# Behavioral tracking to assess neurodegenerative diseases

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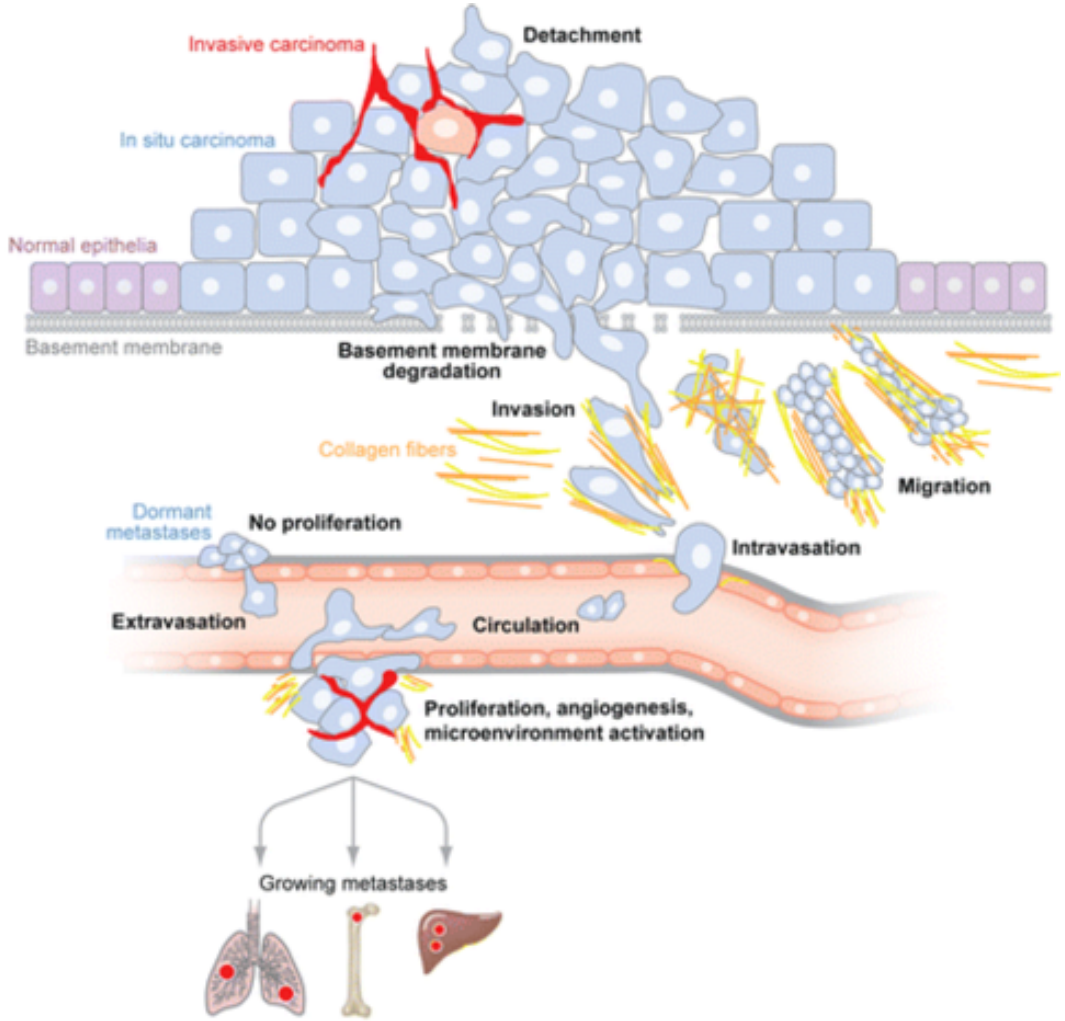
Mar. 29, 2022

