Review of Methods for Cell Tracking

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Overview

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- Applications of cell Tracking
- Cell Tracking Methods
- Approaches Used for Different Methods
- Comparison between different methods
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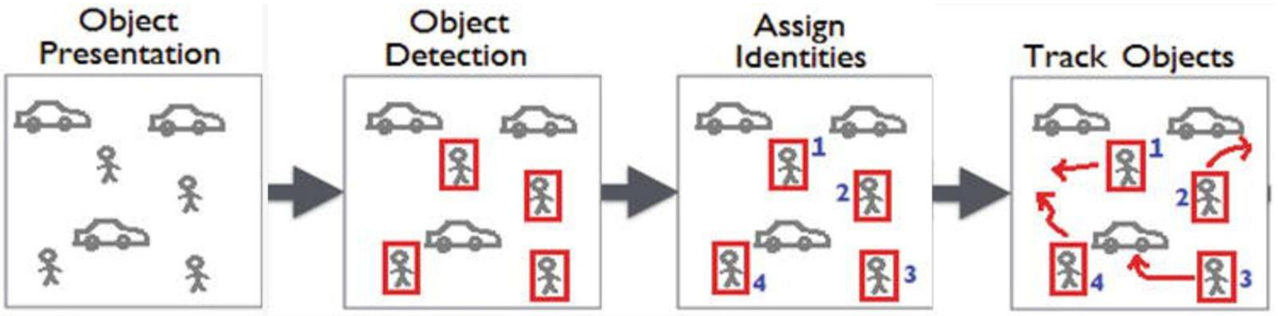
Object Tracking

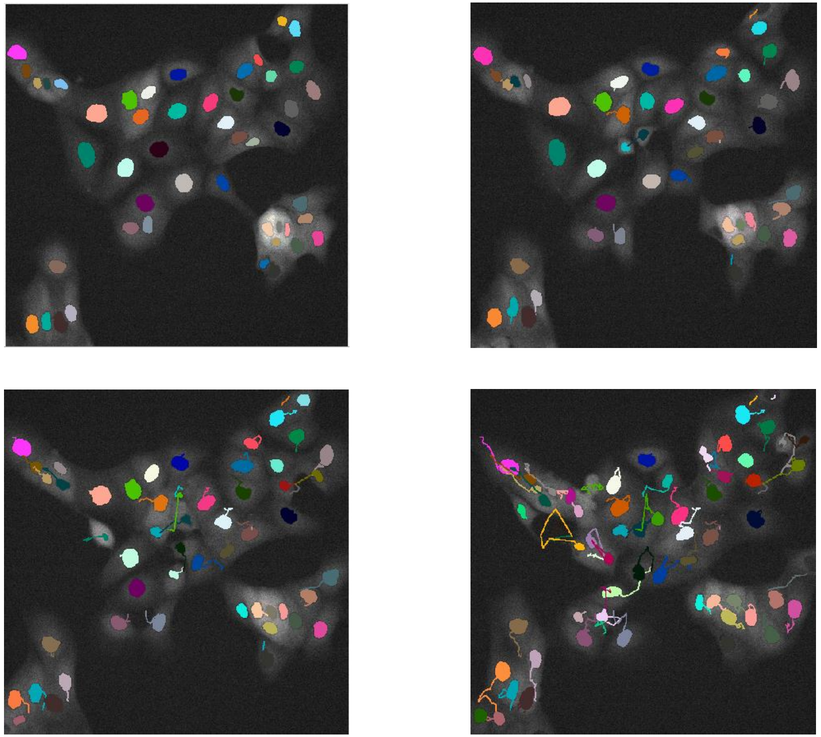
What is Object Tracking?

Object tracking is an application of deep learning where the program takes an initial set of object detections and develops a unique identification for each of the initial detections and then tracks the detected objects as they move around frames in a video.



Cell Tracking

- Cell tracking is a technique used for tracking cell features like cell growth, migration, invasion, and morphological changes.
- Cell tracking aims to portray cell functions like migration and engraftment at the organs, tissue, and molecular levels.



