

# The Anomalous Diffusion Workshop



Results and perspectives of  
the Anomalous Diffusion Challenge 2020

Castelldefels (Barcelona) – December 1–3, 2021

sponsored by:





# Contents

<b>Code of Conduct</b>	<b>3</b>
<b>The Anomalous Diffusion (AnDi) Challenge 2020</b>	<b>4</b>
Objective and tasks . . . . .	4
<b>Dates and Venue</b>	<b>5</b>
<b>Organizers</b>	<b>5</b>
Scientific Committee . . . . .	5
Workshop Secretary . . . . .	5
<b>Acknowledgements</b>	<b>5</b>
<b>Invited Speakers</b>	<b>6</b>
<b>AnDi Challenge 2020 awardees</b>	<b>6</b>
<b>Program</b>	<b>7</b>
<b>Abstracts</b>	<b>8</b>
Invited talks . . . . .	8
Contributed talks . . . . .	21
Posters . . . . .	39
<b>List of Participants</b>	<b>50</b>
<b>List of Online Participants</b>	<b>52</b>

## Code of Conduct

Workshop attendees are expected to adhere to the highest professional standards, according to the OPTICA (Formerly OSA) Anti-harassment Policy and Code of Conduct:

Optica is committed to providing an environment that is conducive to the free and robust exchange of scientific ideas. This environment requires that all participants be treated with equal consideration and respect. While Optica encourages vigorous debate of ideas, personal attacks create an environment in which people feel threatened or intimidated. This is not productive and does not advance the cause of science. All participants in Optica and Optica-managed events and activities are therefore expected to conduct themselves professionally and respectfully.

It is the policy of Optica that all forms of bullying, discrimination and harassment, sexual or otherwise, are prohibited in any Optica or Optica-managed events or activities. This policy applies to every individual at the event, whether attendee, speaker, exhibitor, award recipient, staff, contractor or other. It is also a violation of this policy to retaliate against an individual for reporting bullying, discrimination or harassment or to intentionally file a false report of bullying, discrimination or harassment.

Bullying, discrimination and harassment of any sort by someone in a position of power, prestige or authority is particularly harmful since those of lower status or rank may be hesitant to express their objections or discomfort out of fear of retaliation.

Optica may take any disciplinary action it deems appropriate if, after thorough investigation, it finds a violation occurred.

## The Anomalous Diffusion (AnDi) Challenge 2020

Since Albert Einstein provided a theoretical foundation for Robert Brown's observation of the movement of particles within pollen grains suspended in water, significant deviations from the laws of Brownian motion have been uncovered in a variety of animate and inanimate systems, from biology to the stock market. Anomalous diffusion, as it has come to be called, is a widespread phenomenon connected to non-equilibrium phenomena, flows of energy and information, and transport in living systems. Just focusing on life sciences, identifying its underlying mechanism is a crucial step to understanding, e.g., the motion of sub-cellular components, the uptake of drugs, nonrandom distributions and lateral segregation of plasma membrane components, and the role of chromatin diffusion in gene regulation.

However, the measurement of these properties from the data analysis of trajectories is often limited, especially for trajectories that are short, irregularly sampled, or featuring mixed behaviors. In the last years, several methods have been proposed to quantify anomalous diffusion, going beyond the classical calculation of the mean squared displacement. Through the AnDi Challenge we aimed at establishing a library of computational tools to be used conventionally to characterize diffusion from experimental trajectories from a large variety of fields.

### Objective and tasks

The AnDi Challenge was aimed to assess the performance of methods in quantifying anomalous diffusion, with respect to three different tasks:

- T1 – anomalous exponent inference,
- T2 – model classification,
- T3 – trajectory segmentation,

each for 1D, 2D, and 3D trajectories. The performance was assessed with common metrics on simulated datasets with trajectory length and signal-to-noise level reproducing realistic experimental conditions. The submitted methods were also compared on the blind analysis of experimental trajectories.

The results of the challenge were published in:

G. Muñoz-Gil, G. Volpe, M. A. Garia-March, ... , M. Lewenstein, R. Metzler, and C. Manzo  
*Objective comparison of methods to decode anomalous diffusion*, Nature Communications **12**: 6253 (2021).

## Dates and Venue

The workshop will be held at ICFO premises in Castelldefels (Barcelona) on December 1-3, 2021.

## Organizers

### Scientific Committee

- Carlo Manzo, the QuBI lab – FCT, UVic-UCC
- Giovanni Volpe, Soft Matter Lab – University of Gothenburg
- Gorka Muñoz-Gil & Maciej Lewenstein, Quantum Optics Theory – ICFO – The Institute of Photonic Sciences
- Miguel Angel Garcia-March, Insituito Universitario de Matemática Pura y Aplicada - IUMPA, Universitat Politècnica de València
- Ralf Metzler, Theoretical Physics – University of Potsdam

### Workshop Secretary

- Mercè Latorre, ICFO – The Institute of Photonic Sciences
- Elena Enrique Romero, ICFO – The Institute of Photonic Sciences
- Thomas Charles, ICFO – The Institute of Photonic Sciences

## Acknowledgements

We would like to thank the following sponsors for their support:

- Optica (formerly OSA)
- ICFO – The Institute of Photonic Sciences
- Vicerectorat de Recerca i Transferència de Coneixement de la UVic-UCC
- Societat Catalana de Biologia - Institut d'Estudis Catalans
- European Research Council (through an ERC AdG Grant to Maciej Lewenstein and an ERC StG to Giovanni Volpe)

## Invited Speakers

- Maria F. Garcia-Parajo – ICFO, Spain
- Jean-Baptiste Masson – Institut Pasteur, France
- Diego Krapf – University of Colorado, USA
- Hélène Kabbech – Erasmus MC, The Netherlands
- Zihan Huang – Hunan University, China
- Felix Ritort – Universitat de Barcelona, Spain
- Pietro Tierno – Universitat de Barcelona, Spain

## AnDi Challenge 2020 awardees

- Stefano Bo (Max Planck Institute for the Physics of Complex Systems, Germany)
- Aykut Argun (University of Gothenburg, Sweden)
- Giorgio Volpe (University College London, UK)
- Alessia Gentili (University College London, UK)
- Óscar Garibo i Orts (Universitat Politècnica de València, Spain)
- J. Alberto Conejero (Universitat Politècnica de València, Spain)
- Tom Bland (The Francis Crick Institute, UK)