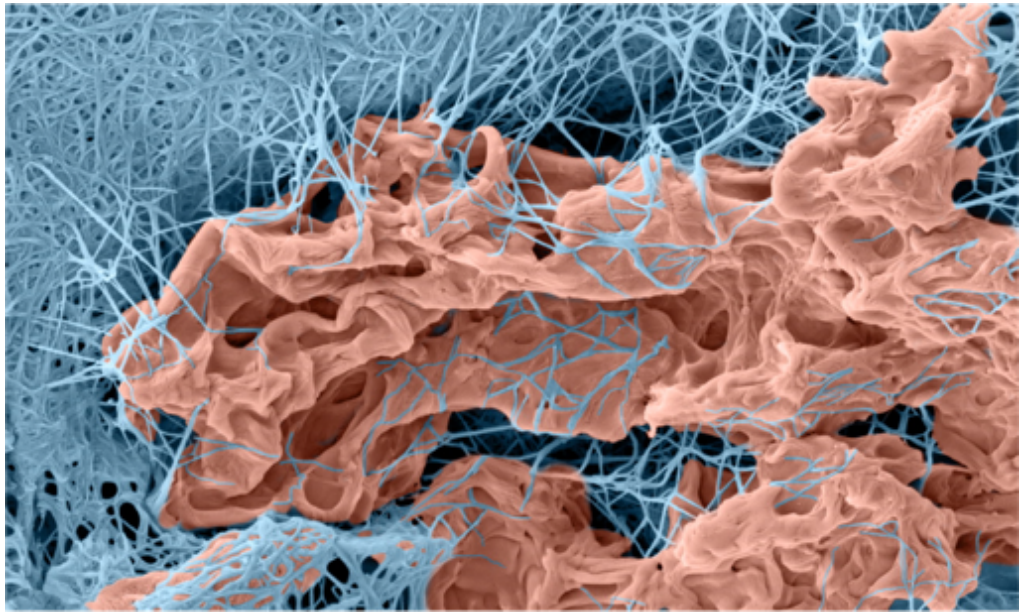
# Biophysical modeling for…

- Cell migration in diseases

# Biophysical modeling of cell migration

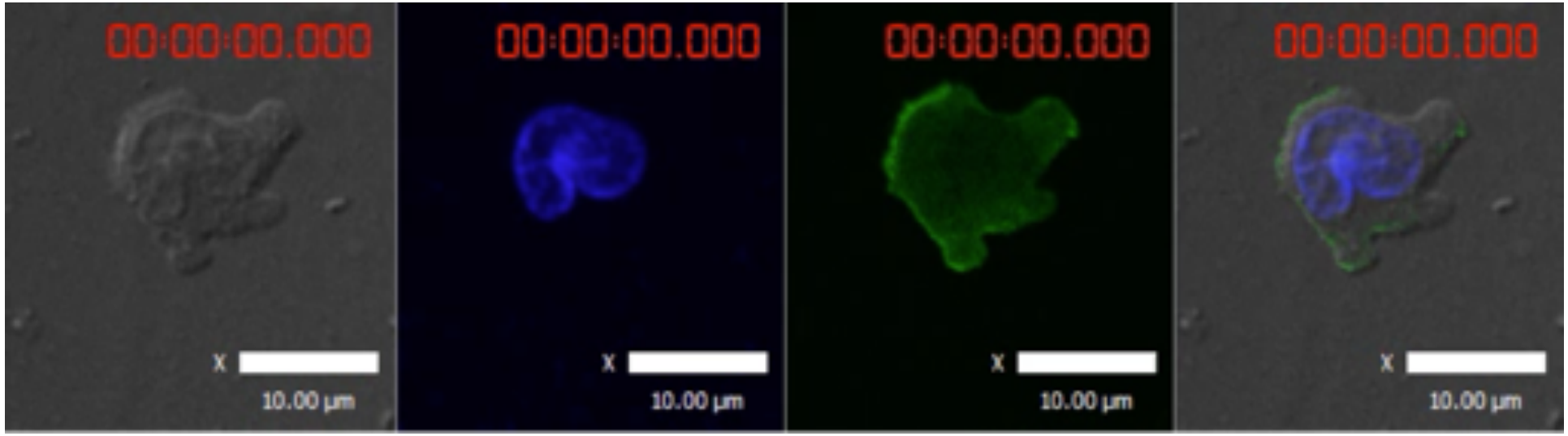



Bacac M, Stamenkovic I. 2008.
Annu. Rev. Pathol. Mech. Dis. 3:221–47

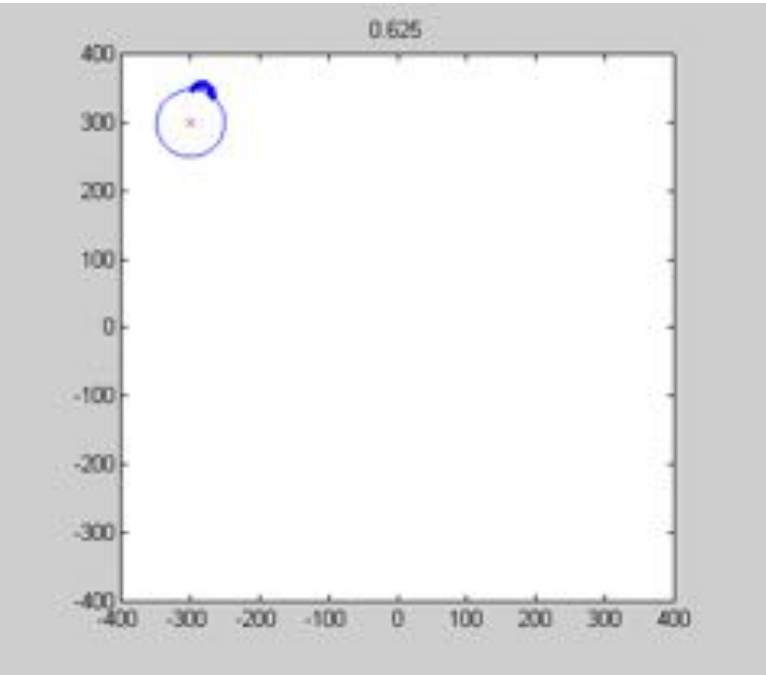


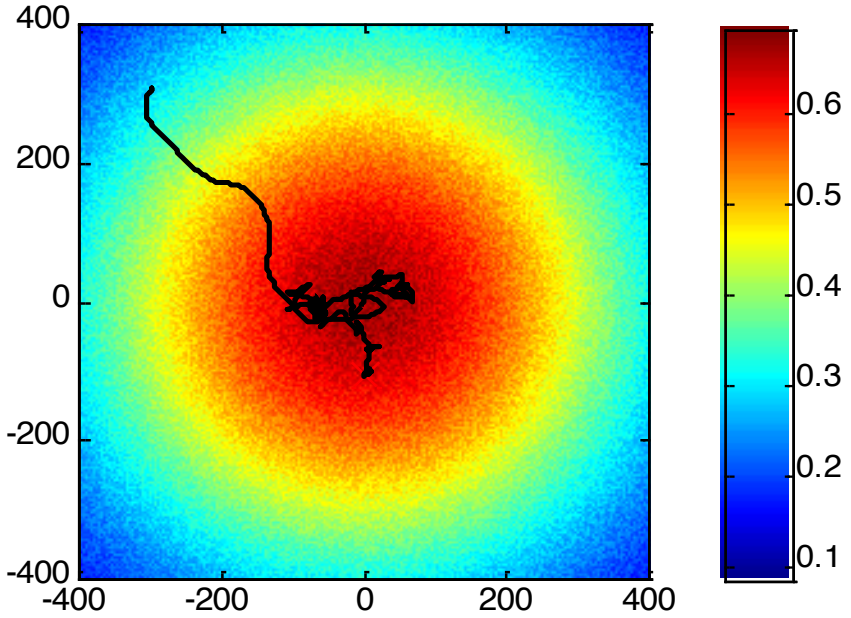
A375 human malignant melanoma cells on collagen-I matrix
J. Cell Sci. 124, 1256 (2011), J. Cell Biol. 185, 11 (2009)