Source: https://imaging.cs.msu.ru/en/research/cell-tracking

Applications of Cell Tracking

Cell tracking finds its application in several spheres of biological research:

- **Intracellular dynamic tracking** - To track intracellular organelles and vesicles for analyzing cellular dynamics
- **Protein Tracking** - To understand the place and dynamic of protein pairs interacting or proteins position
- **Tracking normal and malignant cell cycle** - To track the behavior of cells and to find cells that are defective in their life cycle
- **Tracking of cell death** - To study the tumor growth and to treat the response of malignancies
- **Cell behavior tracking** - This includes tracking cellular behaviors that cause morphogenesis, such as division, migration, or death

Cell Tracking Methods

Cell tracking methods are mainly divided into

- Tracking by Detection
- Tracking by Segmentation
- Point-based Tracking

Tracking by Detection

- On the basis of intensity, texture, or gradient properties, cells are initially detected against the background in all the frames of the video independently.
- Cells are matched between consecutive frames by optimizing certain probabilistic functions.

Cell Tracking via Bounding Box [1]

Tracking by Detection

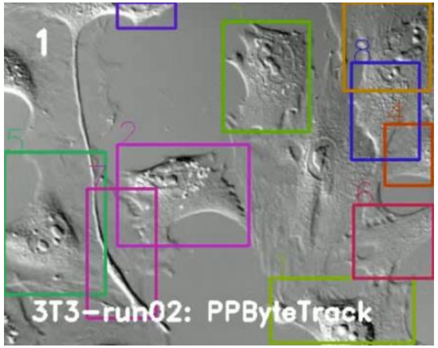
Approach used:

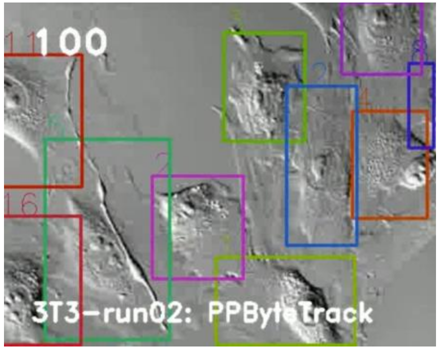
Long Short-Term Memory

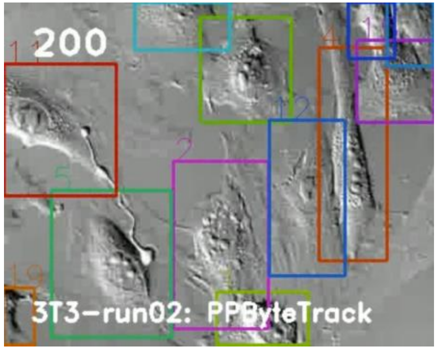
In tracking by detection, a bounding box is incorporated into trackers to train a detector, which detects bounding boxes, and an appearance model that trains the similarity of the bounding boxes.

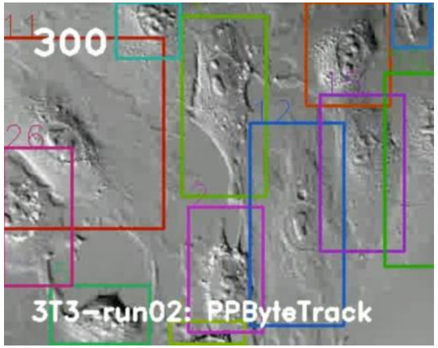
LSTM (Long Short-Term Memory) is used to measure the similarity among the time series of detected bounding boxes.

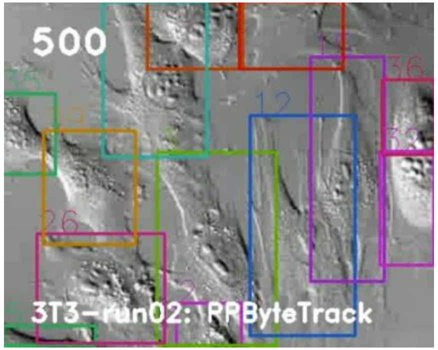
Tracking of cells in Cell Tracking with Mitosis Detection Dataset











Source: https://motchallenge.net/method/CTMC=18&chl=19

Tracking by Detection

Advantages

- Separation of segmentation and tracking tasks
- work on lower imaging frequencies
- advanced tracking data association techniques
- mutual independence of detection and association steps allowing straightforward tracking of new cells entering the field of view

Disadvantages

- Tracking can be problematic during mitosis tracking due to the inability to distinguish between multiple cells touching
- Increase in cell density increases segmentation error rate