## Program

	01/12/2021	02/12/2021	03/12/2021
9:00	Registration & Welcome		
9:30	Maria Garcia-Parajo	Felix Ritort	Diego Krapft
10:10	Hippolyte Verdier	Patrycja Kowalek	Nicolas Mateos
10:35	Benjamin Midtvedt	Borja Requena	Jesus Pineda
11:00	Coffee Break/Posters	Coffee Break/Posters	Coffee Break/Posters
11:30	Pietro Tierno	Hélène Kabbech	Alessia Gentili
12:10	Martin Selin	Juan Andres Torreno Pina	Carlos Mejia-Monasterio
12:35	Enrique Abad	Harshith Bechimanchi	Janusz Szwabinski
13:00	Lunch	Lunch	Lunch
15:00	Aykut Argun	Giorgio Volpe	Óscar Garibo i Orts
15:40	Zihan Huang (online)	Jean Baptiste Masson (online)	Stefano Bo
16:20	Coffee Break/Posters	Coffee Break/Posters	ANDi1 Closing and AnDi2 Kick-off
16:50	Raffaele Pastore	Daniel del Pozo Bueno	Visit of Barcelona City Center
17:15	Gabriel Fernández-Fernández	Eric Cereceda López	Guided by Giovanni Volpe
17:40	Round Table: AnDi2	Ohad Vilks	
18:05		Posters	
19:00	Informal Social Event	Social Event	

Abstracts

Invited talks

---

# Enhanced force-field calibration via machine learning

A. Argun<sup>1</sup>, T. Thalheim<sup>2</sup>, S. Bo<sup>3</sup>, F. Cichos<sup>2</sup>, G. Volpe<sup>1</sup>

<sup>1</sup> *Department of Physics, University of Gothenburg, Origovägen 6B, SE-41296 Gothenburg, Sweden, aykut.argun@physics.gu.se*

<sup>2</sup> *Peter Debye Institute for Soft Matter Physics, Molecular Nanophotonics Group, Leipzig University, Linnestrasse 5, 04103 Leipzig, Germany*

<sup>3</sup> *Max Planck Institute for the Physics of Complex Systems, Nöthnitzer Strasse 38, 01187 Dresden, Germany*

.....

The influence of microscopic force fields on the motion of Brownian particles plays a fundamental role in a broad range of fields, including soft matter, biophysics, and active matter. Often, the experimental calibration of these force fields relies on the analysis of the trajectories of the Brownian particles. However, such an analysis is not always straightforward, especially if the underlying force fields are non-conservative or time-varying, driving the system out of thermodynamic equilibrium. Here, we introduce a toolbox to calibrate microscopic force fields by analyzing the trajectories of a Brownian particle using machine learning, namely, recurrent neural networks. We demonstrate that this machine-learning approach outperforms standard methods when characterizing the force fields generated by harmonic potentials if the available data are limited. More importantly, it provides a tool to calibrate force fields in situations for which there are no standard methods, such as non-conservative and time-varying force fields. In order to make this method readily available for other users, we provide a Python software package named DeepCalib, which can be easily personalized and optimized for specific force fields and applications. This package is ideal to calibrate complex and non-standard force fields from short trajectories, for which advanced specific methods would need to be developed on a case-by-case basis [1].

## References

- [1] Aykut Argun, Tobias Thalheim, Stefano Bo, Frank Cichos and Giovanni Volpe, *Enhanced force-field calibration via machine learning*. Applied Physics Reviews, 7.4 (2020): 041404.

# Characterization of anomalous diffusion with recurrent neural networks

A. Argun<sup>1</sup>, F. Schmidt<sup>2</sup>, R. Eichhorn<sup>3</sup>, G. Volpe<sup>1</sup>, S. Bo<sup>4</sup>

<sup>1</sup> *Department of Physics, University of Gothenburg, Origovägen 6B, SE-41296 Gothenburg, Sweden*

<sup>2</sup> *Friedrich-Schiller-University Jena, Germany*

<sup>3</sup> *Nordita, Royal Institute of Technology and Stockholm University, Roslagstullsbacken 23, SE-106 91 Stockholm, Sweden*

<sup>4</sup> *Max Planck Institute for the Physics of Complex Systems, Nöthnitzer Straße 38, DE-01187 Dresden, Germany. stefabo@pks.mpg.de*

.....

Anomalous diffusion occurs in many physical and biological phenomena, when the growth of the mean squared displacement with time has an exponent different from one and can be due to different mechanisms. We show that long short-time memory (LSTM) recurrent neural networks can efficiently characterize anomalous diffusion by identifying the mechanism causing it and determining the anomalous exponent from a single short trajectory. This method outperforms standard techniques and advanced ones when the available data points are limited, as is often the case in experiments. Furthermore, LSTMs can handle complex tasks where there are no standard approaches, such as determining the anomalous diffusion exponent from a trajectory sampled at irregular times, and measuring intermittent systems that switch between different kinds of anomalous diffusion. We validate the method on experimental data obtained from subdiffusive colloids trapped in speckle light fields and superdiffusive microswimmers. We also discuss the performance of the method in the context of the Anomalous Diffusion Challenge.

## References

- [1] Bo S., Schmidt F., Eichhorn R. and Volpe G., *Measurement of anomalous diffusion using recurrent neural networks*. Phys. Rev. E **100** (1), 010102 (2019).
- [2] Argun A., Volpe G. and Bo S., *Classification, inference and segmentation of anomalous diffusion with recurrent neural networks* J. Phys. A **54** 294003 (2021).

# Efficient recurrent neural network methods for anomalously diffusing single particle short and noisy trajectories

Òscar Garibo-i-Orts<sup>1,2</sup>, Alba Baeza-Bosca<sup>1</sup>, Miguel A. Garcia-March<sup>1</sup>, J. Alberto Conejero<sup>1</sup>

<sup>1</sup> *Instituto Universitario de Matemática Pura y Aplicada, Universitat Politècnica de València, Spain, osgaor@upv.es, abaebos@posgrado.upv.es, garciamarch@mat.upv.es, aconejero@upv.es*

<sup>2</sup> *Valencian Research Institute for Artificial Intelligence, Universitat Politècnica de València, Spain.*

.....

Anomalous diffusion occurs at very different scales in nature, from atomic systems to motions in cell organelles, biological tissues or ecology, and also in artificial materials, such as cement. Being able to accurately measure the anomalous exponent associated to a given particle trajectory, thus determining whether the particle subdiffuses, superdiffuses or performs normal diffusion, is of key importance to understand the diffusion process. Also, it is often important to trustingly identify the model behind the trajectory, as this gives a large amount of information on the system dynamics. Both aspects are particularly difficult when the input data are short and noisy trajectories. It is even more difficult if one cannot guarantee that the trajectories output in experiments are homogeneous, hindering the statistical methods based on ensembles of trajectories. We present a data-driven method able to infer the anomalous exponent and to identify the type of anomalous diffusion process behind single, noisy and short trajectories, with good accuracy [3]. This model was used in our participation in the Anomalous Diffusion (AnDi) Challenge. A combination of convolutional and recurrent neural networks was used to achieve state-of-the-art results when compared to methods participating in the AnDi Challenge, ranking top 4 in both classification and diffusion exponent regression [2].