# Biophysical modeling of cell migration



# Biophysical modeling of cell migration



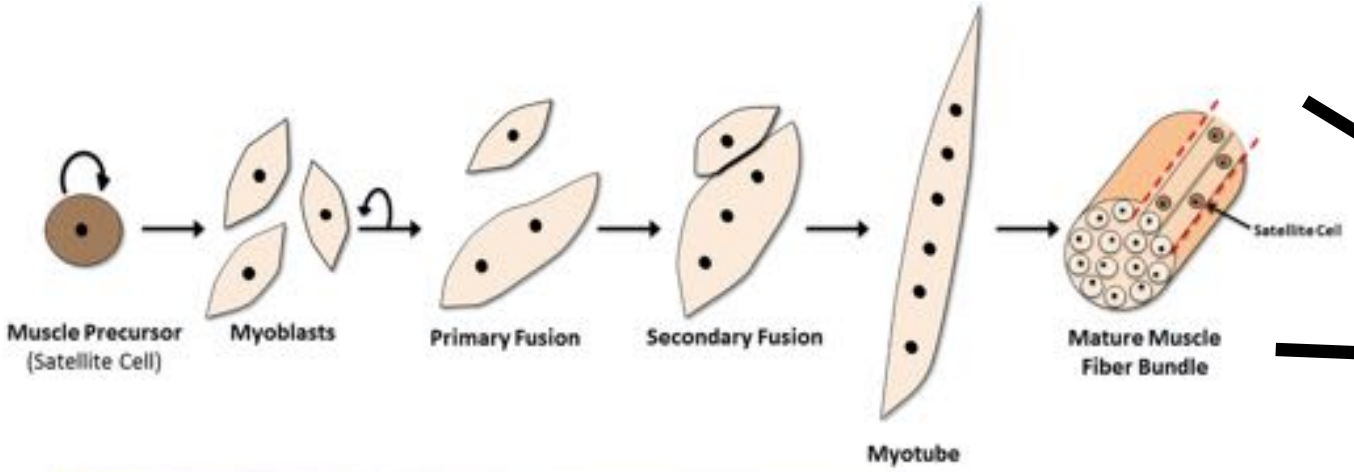



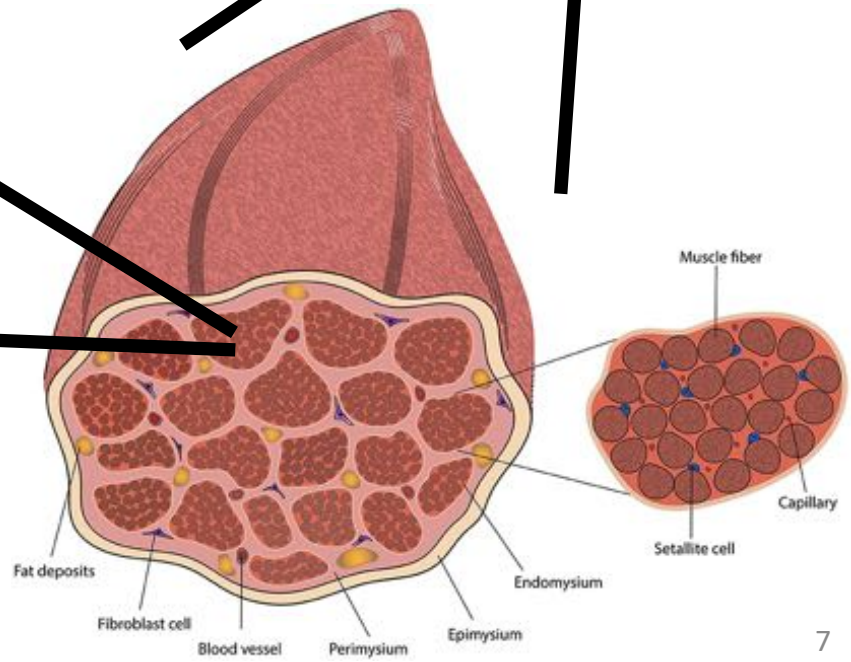
# Biophysical modeling for…

- Cell migration in diseases
- Cultured meat production
- Behavioral tracking

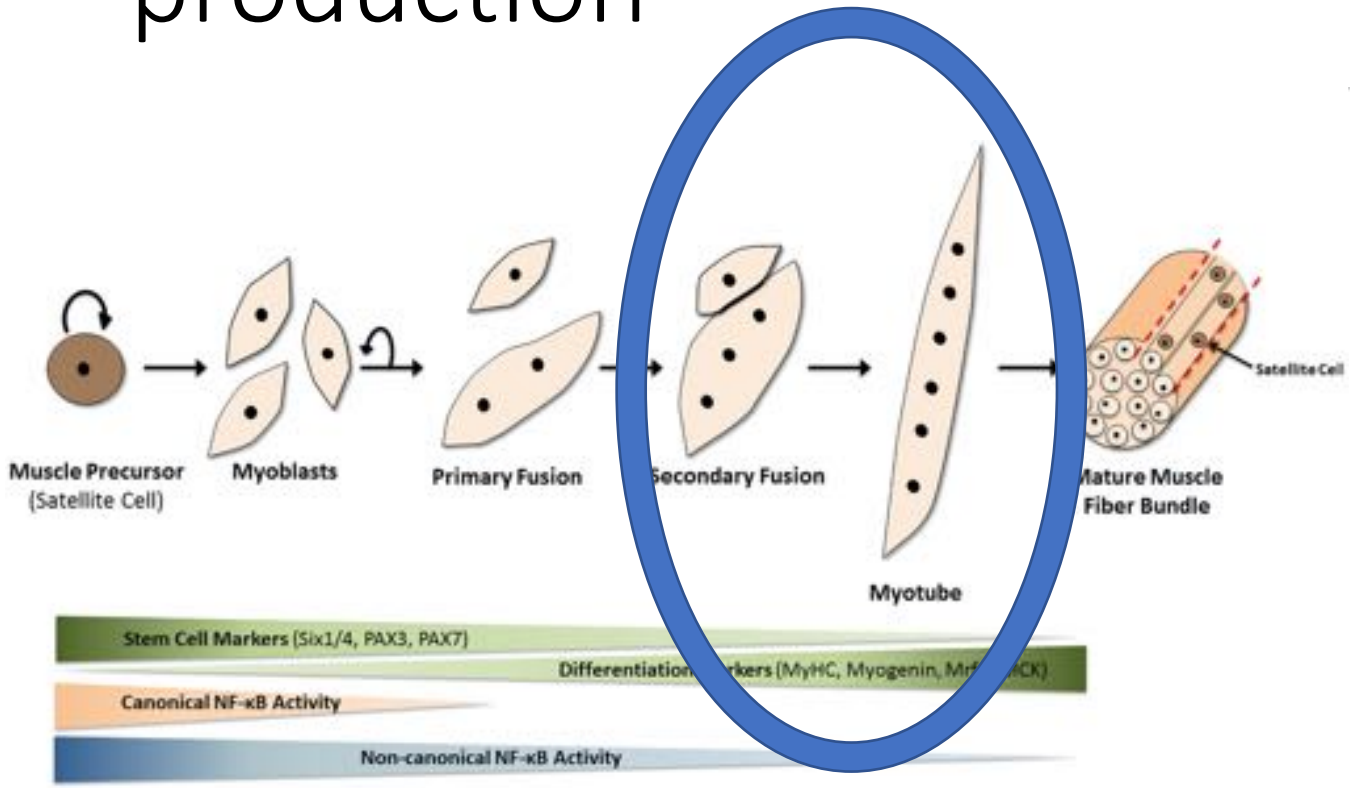
# Biophysical modeling for cultured meat production

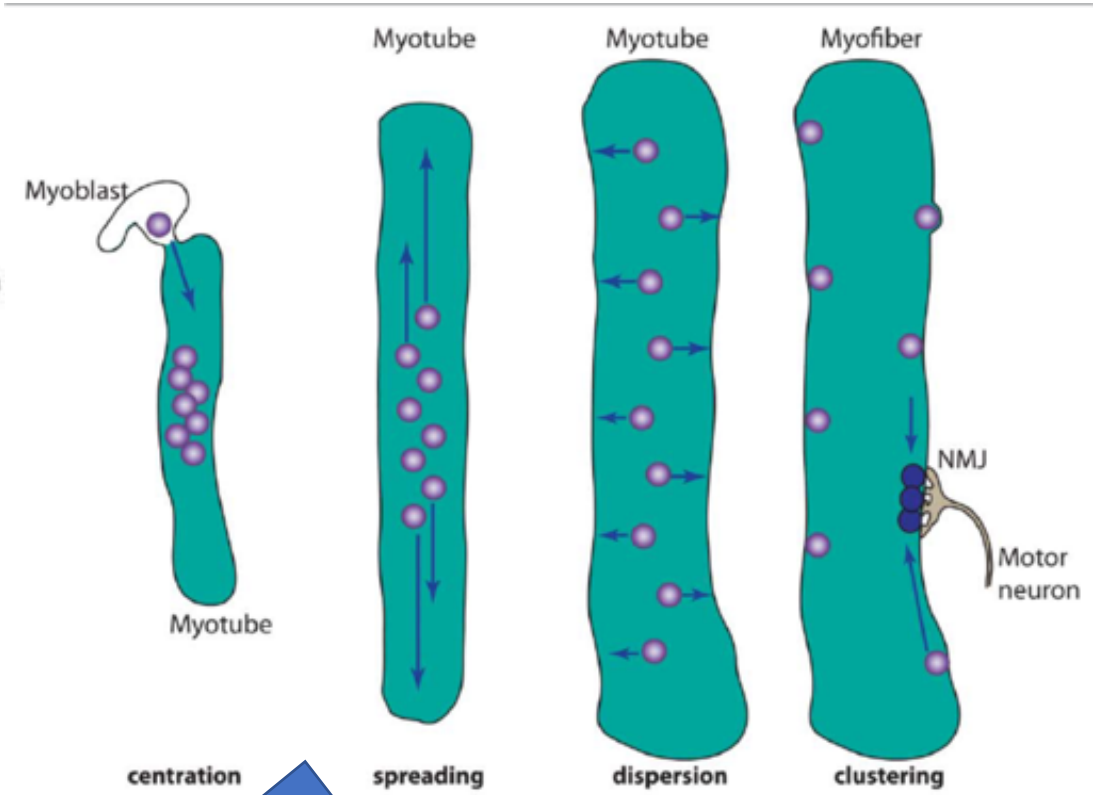
- What is meat?
- Striated muscle fibers
- plus fat cells, connective tissues, blood vessels