Tracking by Segmentation

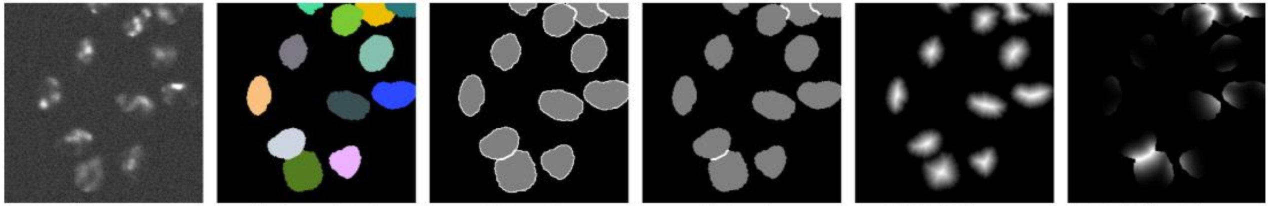
- Cells are segmented and tracked using the final outcome of every frame as an initial condition for the following frame.
- This method searches for similarities of objects in each image, and it is applied to applications like object tracking, edge detection, and handling cell division by providing a primary segmentation for the first frame.

Tracking by Segmentation

Approach used:

CNN based distance prediction

For cell segmentation, a deep learning model is trained to predict cells and cell borders. Instead of discrete cell boundary and cell border representations, the approach combines **cell distances** with novel **neighbor distances**.

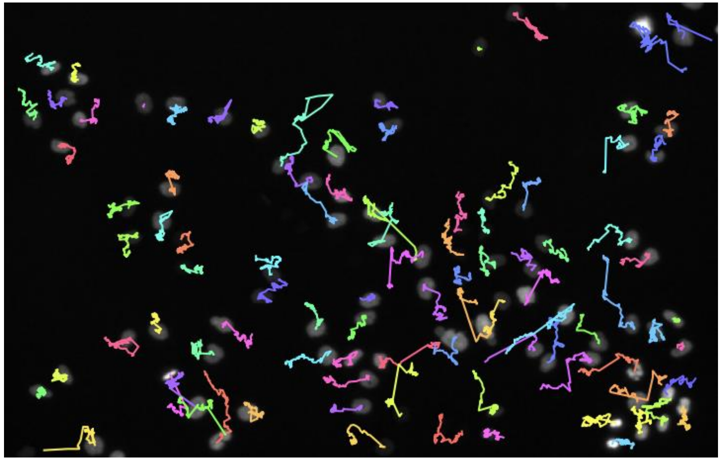


(a) Image (b) Ground Truth (c) Boundary (d) Border (e) Cell Distance (f) Neighbor Distance

Simulated Cell Tracking Challenge data set Fluo-N2DH-SIM+ [2].

Tracking by Segmentation

- The cell tracking algorithm used on the Cell Tracking Challenge (CTC) dataset traverses the image sequences.
- For each tracked object, a rectangular region of interest (ROI) is defined. The initial center of each ROI is set to the median position.
- To estimate the movement of an object, the consecutive image frames are cropped to the object ROI.
- Then, a phase correlation is calculated between the image crops to estimate a shift.
- Tracks with missing segmentation masks can be re-linked using a Graph-based matching strategy.



Tracking result on the CTC dataset [2]

Tracking by Segmentation

Advantage

- This method is very popular and it provides easy accommodation of morphological cues into the model to deal with the topologically flexible behaviour of live cells.

Disadvantage

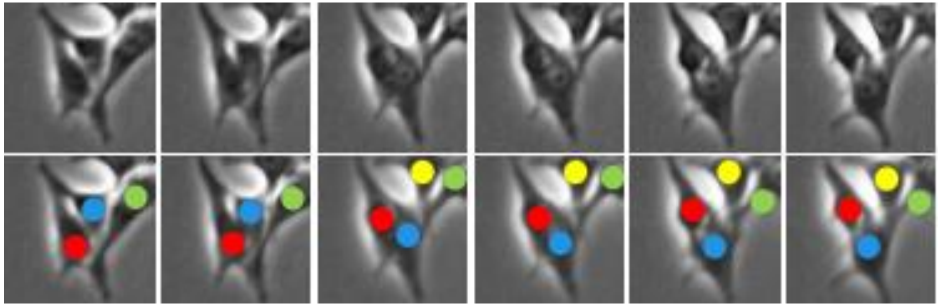
- Low contrast edges or noise pollution leads to incorrect segmentation

Point-based Tracking

- Point-based tracking is used for jointly estimating the center positions of objects and their attributes as points
- Point-based methods for detection and motion estimation are used for effective use in the spatial context.