## References

- [1] Ó. Garibo-i-Orts, A. Baeza-Bosca, M.A. Garcia-March, Miguel and J. Alberto Conejero. *Efficient recurrent neural network methods for anomalously diffusing single particle short and noisy trajectories*. Journal of Physics A: Mathematical and Theoretical. DOI: 10.1088/1751-8121/AC3707 (November 2021).
- [2] G. Muñoz-Gil, G. Volpe, G., M.A. Garcia-March, et al. *Objective comparison of methods to decode anomalous diffusion*. Nature Communications. DOI: 10.1038/S41467-021-26320-W (November 2021).

# Single molecule imaging tools to unravel spatiotemporal compartmentalisation in living cells

Maria Garcia-Parajo<sup>1,2</sup>

<sup>1</sup> *ICFO-Institut de Ciències Fotoniques, The Barcelona Institute of Science and Technology, Barcelona, Spain*

<sup>2</sup> *ICREA-Institució Catalana de Recerca i Estudis Avançats, Barcelona, Spain*

*maria.garcia-parajo@icfo.eu*

.....

Organization by compartmentalization is a general property of natural systems that efficiently facilitates and orchestrates biological events in space and time. In the last decade, compartmentalization of the plasma membrane of living cells has emerged as a dominant feature present at different spatiotemporal scales and regulating key cell functions [1]. In parallel, recent experimental evidence points to the notion that the nucleus of living cells is highly compartmentalized. The advent of super-resolution microscopy and single molecule dynamic approaches has allowed the study of living cell membranes and intact nuclei with unprecedented levels of details [2, 3]. In particular, single particle tracking (SPT) approaches have revealed that most cell membrane receptors and/or molecules inside the cell nucleus exhibit anomalous diffusion and weak ergodicity breaking [4]. The manifestation of such behavior is directly linked to molecular function and result from the nano- and meso-scale interaction of molecules with their surrounding environment [4, 5]. In this talk, I will discuss evidence for anomalous diffusion on prototypical membrane receptors and in the cell nucleus and will show a direct correlation between these phenomena and biological function. Moreover, I will describe the combination of SPT at different labelling densities. Low density conditions allow us to reconstruct the mobility of individual molecules and their transient interaction with other molecular partners, while high density labeling conditions provide complementary information on the spatial and temporal length scales of cellular regions re-visited (or forbidden) for molecules. We find that both molecular diffusion and dynamic re-modelling of the environment play key roles regulating biological function.

## References

- [1] M.F. Garcia-Parajo et al, *J. Cell Sci.* **127**: 4995–5005 (2014).
- [2] M.A Ricci et al, *Cell* **160**: 1145-1158 (2015).
- [3] C. Manzo and M.F. Garcia-Parajo, *Rep. Prog. Phys.* **78**: 124601 (2015).
- [4] C. Manzo et al., *Phys. Rev. X* **5**: 011021 (2015).
- [5] P. Sil et al., *Mol. Biol. Cell* **31**: 561-579 (2020).

# CONDOR: Characterising anomalous diffusion with classical statistics and deep learning

A. Gentili<sup>1</sup>, G. Volpe<sup>1</sup>

<sup>1</sup> *Department of Chemistry, University College London, 20 Gordon Street, London WC1H 0AJ, United Kingdom*

.....

In many natural phenomena, deviations from Brownian diffusion, known as anomalous diffusion, can be often observed. Examples of these deviations can be found in cellular signalling, in animal foraging, in the spread of diseases, and even in trends in financial markets and climate records. The characterisation of anomalous diffusion remains challenging to date. In this talk, I will discuss a new method that we introduced in response to the Anomalous Diffusion (AnDi) Challenge [1, 2] based on combining classical statistics and deep learning to characterise anomalous diffusion in single trajectories [3]. Our method can efficiently characterize, without any a priori information, the underlying anomalous diffusion model with high accuracy, and infer its anomalous exponent with a small absolute error in single 1D, 2D and 3D trajectories corrupted by localization noise. Moreover, I will show how CONDOR can be extended to the segmentation of trajectories, where the diffusion model and/or its anomalous exponent vary in time. Our method was developed following the idea that different trajectories generated by the same diffusion model should present similar statistical properties to distinguish them from other models. In realistic scenarios, these proprieties could be well hidden in single trajectories because of, e.g., environmental noise or limited data points. As a result, CONDOR processes single trajectories to retrieve the underlying statistical information, which is then analyzed and clustered using the power of deep learning. While most advanced machine learning techniques work as black boxes, we believe that CONDOR, which is partially based on classical statistics analysis, can enhance the understanding of the underlying diffusion processes in single trajectories shedding light on their physical nature.

## References

- [1] G. Muñoz-Gil, *et al.*, *The anomalous diffusion challenge: single trajectory characterisation as a competition*. Emerging Topics in Artificial Intelligence 2020. Vol. 11469. International Society for Optics and Photonics (2020).
  - [2] G. Muñoz-Gil, G. Volpe, M.A. Garcia-March, *et al.*, *Objective comparison of methods to decode anomalous diffusion*. Nat. Commun. 12, 6253 (2021).
  - [3] A. Gentili and G. Volpe, *Characterization of anomalous diffusion classical statistics powered by deep learning (CONDOR)*, J. Phys. A 54 314003 (2021).
-

# WaveNet-Based Deep Neural Networks for the Characterization of Anomalous Diffusion (WADNet)

Zihan Huang

School of Physics and Electronics, Hunan University, Changsha 410082, China, huangzih@hnu.edu.cn

.....

Anomalous diffusion, which shows a deviation of transport dynamics from the framework of standard Brownian motion, is involved in the evolution of various physical, chemical, biological, and economic systems. The study of such random processes is of fundamental importance in unveiling the physical properties of random walkers and complex systems. However, classical methods to characterize anomalous diffusion are often disqualified for individual short trajectories, leading to the launch of the Anomalous Diffusion (AnDi) Challenge. This challenge aims at objectively assessing and comparing new approaches for single trajectory characterization. In this work, to address the inference and classification tasks in the challenge, we develop a WaveNet-based deep neural network (WADNet) by combining a modified WaveNet encoder with long short-term memory networks, without any prior knowledge of anomalous diffusion. The results show that WADNet could be the part of state-of-the-art techniques to decode the AnDi database. Our method presents a benchmark for future research, and could accelerate the development of a versatile tool for the characterization of anomalous diffusion.