# Biophysical modeling for cultured meat production



# Biophysical modeling for…

- Cell migration in diseases
- Cultured meat production
- Behavioral tracking

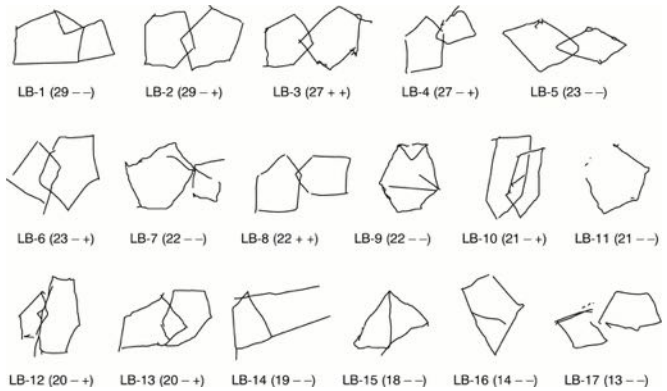
# Behavioral tracking

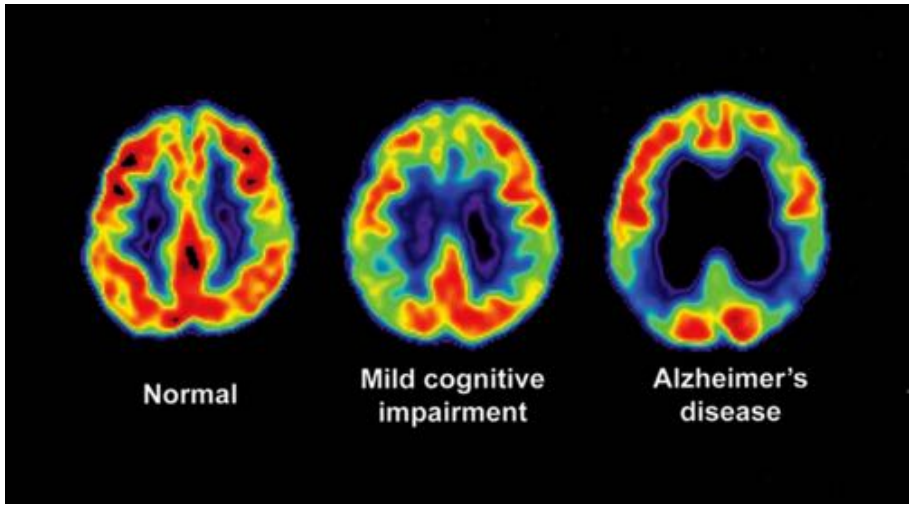
Clinical & cognitive assessments

MRI & PET images

Behavioral patterns

| Maximum Score | Patient's Score | Questions |
|---|---|---|
| 5 | | "What is the year? Season? Date? Day? Month?" |
| 5 | | "Where are we now? State? County? Town/city? Hospital? Floor?" |
| 3 | | The examiner names three unrelated objects clearly and slowly, then the instructor asks the patient to name all three of them. The patient's response is used for scoring. The examiner repeats them until patient learns all of them, if possible. |
| 5 | | "I would like you to count backward from 100 by sevens." (93, 86, 79, 72, 65, …)<br>Alternative: "Spell WORLD backwards." (D-L-R-O-W) |
| 3 | | "Earlier I told you the names of three things. Can you tell me what those were?" |
| 2 | | Show the patient two simple objects, such as a wristwatch and a pencil, and ask the patient to name them. |
| 1 | | "Repeat the phrase: 'No ifs, ands, or buts.'" |
| 3 | | "Take the paper in your right hand, fold it in half, and put it on the floor." (The examiner gives the patient a piece of blank paper.) |
| 1 | | "Please read this and do what it says." (Written instruction is "Close your eyes.") |
| 1 | | "Make up and write a sentence about anything." (This sentence must contain a noun and a verb.) |
| 1 | | "Please copy this picture." (The examiner gives the patient a blank piece of paper and asks him/her to draw the symbol below. All 10 angles must be present and two must intersect.)  |
| 30 | | TOTAL |



THE STRAITS TIMES SINGAPORE

# Kebun Baru pilots tech-integrated facility for the elderly living alone

The facility has two cameras and a sound sensor that monitor the elderly. ST PHOTO: KUA CHEE SIONG

# Behavioral tracking

**Nose-nose sniff**

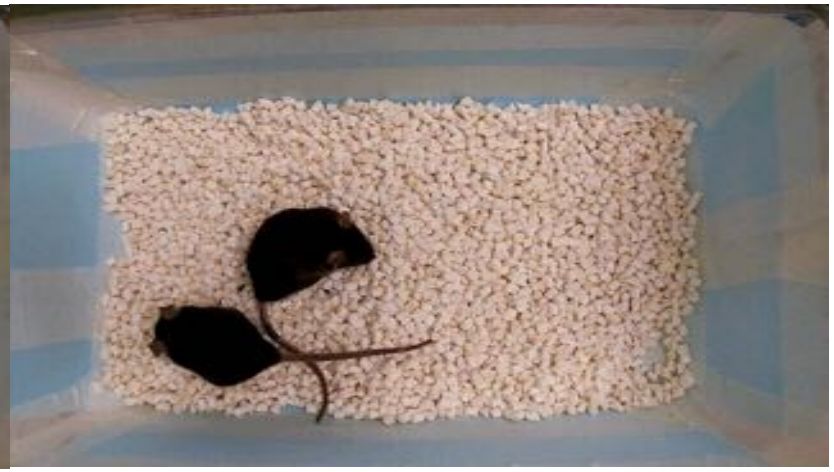
**Anogenital sniff**

**Body sniff**

**Affiliative**

**Following**

**Exploration**



# Behavioral tracking

Automated behavioral classification using machine learning:

1. Feature extraction
   - Pose estimation, i.e. tracking of positions of key points of the body
   - Features extracted directly from image, e.g. output of convolutional neural network trained on images
2. Classification
   - Supervised learning
   - Unsupervised learning

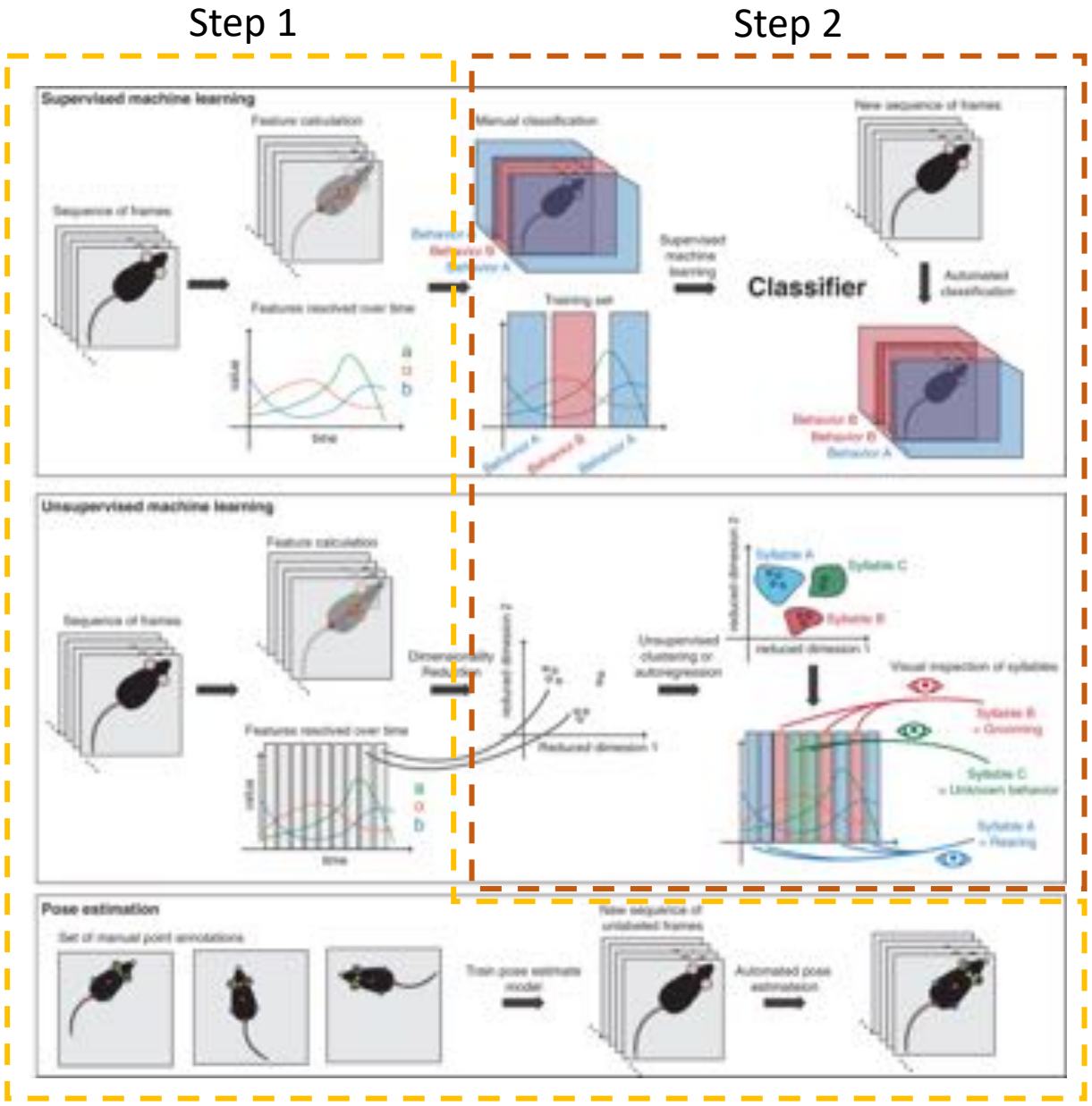
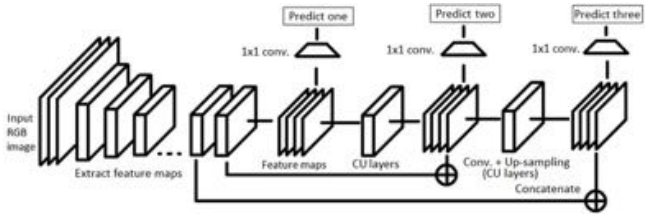