Point-based Tracking

- Point-based methods directly extract the common image features from the image to estimate the position and motion map image by using a single network.
- In the first step of this method, the detected objects are associated between successive frames using one-by-one matching. This leads to errors in the detection step directly propagating to the association steps.
- It is difficult to detect cells and estimate cell motion of cells having blurry intercellular boundaries forming cluster regions under high-density regions



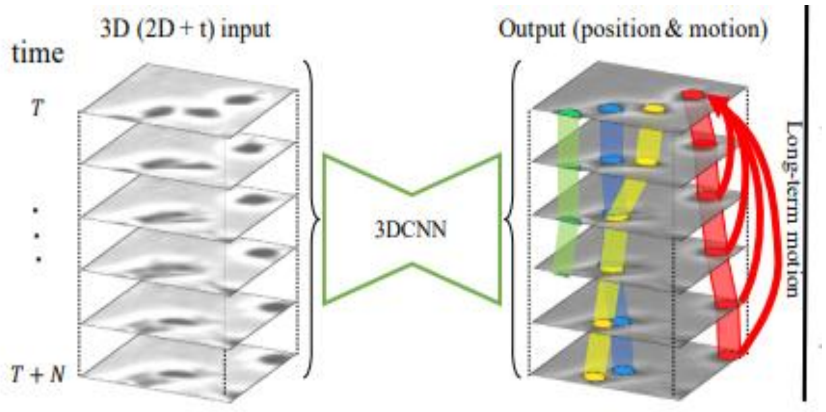
Top: original images
Bottom: ground-truth of trajectories. It is difficult to identify cells from the 3rd and the 4th frame. The individual cells can be identified if the entire frame is observed [3].

Point-based Tracking

Approach used

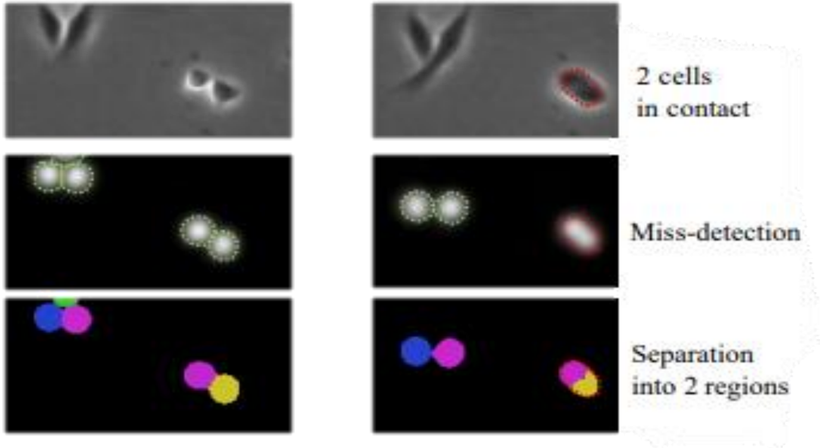
In order to overcome the difficulties of cell overlap in multiple frames, the **long-term spatial-temporal context is used using 3DCNN**.

- The short-term and long-term motion and position of each cell in multi-frames using 3DCNN.
- The long-term motion helps to extract the long-term spatial-temporal context and is also used for the interpolation of false negatives.

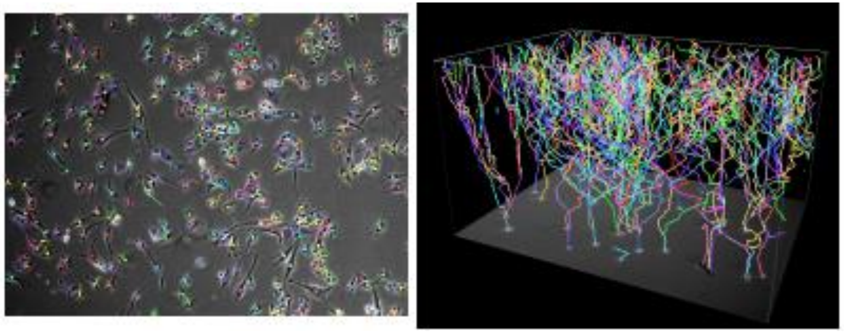


Long-term motion to obtain spatial-temporal context [3].

Point-based Tracking



Tracking using Spatio-Temporal Context reduced miss detection [3].