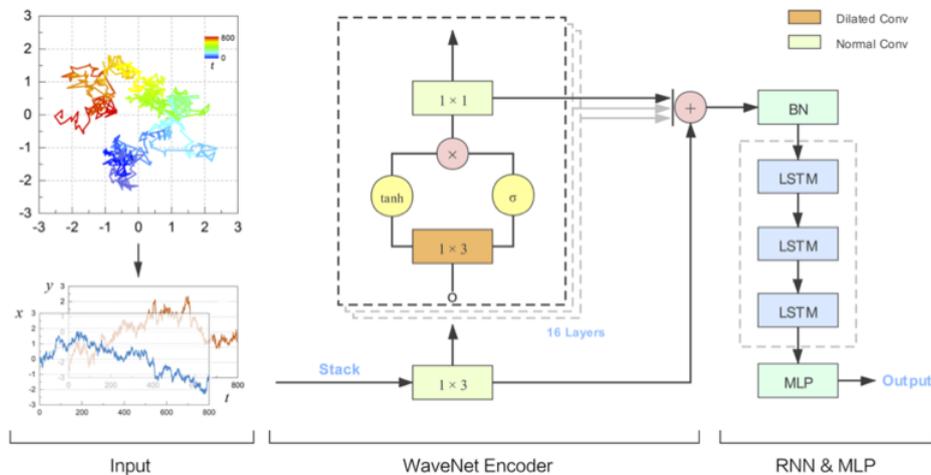


Figure 1: Overview of the workflow of WADNet.

## References

- [1] Gorka Muñoz-Gil, et al., *Objective comparison of methods to decode anomalous diffusion*, Nature Communications **12**: 6253 (2021).
- [2] Dezhong Li, Qiuji Yao and Zihan Huang, *WaveNet-based deep neural networks for the characterization of anomalous diffusion (WADNet)*, Journal of Physics A **54**: 404003 (2021).

# Biological applications of single-particle tracking data: from processing to data analysis

H. Kabbech, I. Smal

Erasmus University Medical Center Rotterdam, Department of Cell Biology,  
Dr. Molewaterplein 40, 3015 GD Rotterdam, The Netherlands,  
h.kabbech@erasmusmc.nl

.....

Does a specific mutation on the BRCA2 DNA-repaired protein modify its capability to bind to the DNA? Will the induction of light during an optogenetics experiment affect the movement of DCC receptors? How does the interaction between an enhancer and a promoter on the chromatin occurs through time? These types of biological questions can be solved by quantitatively assessing the dynamics of fluorescently labeled biological entity captured during single-particle tracking (SPT) experiments. Our group aims at developing state-of-the-art deep-learning tools for the processing and analysis of SPT data.

Estimation of the anomalous exponent  $\alpha$  from the mean squared displacements (MSD) and the methods developed for the task 1 of the AnDi challenge [1] are valid for a population of trajectories exhibiting a single type of motion (i.e., super, freely or sub-diffusive), which does not describe the reality as biological particles can behave according to a mixture of various dynamics (states). We define the state of a given trajectory segment by its motion parameters: the diffusion  $D$  and level of confinement  $\alpha$ . There might be transitions between states along a trajectory, which can be caused by a property of the particle (e.g., bound/unbound to the DNA) or a heterogeneity of the environment (e.g., overcrowded/void). The development of advanced and robust tools to improve the analysis of SPT data (segmentation and estimation of motion parameters) is still of great importance for the scientific community.

Segmentation of trajectories with a supervised method [2] often requires to know in advance the number of states and some physical parameters to simulate labeled trajectories. We overcome this issue by developing an unsupervised method for segmenting trajectories into diffusive states. We applied noise2noise [3], a state-of-the-art image denoising approach, on SPT data, which allows us to recover “smoothed” displacements, corresponding to MSD values. This results in successful identification of the number of diffusive states in SPT data and segmentation of trajectories using automatically computed thresholds.

## References

- [1] G. Muñoz-Gil, G. Volpe, M.A. Garcia-March, et al., *Objective comparison of methods to decode anomalous diffusion*, Nat Commun **12**, 6253 (2021).
- [2] M. Arts, I. Smal, M. W. Paul, C. Wyman, and E. Meijering, *Particle mobility analysis using deep learning and the moment scaling spectrum*, Scientific reports **9**, 17160 (2019).
- [3] J. Lehtinen, J. Munkberg, J. Hasselgren, S. Laine, T. Karras, M. Aittala, and T. Aila, *Noise2Noise: Learning image restoration without clean data*, arXiv preprint arXiv:1803.04189 (2018).

# Identifying diffusion states in the cytoplasm of mammalian cells

Michał Balcerek<sup>1</sup>, Krzysztof Burnecki<sup>1</sup>, Joanna Janczura<sup>1</sup>, Diego Krapf<sup>2</sup>, Adal Sabri<sup>3</sup>, Matthias Weiss<sup>3</sup>, Xinran Xu<sup>2</sup>

<sup>1</sup> Faculty of Pure and Applied Mathematics, Hugo Steinhaus Center, Wrocław University of Science and Technology, Wrocław, Poland

<sup>2</sup> Department of Electrical and Computer Engineering and School of Biomedical Engineering, Colorado State University, Fort Collins, Colorado, USA, [diego.krapf@colostate.edu](mailto:diego.krapf@colostate.edu)

<sup>3</sup> Experimental Physics I, University of Bayreuth, Bayreuth, Germany

.....

The diffusion of nanoparticles in the cytoplasm of live cells has frequently been reported to exhibit an anomalous and even heterogeneous character, i.e. particles seem to switch gears during their journey. Despite considerable efforts, the mechanisms behind these observations have remained largely elusive. To gain insight into this problem, we performed extensive single-particle tracking experiments using quantum dots in the cytoplasm of living HeLa cells at varying conditions [1]. Statistical analyses of the trajectories reveal a marked, microtubule-dependent subdiffusion with antipersistent increments and substantial heterogeneities. Furthermore, particles randomly switch between different mobility states. Our data indicate that one of these states is rooted in the transient associations with the cytoskeleton-shaken endoplasmic reticulum network. In addition, a hidden Markov model indicates that individual quantum dot trajectories feature a dichotomous switching between two mobility states with an overall subdiffusive mode of motion of the fractional Brownian motion type[2].

## References

- [1] A. Sabri, X. Xu, D. Krapf, and M. Weiss, *Elucidating the origin of heterogeneous anomalous diffusion in the cytoplasm of mammalian cells*, Physical Review Letters **125**: 058101 (2020).
- [2] J. Janczura, M. Balcerek, K. Burnecki, A. Sabri, M. Weiss, and D. Krapf, *Identifying heterogeneous diffusion states in the cytoplasm by a hidden Markov model*, New Journal of Physics **23**: 053018 (2021)

# Statistical signature of interactions in heterogeneous cellular environments

Hippolyte Verdier<sup>1,2</sup>, François Laurent<sup>1,2</sup>, Christian Vestergaard<sup>1,2</sup>, Jean-Baptiste Masson<sup>1,2</sup>

<sup>1</sup> *Decision and Bayesian Computation, Neuroscience Department - UMR 3571 & USR 3756, Institut Pasteur, Paris, France.*

<sup>2</sup> *Institut Prairies, Paris, France*

*Email: jean-baptiste.masson@pasteur.fr*

.....