Diagram reproduced from Ziegler, Sturman & Bohacek, 2020. Big behavior: challenges and opportunities in a new era of deep behavior profiling

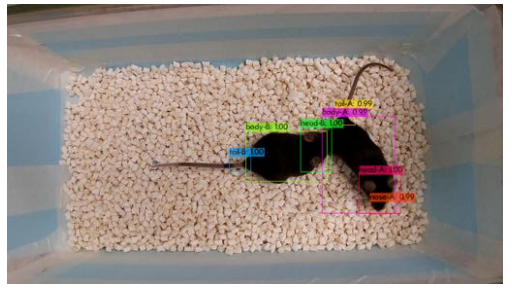
# Illustration of typical supervised learning workflow

Video of interacting animals

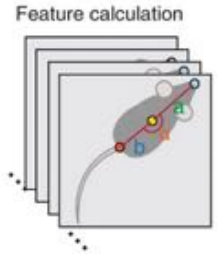
Deep learning pose estimation




Obtain pose

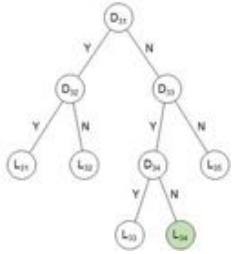


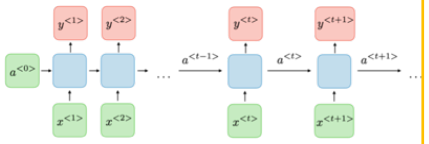
Compute features




- distances
- velocities
- angles
- etc …

Behavior classifier





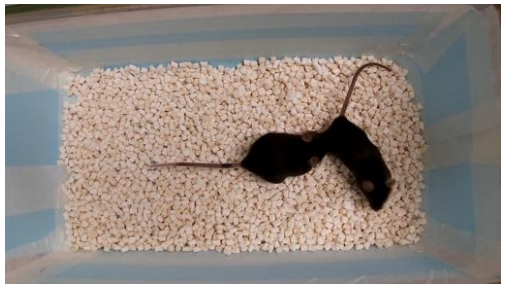
Neural network

Behavior

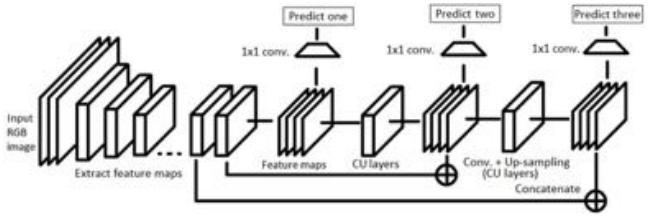
Mice 1: Body Sniff
Mice 2: Affliative

# Illustration of typical unsupervised learning workflow

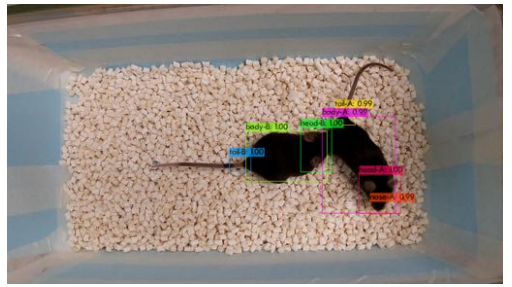
Video of interacting animals



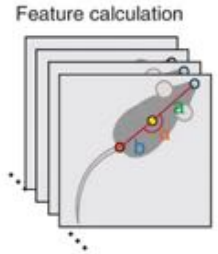
Deep learning pose estimation




Obtain pose



Compute features

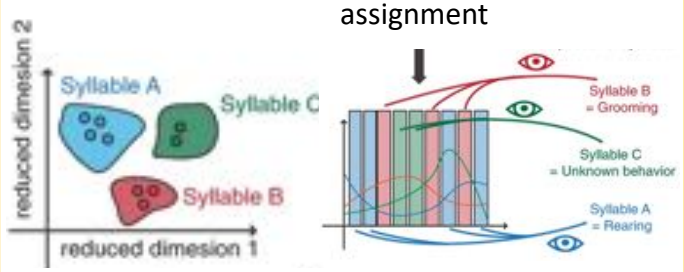



- distances
- velocities
- angles
- etc …

Behavior classifier

Clustering

Visual inspection and assignment



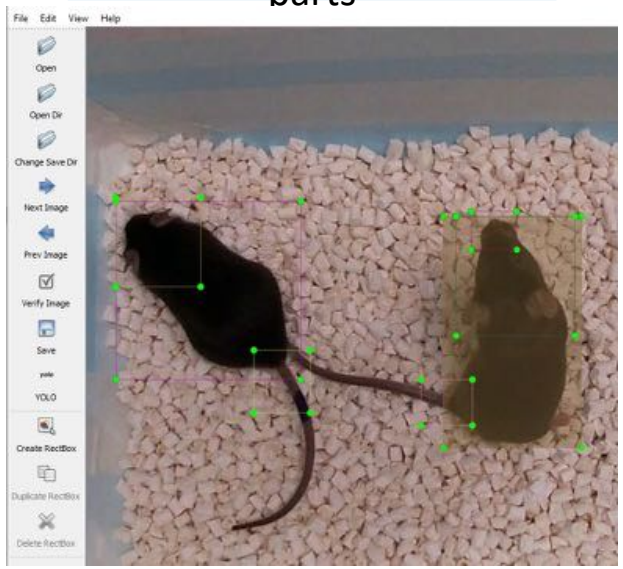

Behavior

Mice 1: Body Sniff
Mice 2: Affliative

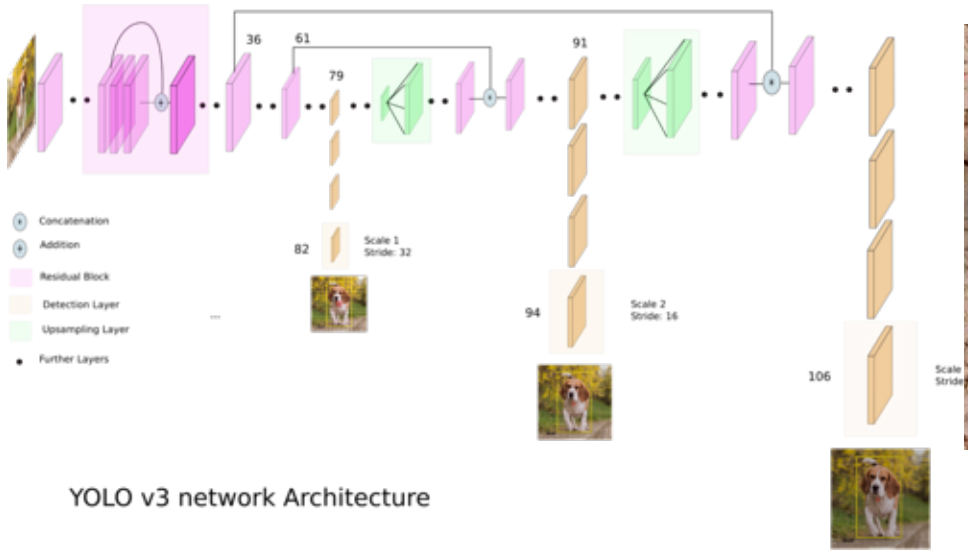
# Pose Estimation using Deep Learning

- Bounding box object detection method based on YOLO[1,2,3]