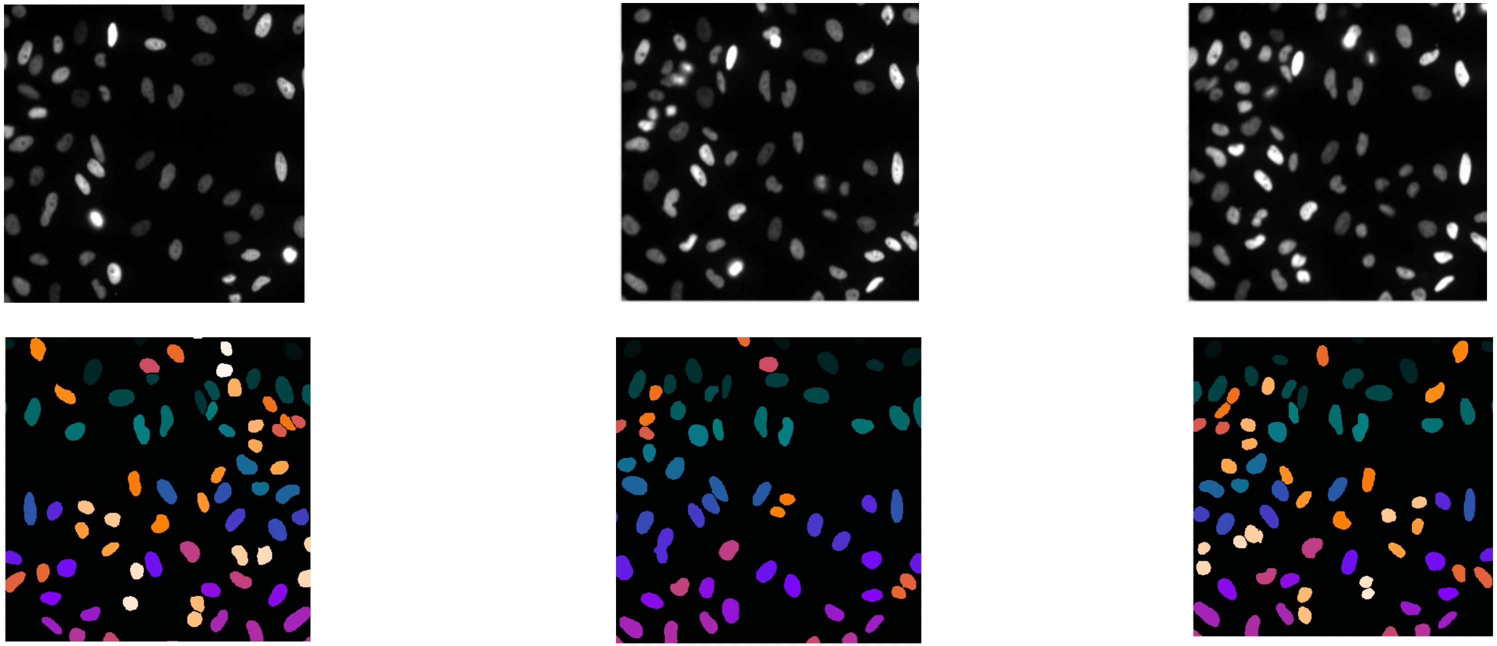
Tracking Result using Spatio-Temporal Context [3]. (a) indicates the entire image, (b) 3D view of estimated cell trajectories

Comparison between Different Methods

Method	Time taken	Analysis
Tracking by detection	7 seconds for each cell	• More information about the cell than point-based but less than segmentation based • Saves more time and money to annotate than a segmentation-based approach
Tracking by segmentation	46 seconds for each cell	• More information about the cell than tracking by detection and point-based approach as the cell shape is preserved. • Time consuming and costly
Point based tracking	0.9 seconds for each cell	• Least information about cell as the cell shape is lost. • Saves most time and money than the other methods