Single biomolecule trajectories offer the possibility to probe the physical properties of their environment by having random walkers sampling it spatially. However, a recurring problem with these measures is resolving inverse problems of finding the nature of random walks from usually short realizations. Inferring reliable information from short trajectories is made difficult by the stochasticity of movements, experimental noises and by the degeneracy of characteristics for short trajectories. It is also made difficult as the main properties of some random walks are defined asymptotically. Here, we introduce two approaches to infer the subtle interactions between biomolecules and their environment by simultaneously mapping the physical properties of random walks in space and time by learning a random walk latent space able to characterize them without a known underlying model. In the former, we combine physics-informed Bayesian inference to the approximate solution of the Fokker-Planck to map diffusion and interaction in space and time. In the latter, we introduce a new simulation-based inference approach to perform fast and reliable estimates of random walk properties. By associating graphs to trajectories and using a graph neural network to perform learning on these, we show that we can reliably infer the nature of random walks along with their anomalous exponent. Moreover, the method can naturally be applied to trajectories of any length. Finally, we combine these two approaches to a Maximum Mean Discrepancy (MMD) based statistical testing method to probe subtle interactions modifications upon the change in biological conditions. We discuss the application of this approach to Glycine receptor dynamics in synapses and Gag dynamics during virion formation.

---

# Mechanical unzipping studies of nucleic acid folding

Felix Ritort<sup>1</sup>

<sup>1</sup> *Small Biosystems Lab, Departament de Física de la Matèria Condensada, Facultat de Física, Universitat de Barcelona, C/ Martí i Franquès 1, 08028 Barcelona (Spain)*

*Lab website: <http://fmc.ub.edu/ritort>*

.....

DNA, RNA, and proteins are polymers that fold into three-dimensional structures to perform their biological function. How these molecules fold is, however, not understood. Although some models advocate for funnel-like energy landscapes, other models envision folding as cooperative process mediated by the sequential formation of intermediates. Here I will address the question of molecular folding by considering nucleic acid (DNA and RNA) hairpins unzipped with optical tweezers. In particular, I will introduce a simple helix-coil model for the cooperative formation of non-specific secondary structures in DNA that reproduces the experimental force-extension curves and which agrees with energy predictions by MFold [1]. For the case of RNA unzipping I will show the importance of stem-loop structures along the single strands that compete with the native stem, favoring the formation of alternative structures and misfolding [2]. The diversity of structures that RNA can form correlates with its many biological functions and the complexity of RNA biophysics.

## References

- [1] X. Viader-Godoy, C. R. Pulido, B. Ibarra, M. Manosas and F. Ritort, *Cooperativity-dependent folding of single-stranded DNA*, Phys. Rev. X **11**, 031037 (2021)
- [2] P. Rissone, C. V. Bizarro, F. Ritort, *Stem-loop formation drives RNA folding in mechanical unzipping experiments*, submitted

# Emergent colloidal currents generated via exchange dynamics in a broken dimer state

Antonio Ortiz-Ambriz<sup>1,2</sup>, Helena Massana-Cid<sup>1,3</sup>, Mattia Ostinato<sup>1,2</sup>, P. Tierno<sup>1,2,3</sup>

<sup>1</sup> *Departament de Física de la Matèria Condensada, Universitat de Barcelona, 08028 Barcelona, Spain: Email: ptierno@ub.edu*

<sup>2</sup> *Universitat de Barcelona Institute of Complex Systems (UBICS), Universitat de Barcelona, 08028 Barcelona, Spain*

<sup>3</sup> *Institut de Nanociència i Nanotecnologia, Universitat de Barcelona, 08028 Barcelona, Spain*

.....

In this talk, I will describe a general strategy to assemble and transport polarizable magnetic microspheres in fluid media through a combination of confinement [1] and magnetic dipolar interactions [2]. We use a homogeneous magnetic modulation to assemble dispersed particles into rotating dimeric state and frustrated binary lattices and generate collective edge currents that arise from a novel, field-synchronized particle exchange process [3]. The observed, net bidirectional current is composed of colloidal particles which periodically meet assembling into rotating dimers, and exchange their positions in a characteristic, "ceilidh"-like dance. We develop a theoretical model that explains the physics of the observed phenomena as dimer rupture and the onset of current, showing agreement with Brownian dynamic simulations [4]. Further, we explore recently the transport of defects as non-magnetic inclusions in ferrofluids media and the anomalous dynamics of the broken/recombining dimers during the exchange process. Overall, we demonstrate an effective technique to drive microscale matter by using the interplay of steric confinement and dipolar forces, not based on any gradient of the applied field.

## References

- [1] N. Osterman, I. Poberaj, J. Dobnikar, D. Frenkel, P. Zihlerl, and D. Babic *Field-Induced Self-Assembly of Suspended Colloidal Membranes*, Phys. Rev. Lett. **103**:228301 (2009).
- [2] P. Tierno, R. Muruganathan and T. M. Fischer, *Viscoelasticity of Dynamically Self-Assembled Paramagnetic Colloidal Clusters*, Phys. Rev. Lett. **98**:028301 (2007).
- [3] H. Massana-Cid, A. Ortiz-Ambriz, A. Vilfan and P. Tierno, *Emergent collective colloidal currents generated via exchange dynamics in a broken dimer state*, Science advances **6**:eaaz2257 (2020).
- [4] F. Meng, A. Ortiz-Ambriz, H. Massana-Cid, A. Vilfan, R. Golestanian and P. Tierno, *Field synchronized bidirectional current in confined driven colloids*, Physical Review Research **2**: 012025 (2020).

# Role of Topography on Surface Propagation of Motile Bacteria

Giorgio Volpe<sup>1</sup>

<sup>1</sup> *Department of Chemistry, University College London, 20 Gordon Street, WC1H 0AJ London, UK Email: g.volpe@ucl.ac.uk*

.....

Only two decades ago, bacterial cells were considered as well-characterized biophysical entities, which offered little room for new discoveries. We now know that this picture is truly wrong and naïve. In recent years, bacterial cells have come back to the spotlight due to many bacterial species developing antimicrobial resistance even to last-resort antibiotics. The way bacterial cells localize near a surface is particularly important as it determines the emergence of several phenomena of biological, ecological, and medical relevance, including biofilm formation. In this talk, I will show how the microscopic features of a surface have a non-negligible effect in determining the propagation and localization dynamics of bacterial cells on it. Beyond demonstrating the critical role played by surface defects on the near-surface motion of bacterial cells, our results can inspire novel routes to control microbial ecology in natural habitats and to engineer materials for the control and prevention of bacterial adhesion to surfaces.