Manually label the training set for body parts

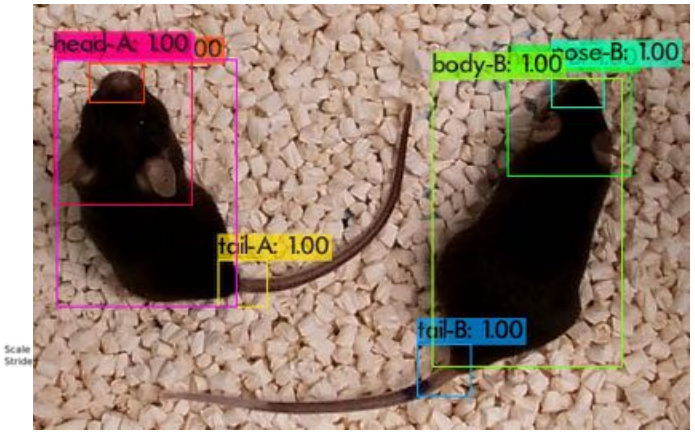



Train the YOLO network



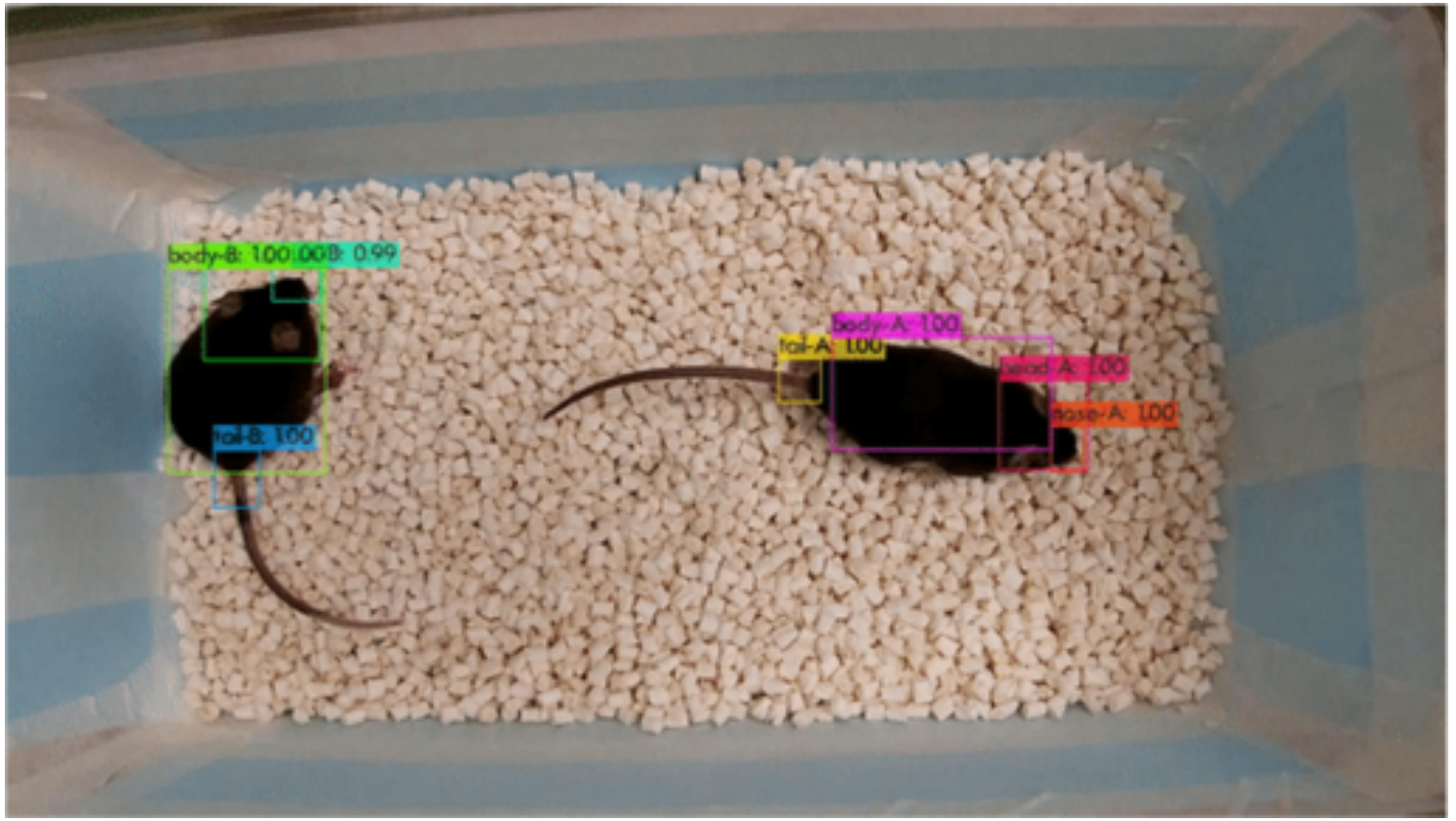

YOLO v3 network Architecture

Apply the trained model




1. Arac et al. 2019. DeepBehavior: A Deep Learning Toolbox for Automated Analysis of Animal and Human Behavior Imaging Data
2. Redmon et al. 2015. You Only Look Once: Unified, Real-Time Object Detection
3. Redmon & Farhadi, 2018. YOLOv3: An Incremental Improvement

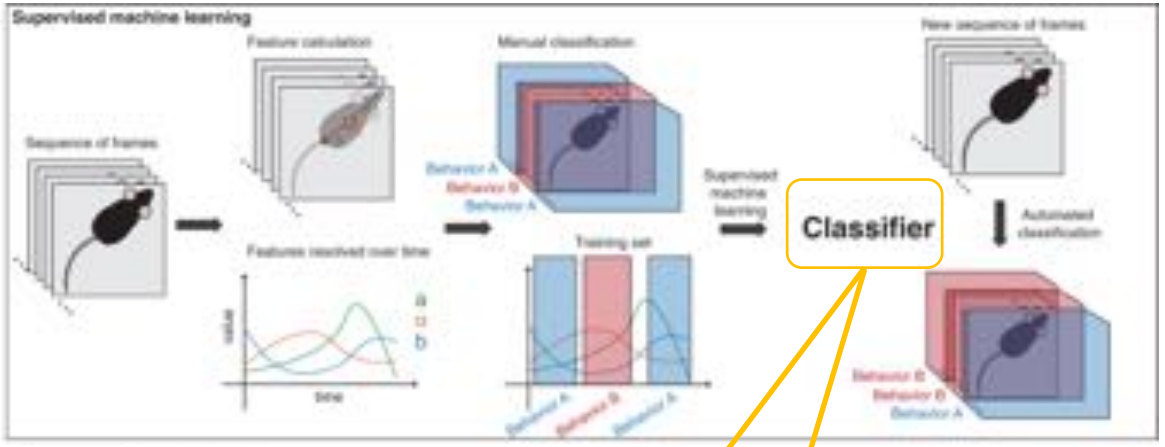
# Pose Estimation using Deep Learning Object Detection



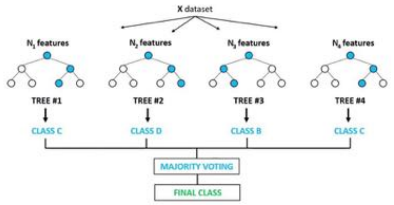

Example generated using YOLO network

# Supervised classification of behavior using pose information

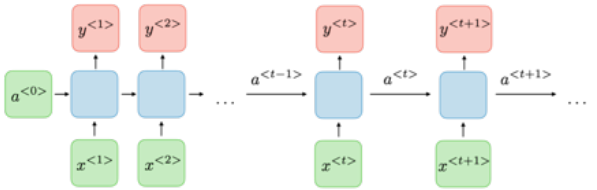
1. Calculation of features from pose estimation data
   - Distance between points, velocity, relative orientation etc.
2. Classification
   - Tree-based ensemble methods[1,2,3] are the most popular in literature. There has also been a few works using neural networks such as RNN[4] and CNNs
   - From results in literature and our own experiments, random forest model generally perform quite well




