sizes uniformly moderate

Cancer cell migration is a key process in development, physiology and diseases where

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