## References

- [1] S. Makarchuk, V.C. Braz, N.A.M. Araújo, L. Ciric and G. Volpe, *Nature Communications* **10**, 4110 (2019).

Abstracts

Contributed talks

---

# Diffusion in a pseudo-two-dimensional system of macroscopic rolling spheres

M. A. López-Castaño<sup>1</sup>, J. F. González-Saavedra<sup>2</sup>, A. Rodríguez Rivas<sup>3</sup>, E. Abad<sup>4</sup>, S. B. Yuste<sup>5</sup>, F. Vega Reyes<sup>6</sup>

<sup>1</sup> *University of Extremadura, Department of Physics, Badajoz, Spain, malopez00@unex.es*

<sup>2</sup> *University of Extremadura, Department of Physics, Badajoz, Spain, jfgsaavedra@gmail.com*

<sup>3</sup> *Pablo de Olavide University, Department of Physical, Chemical and Natural Systems, Seville, Spain, arodriw1@upo.es*

<sup>4</sup> *University of Extremadura, Department of Applied Physics & ICCAEx, Mérida, Spain, eabad@unex.es*

<sup>5</sup> *University of Extremadura, Department of Physics & ICCAEx, Badajoz, Spain, santos@unex.es*

<sup>6</sup> *University of Extremadura, Department of Physics & ICCAEx, Badajoz, Spain, fvega@unex.es*

.....

We consider a collection of fluidized identical hollow spheres (ping-pong balls) resting on a horizontal metallic grid [1]. Fluidization is achieved by means of a turbulent air current coming from below. The upflow is adjusted so that the particles do not levitate over the grid, resulting in quasi-two-dimensional dynamics. The intricate diffusive behaviour displayed by this granular system is related to the effective potential characterizing the hydrodynamic interactions between the constituents. Changes in the effective potential can be induced by tuning the granular temperature  $T$  and the packing fraction  $\Phi$ , which results in a rich variety of spatial structures. We discuss the error sources characterizing the experimental trajectories of the spheres and provide realistic estimates for the total localization error (see Supplemental Material in [1]).

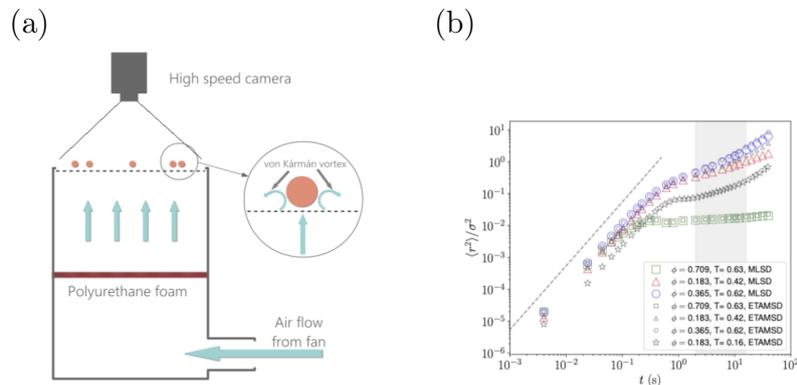


Figure 1: (a) Experimental setup. (b) Time dependence of the mean logarithmic square displacement (MLSD) and of the ensemble average of the time averaged mean square displacement (ETAMSD) in units of sphere diameter  $\sigma$  for different  $T$  and  $\Phi$ .

## References

- [1] Miguel Ángel López-Castaño, Juan Francisco González-Saavedra, Álvaro Rodríguez-Rivas, Enrique Abad, Santos Bravo Yuste and Francisco Vega Reyes, *Pseudo-two-dimensional dynamics in a system of macroscopic rolling spheres*, Phys. Rev. E **103**: 042903 (2021).

# Characterising micro-plankton behaviours using deep learning powered inline holography

Harshith Bachimanchi<sup>1</sup>, Benjamin Midtvedt<sup>1</sup>, Daniel Midtvedt<sup>1</sup>, Erik Selander<sup>2</sup>, Giovanni Volpe<sup>1</sup>

<sup>1</sup> Department of Physics, University of Gothenburg, SE-41296 Gothenburg, Sweden, harshith.bachimanchi@physics.gu.se

<sup>2</sup> Department of Marine sciences, University of Gothenburg, SE-41296 Gothenburg, Sweden,

.....

Phytoplankton are responsible for approximately half of the biological fixation of atmospheric carbon dioxide on Earth. The main consumers of the phytoplankton are microscopic unicellular grazers, microzooplankton. The microzooplankton consume around 60 percent of what the phytoplankton produce and constitute an important route in the global carbon cycle [1]. Yet we know surprisingly little about the whereabouts of marine microzooplankton, and their grazing and reproductive behaviours are mainly inferred from indirect techniques. A simplistic laboratory alias to gain a mechanistic understanding for the above scenario is to have an ensemble of phytoplankton and zooplankton in a controlled environment and capture their dynamics using digital cameras. However, this is only feasible for short term observations of few individuals, and unless the individual plankton are tracked simultaneously from different angles, the three-dimensional position of the plankton will not be recorded. As an alternative to standard approaches, holography offers particle tracking in a 3D volume thereby allowing longer tracking times with improved sample volumes. Moreover, integration of holography with deep learning allows an automatized detection of plankton species and facilitates the monitoring of cell properties.

Our approach is to observe a small ensemble of prey (*Dunaliella tertiolecta*) and predator (*Oxyrrhis marina*) cells in a semi-controlled environment and to capture their interactions through lens-less holography. The holographic data is then analyzed with artificial neural networks developed with a custom software package called DeepTrack 2.0 [2] for further results. We employ a neural network with U-net architecture to detect and assign the planktons to their species. Thereby followed by a tracking algorithm, we use a weighted average convolutional neural network (WAC-Net) to predict the radius, refractive index, vertical positions, and the dry mass for each plankton, enabling the prediction of temporal changes of the properties. In practice, this allows us to follow ensembles of individual microzooplankton and observe their detailed behaviour at different stages in their life span. Our preliminary benchmarking reveal a good correlation with standard approaches for different species of microzooplanktons and diatoms.

## References

- [1] Michael J. Behrenfeld, and Paul G. Falkowski, *Photosynthetic rates derived from satellite-based chlorophyll concentration*, *Limnology and oceanography* **42**, 1, 1-20 (1997).
- [2] Benjamin Midtvedt, Saga Helgadottir, Aykut Argun, Jesús Pineda, Daniel Midtvedt, and Giovanni Volpe, *Quantitative Digital Microscopy with Deep Learning*, **8** :011310 (2021).