Random Forest Classifier




Recurrent neural network

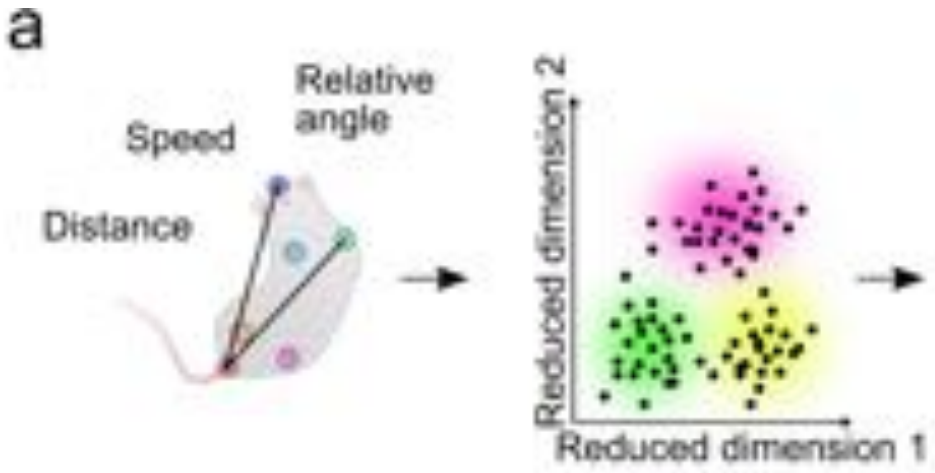



1. Hong at al. 2015. Automated measurement of mouse social behaviors using depth sensing, video tracking, and machine learning
2. Nilsson et al. 2020. Simple Behavioral Analysis (SimBA)
3. Segalin et al. 2020. The Mouse Action Recognition System (MARS): a software pipeline for automated analysis of social behaviors in mice
4. Arac et al. 2019. DeepBehavior: A Deep Learning Toolbox for Automated Analysis of Animal and Human Behavior Imaging Data

# Unsupervised classification of behavior using pose information

1. Calculation of features from pose estimation data
   - Distance between points, velocity, relative orientation etc.
2. Classification
   1. Dimensionality reduction and clustering
   2. Nonlinear dimensionality algorithms such as tSNE1, UMAP2
   3. Autoencoders type network that was trained with simulation data3, or on self-supervised task4

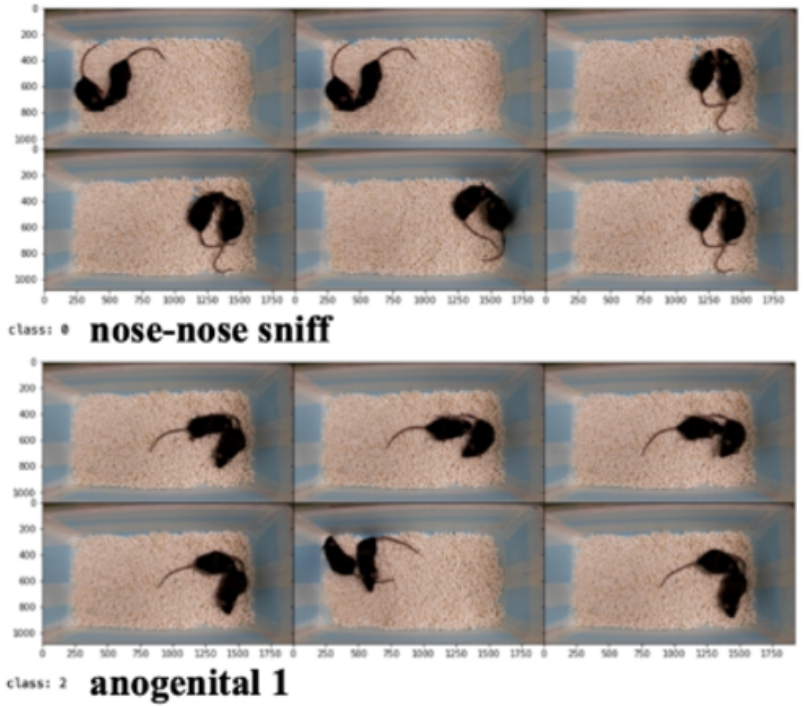
- Advantages of unsupervised learning
  - Remove potential biases introduced by humans in defining and labelling behavior



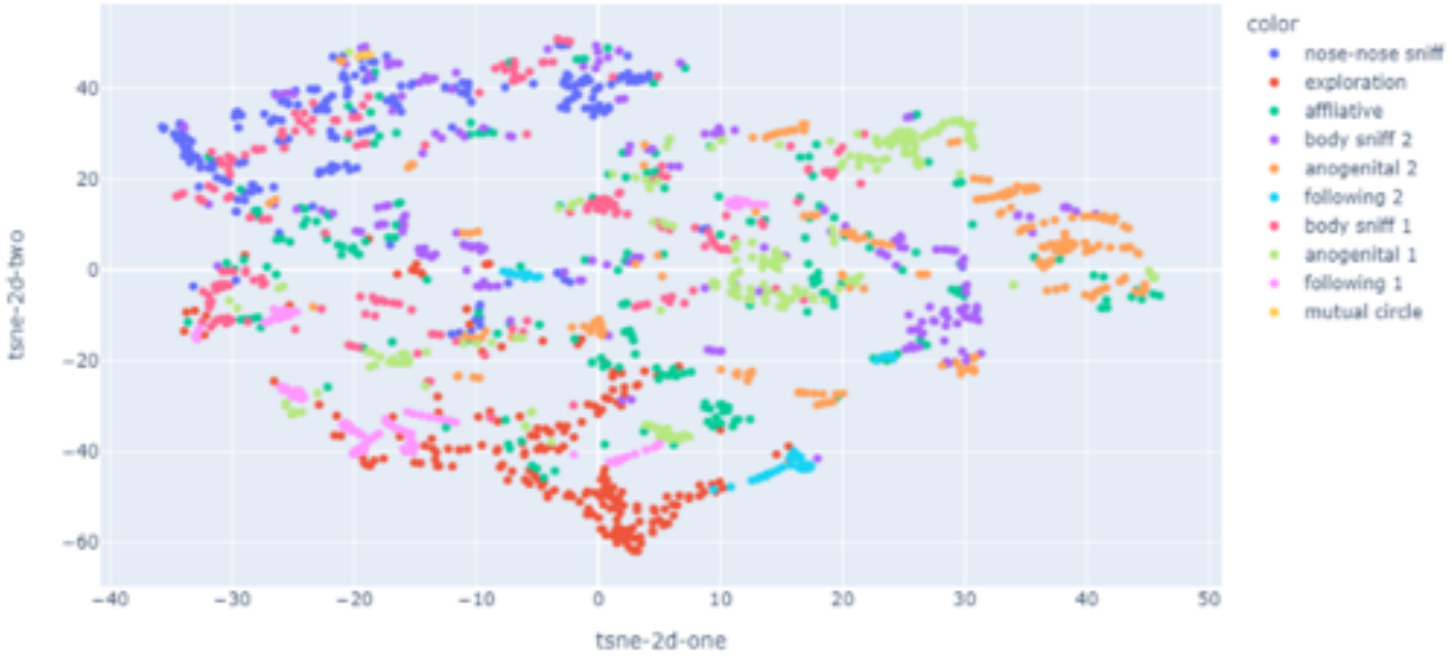


1. Berman et al. 2014. Mapping the stereotyped behaviour of freely moving fruit flies
2. Xu & Yttri 2021. B-SOiD, an open-source unsupervised algorithm for identification and fast prediction of behaviors
3. Batpurev et al. 2021. Automatic Identification of Mice Social Behavior through Multi-Modal Latent Space Clustering
4. Luxem et al. 2020. Identifying Behavioral Structure from Deep Variational Embeddings of Animal Motion