Datasets used for Cell Tracking

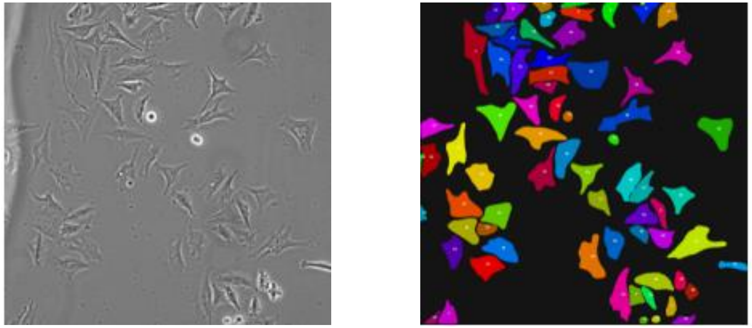
- **DeepCell** – It comprises a PhC (Phase Contrast) image sequence of HeLa-S3 cells. The annotations are given in terms of cell and nuclei segmentation masks for each image



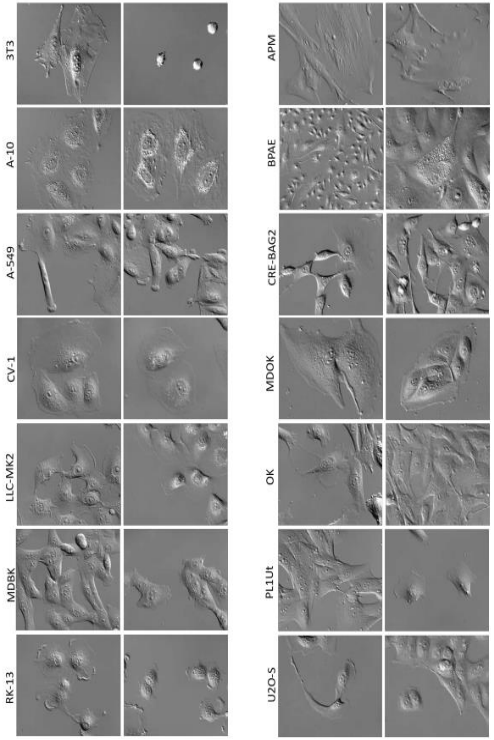
Source: https://deepcell.readthedocs.io/en/latest/

Datasets used for Cell Tracking

- **Cell Tracking with Mitosis Detection Challenge** - This consists of 152,584 frames in total, adding up to 86 live-cell imaging videos.
- **Usiigaci** – This includes 37 PhC images of T98G cells. The annotations comprise indexed masks with an index for each cell followed in time.



Example data from the Usiigaci dataset [1].



Examples of frames for each of the 14 cell lines in CTMC dataset [4].

Datasets used for Cell Tracking

- **Cell Tracking Challenge (CTC)** – CTC dataset includes 2D and 3D time-lapse videos of fluorescently marked nuclei or cells moving on top of or within a substrate, together with 2D PhC (Phase Contrast) and DIC (Differential Interphase Contrast) microscopy videos of cells that are moving on a flat substrate.
- **The dataset by Ker et al. [5]** comprises 48 PhC image sequences of mouse C2C12 cells under various treatments. Every cell in the dataset is annotated automatically.
- **C2C12-16** - This dataset is an extension of the Ker et al. dataset [5] with manual annotations of mitosis. This dataset comprises 16 sequences of 1013 frames per sequence with a total of 7159 mitosis events within the images

Conclusion

The key factors that cause errors in tracking results

- Noise - When images have a high noise ratio, it is difficult to detect objects. In some cases, the noise is followed instead of the objects, and this happens when the noise level is almost equal to the object's intensity.
- Information loss- Information loss occurs when converting 3D images to 2D.

In order to solve numerous biological challenges, such as deciphering complex cellular activities, it is necessary to create multitasking systems that can track several objects and simultaneously visualize the cell's environment.

References

1. Maddalena, L.; Antonelli,L.; Albu, A.; Hada, A.; Guarracino, M.R. Artificial Intelligence for Cell Segmentation, Event Detection, and Tracking for Label-Free Microscopy Imaging. Algorithms 2022, 15, 313.

2. Scherr T, Löffler K, Böhland M, Mikut R. Cell segmentation and tracking using CNN-based distance predictions and a graph-based matching strategy. Plos One. 2020 Dec 8;15(12):e0243219.

3. Hayashida J, Nishimura K, Bise R. MPM: Joint representation of motion and position map for cell tracking. InProceedings of the IEEE/CVF Conference on Computer Vision and Pattern Recognition 2020 (pp. 3823-3832).

4. Anjum S, Gurari D. CTMC: Cell tracking with mitosis detection dataset challenge. InProceedings of the IEEE/CVF Conference on Computer Vision and Pattern Recognition Workshops 2020 (pp. 982-983).

Thank You