# Hydrodynamic interactions can induce jamming in flow-driven systems

E. Cereceda-López<sup>1,2,\*</sup>, D. Lips<sup>3</sup>, A. Ortiz-Ambriz<sup>1,2,4</sup>, A. Ryabov<sup>5</sup>, P. Maass<sup>3</sup>, and P. Tierno<sup>1,2,4</sup>

<sup>1</sup> *Departament de Física de la Matèria Condensada, Universitat de Barcelona, 08028, Spain*

<sup>2</sup> *Institut de Nanociència i Nanotecnologia, Universitat de Barcelona (IN2UB), 08028, Barcelona, Spain*

<sup>3</sup> *Universität Osnabrück, Fachbereich Physik, Barbarastrasse 7, D-49076 Osnabrück, Germany*

<sup>4</sup> *University of Barcelona Institute of Complex Systems (UBICS), 08028, Barcelona, Spain*

<sup>5</sup> *Charles University, Faculty of Mathematics and Physics, Department of Macromolecular Physics, V Holešovičkách 2, CZ-18000 Praha 8, Czech Republic*

\* *ecereceda@ub.edu*

.....

In the present work, we experimentally study the transport of particles in a quasi-one-dimensional (q1D) periodic potential. We compare the experimental results with simulations based on the Brownian Asymmetric Simple Exclusion Process [1, 2], and we discuss the importance of hydrodynamic interactions (HI) in flow-driven particle transport.

The experimental setup consists of 27 time-shared optical tweezers, which create individual Gaussian potential wells, uniformly distributed in a ring-shape confining up to 27 colloidal particles. We rotate the optical traps at constant angular velocity to create a quasi-sinusoidal traveling potential landscape. Varying the number of particles in the potential landscape allows us to measure the fundamental diagram of the system, which is the colloidal current as a function of the particle density. We find that for different potential landscape barrier heights the particle current density decreases after reaching a maximum value.

We compare the experimental results with simulations, and we attribute the decrease of the current density relationship to the jamming produced by the HI between particles. We explain this phenomenon using the equations of motion that include HI and show that the latter enhances the potential barrier in flow-driven systems. This is opposed to previous observations in force-driven systems, which remark the fundamental difference with our flow-driven system.

## References

- [1] Dominik Lips, Artem Ryabov, and Philipp Maass, *Brownian Asymmetric Simple Exclusion Process*, Phys. Rev. Lett. **121**, 160601 (2018).
- [2] Dominik Lips, Artem Ryabov, and Philipp Maass, *Single transport in periodic potentials: The Brownian asymmetric simple exclusion process*, Phys. Rev. E textbf100, 052121 (2019).

# Transition Metals Electron Energy-Loss Spectra classified via Support Vector Machines

D. del-Pozo-Bueno<sup>1,2</sup>, F. Peiró<sup>1,2</sup>, S. Estradé<sup>1,2</sup>.

<sup>1</sup> *LENS-MIND, Dept. Enginyeries Electrónica i Biomèdica, Universitat de Barcelona, Barcelona, Spain.*

<sup>2</sup> *Institute of Nanoscience and Nanotechnology (IN<sup>2</sup>UB), Universitat de Barcelona, Barcelona, Spain.*

.....

Electron Energy-Loss Spectroscopy (EELS) is a powerful and functional spectroscopic technique to study locally the composition and properties of materials at the nanoscale, which is carried out in the Scanning and Transmission Electron Microscopes (S/TEM). In this sense, the recent technological advances in STEM devices are leading to higher spatial and energy resolution resulting in an enormous increase of the total amount of data acquired in EELS measurements. Thus, currently this technique offers better energy and spatial resolutions making possible a better nanometric characterization, at the cost of producing large spectral datasets, hindering the spectra analysis for the spectroscopist.

The machine learning methods provide a large variety of tools to properly deal with these large amounts of spectral data in an automated manner, at the same time that allow for extracting valuable physical information. In this sense, a promising machine learning strategy for identifying EELS data is the Support Vector Machine (SVM) [1], in particular the soft-margin SVM, which is a supervised machine learning algorithm allowing the multiclass classification, even with non-linear data, and that can be used as a probabilistic classifier.

The soft-margin SVM has shown promising results identifying the oxidation state in transition metal (TM) oxides, manganese and iron oxides, through the study of their EELS spectra, concretely, their white lines ( $L_3$  and  $L_2$ ) [2]. The algorithm has been implemented in Python from the library Scikit-learn [3], concretely, the LIBSVM library [4]. It has presented a performance above 90% classifying the TM oxidation state, and additionally, it has exhibited a good performance classifying these EEL spectra considering the usual level of noise and additional instrumental energy shifts.

In conclusion, the SVM applied to EEL spectra makes the most of the simplicity (few parameters to optimize) and short computation times of it to identify correctly and automatically the oxidation state of the transition metals. Furthermore, for large spectral datasets the computing times can even be reduced by implementing the Stochastic Gradient Descend (SDG), which is an iterative method that optimizes, and so, accelerates model training enabling also faster parameter optimization.

## References

- [1] C. Cortes and V. Vapnik, *Support-vector networks*, Machine Learning 20 (1995), pp. 273-297.
- [2] D. del-Pozo-Bueno, F. Peiró and S. Estradé, *Support vector machine for EELS oxidation state determination*, Ultramicroscopy 221 (2021), p. 113190.
- [3] F. Pedregosa et al., *Scikit-learn: Machine Learning in Python*, Journal of Machine Learning Research 12 (2011), pp. 2825-2830.
- [4] C. C. Chang and C. J. Lin, *LIBSVM: A Library for Support Vector Machines*, ACM Trans. Intell. Syst. Technol. 2 (2011), pp. 1-39.

# Extracting relevant parameters from anomalous diffusion trajectories

Gabriel Fernández-Fernández<sup>1\*</sup>, Alexandre Dauphin<sup>1</sup>, Gorka Muñoz-Gil<sup>2</sup>

<sup>1</sup> ICFO - Institut de Ciències Fotoniques, The Barcelona Institute of Science and Technology, Av. Carl Friedrich Gauss 3, 08860 Castelldefels (Barcelona), Spain, \* gabriel.fernandez@icfo.eu

<sup>2</sup> Institute for Theoretical Physics, University of Innsbruck, Technikerstr. 21a, A-6020 Innsbruck, Austria

.....

Anomalous diffusion trajectories arise from different stochastic processes that, in general, lack a universal model to gather all the current subtypes. Last year, the ANDI Challenge was created with the aim to bring computational tools to characterize these trajectories. However, up to the moment, the machine learning (ML) methods used in this challenge were only supervised. In contrast, in recent years, some unsupervised ML techniques have been proposed to learn a map to the relevant variables of simple physical problems [1]. These techniques are directed towards the extraction of hidden parameters from data rather than making accurate predictions. Yet, it is still unclear if this sort of algorithms can extract relevant physical parameters behind stochastic processes, as the ones we deal with in anomalous diffusion.