# Unsupervised classification of behavior using pose information



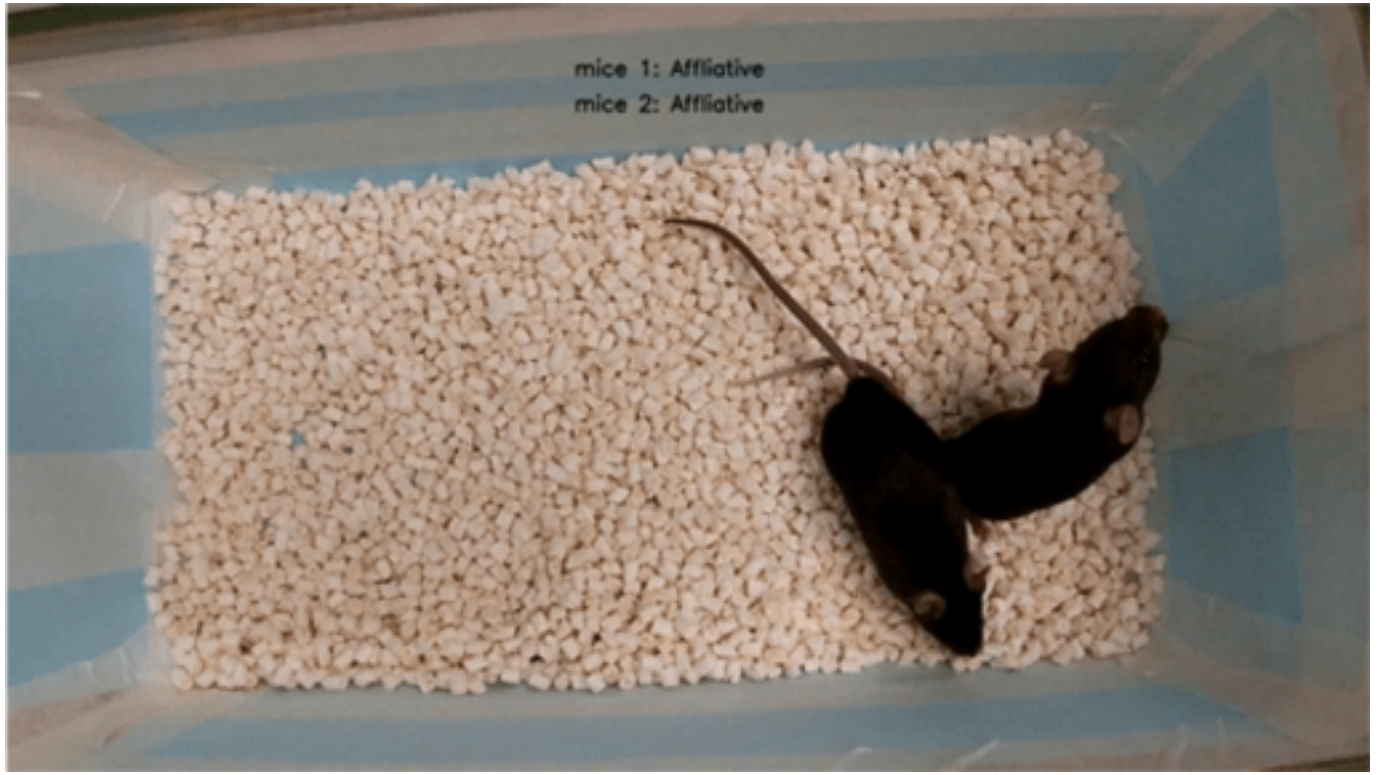

Visual inspection of clusters



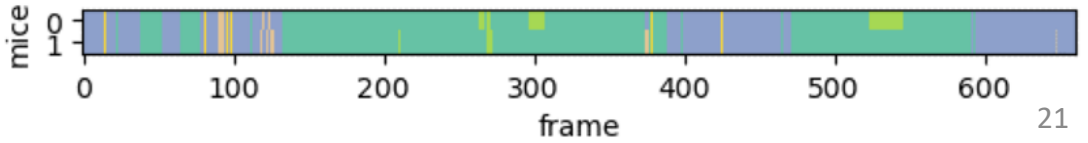

Assignment of behaviors to clusters

# Unsupervised classification of behavior using pose information

- Behavior classification for video can then be used for further analysis by researchers
- Example video shows demo of an automated behavior annotation







# Results

1. Supervised classification was done using random forest model on features extracted from pose estimation
2. Unsupervised classification was done using UMAP or autoencoder to perform dimensionality reduction, followed by agglomerative clustering algorithm. Then manually inspect random samples from each cluster and assign a class to the cluster
    - Lower accuracy and F1 than supervised method. However, do not require manual labelling. Accuracy is measured in behaviors as defined for the supervised learning, so biases may be present

| Metrics | Supervised classification (Random Forest) | Unsupervised classification (Autoencoder + agglomerative clustering) | Unsupervised classification (UMAP + agglomerative clustering) |
|---|---|---|---|
| **Accuracy** | 0.75 | 0.65 | 0.65 |
| **F1 Score** | 0.64 | 0.58 | 0.60 |

In-house dataset
(10 behavior classes)

| Metrics | Supervised classification (Random Forest) | Unsupervised classification (UMAP + agglomerative clustering) |
|---|---|---|
| **Accuracy** | 0.90 | 0.84 |
| **F1 Score** | 0.65 | 0.58 |

Public dataset (CalMS21)
(4 behavior classes)

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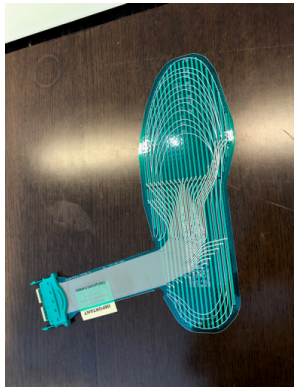
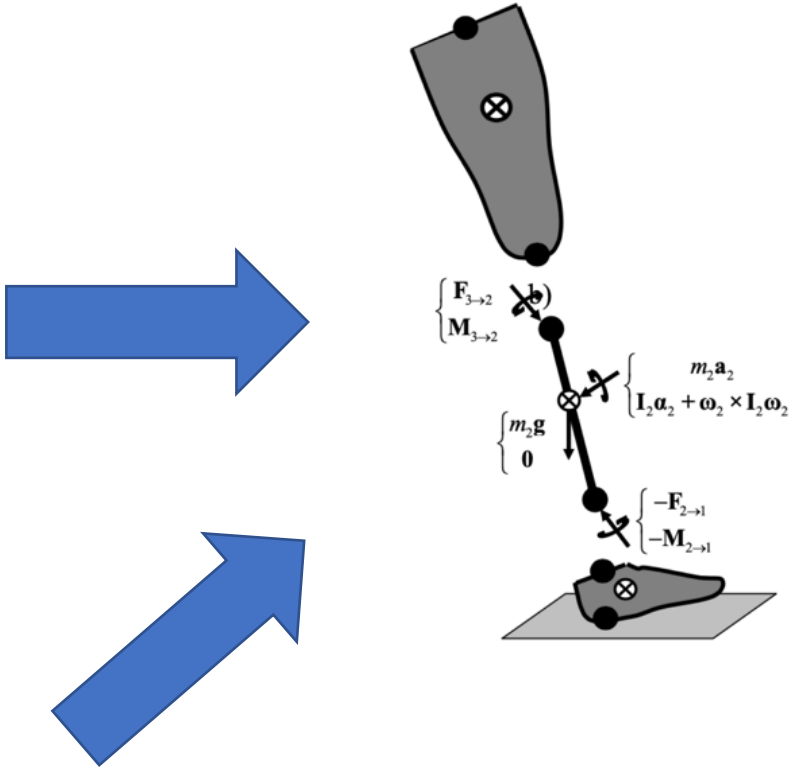
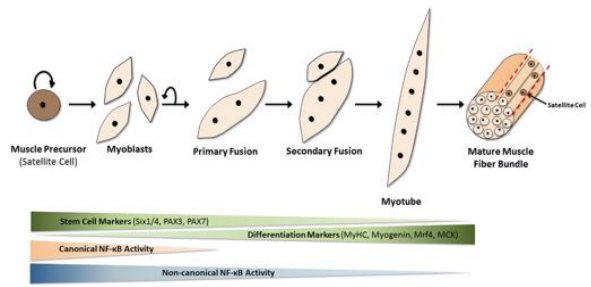
# Kebun Baru pilots tech-integrated facility for the elderly living alone

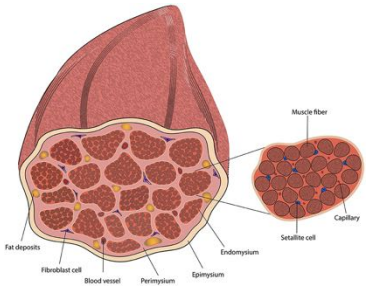
The facility has two cameras and a sound sensor that monitor the elderly. ST PHOTO: KUA CHEE SIONG

# From behavior to mechanisms





# Acknowledgment

Zhou Tianxun
Farm Hui Jia
Chen Jie (NTU SBS)

Eyleen Goh (NTU LKC) & her group members