Using these unsupervised ML techniques, we aim at extracting relevant physical parameters and yield theoretical descriptions for simulated and experimental data. To this end, we use an architecture called Variational Autoencoder (VAE). The task of VAEs is to compress the input data and then recover the input by looking only at this compressed representation. In usual applications, VAEs are used as generative models. To do so, they first compress the data in the so called latent neurons which, by construction, are enforced to be statistically independent. This property allows the latent neurons to represent independent features of the input data.

More concretely, we study how VAEs compress Brownian diffusion trajectories at different conditions. Our goal here is to find a theoretical representation of the trajectories which, in this case, depends only on the diffusion coefficient. The machine is given as input raw trajectories and then, is asked to reconstruct each of them. After the training process, we study the variables arising in the latent neurons and analyze its relation with the factors of variation in the generated data which, as commented, is the diffusion coefficient. Finally, we take the aforementioned method a step further. As these trajectories are stochastic, we propose the use of an autoregressive model as the decoder part of the VAE. These autoregressive architectures allow to reproduce the statistic of the input data rather than reconstructing its exact values. Due to their ease in extracting both local and long range correlations, they are commonly used in timeseries, from the analysis and generation of audio signals to economics forecasting. We expect these methods will heavily boost the present procedure, but also other applications of ML in anomalous diffusion data.

## References

- [1] Raban Iten, Tony Metger, Henrik Wilming, Lidia del Rio, and Renato Renner, *Discovering Physical Concepts with Neural Networks*, Physical Review Letters **124**: 010508 (2020).

# Ensemble machine learning classification of non-ergodic anomalous diffusion

P. Kowalek<sup>1</sup>

<sup>1</sup> Faculty of Pure and Applied Mathematics,  
Wrocław University of Science and Technology,  
Janiszewskiego 14a, 50-372 Wrocław, Poland  
patrycja.kowalek@pwr.edu.pl

.....

Single Particle trajectories measured in microscopy experiments contain essential information about dynamic processes undergoing in a range of materials, including living cells and tissues. Understanding and identifying the diffusion type of molecules in living cells can be important for gaining insight into the cells' features and physical qualities and properties.

Apart from the most well-known and pure statistical methods, the scientific community is attempting to determine the optimum methodology and solution for the classification problem of diffusion models, which has resulted in the introduction of the anomalous diffusion (AnDi) challenge. One of the solutions produced during the ANDi challenge and improved after the event is presented in this study. Model combines classical statistical methods with an ensemble machine learning algorithm.

A stochastic process classifier based on various statistics, each of which describes a distinct aspect of the process. We can integrate all statistics and achieve satisfactory classification accuracy using the Gradient Boosting approach used in that study.

## References

- [1] J. Janczura, P. Kowalek, H. Loch-Olszewska, J. Szwabiński and A. Weron, *Classification of particle trajectories in living cells: Machine learning versus statistical testing hypothesis for fractional anomalous diffusion*, Phys. Rev. E 102, 032402 (2020).
- [2] P. Kowalek, H. Loch-Olszewska, J. Szwabiński, *Classification of diffusion modes in single-particle tracking data: Feature-based versus deep-learning approach*, Phys. Rev. E 100, 032410 (2019).

# HiDenMaps: a biophysical tool to understand how molecules interact with their environment

N. Mateos<sup>1</sup>, P. Sil<sup>2</sup>, S. Talluri<sup>3</sup>, S. Mayor<sup>4</sup>, C. Manzo<sup>5</sup>, M. Garcia-Parajo<sup>6,7</sup>

<sup>1</sup> ICFO-The Institute of Photonic Sciences, The Barcelona Institute of Science and Technology, Castelldefels 08860, Spain, [nicolas.mateos@icfo.eu](mailto:nicolas.mateos@icfo.eu)

<sup>2</sup> Devenport lab, Dept. of Molecular Biology - Princeton University, Princeton, USA, [ps7251@princeton.edu](mailto:ps7251@princeton.edu)

<sup>3</sup> National Centre for Biological Sciences (NCBS), Institute of Stem Cell and Regenerative Medicine, Bangalore 560065, India, [sankarshant@ncbs.res.in](mailto:sankarshant@ncbs.res.in)

<sup>4</sup> National Centre for Biological Sciences (NCBS), Institute of Stem Cell and Regenerative Medicine, Bangalore 560065, India, [mayor@ncbs.res.in](mailto:mayor@ncbs.res.in)

<sup>5</sup> Facultat de Ciències i Tecnologia, Universitat de Vic - Universitat Central de Catalunya, Vic 08500, Spain [carlo.manzo@uwic.cat](mailto:carlo.manzo@uwic.cat)

<sup>6</sup> ICFO-The Institute of Photonic Sciences, The Barcelona Institute of Science and Technology, Castelldefels 08860, Spain, [maria.garcia-parajo@icfo.eu](mailto:maria.garcia-parajo@icfo.eu)

<sup>7</sup> Institució Catalana de Recerca i Estudis Avançats (ICREA), 08010 Barcelona, Spain

.....

Understanding the spatiotemporal organization of receptors at the plasma membrane of living cells is crucial to elucidate their functions. However, spatial and temporal studies at the single molecule level are typically conducted separately. On the one hand, super-resolution (SR) techniques can reveal the nanoscale spatial organization of receptors, but at the expense of poor temporal resolution. On the other hand, single particle tracking (SPT) has access to the dynamics of individual receptors with ms temporal resolution, but it requires sparse labeling which results in low statistics. Here, we propose a novel methodology based on high-density single particle tracking to generate high density maps (HiDenMaps) of regions dynamically explored by receptors as they diffuse in their environment. The methodology combines nanometer scale localization accuracy of the receptor positions together with ms temporal resolution, bridging between SR and SPT. To validate the technical requirements and algorithms, we performed in-silico simulations of molecules diffusing in a Brownian fashion or interacting with the environment by binding to an imposed network. We further performed experiments to generate HiDenMaps from (i) supported lipid bilayers as a control of Brownian motion and (ii) transmembrane proteins that can interact with the cortical actin cytoskeleton with different strengths. While the HiDenMaps from the supported lipid bilayers rendered homogeneous maps consistent with Brownian motion, the HiDenMaps of those receptors that interact with the underlying cortical actin revealed a dynamic meshwork-like pattern. We quantified the temporal decays from autocorrelation curves inside and outside the meshwork and obtained two distinct temporal scales:  $\sim 30$  s and  $\sim 4$  s with different strengths depending on the receptor investigated. Overall, our data not only indicate that receptors actively interact with their environment, but importantly, HiDenMaps reveal the existence of an environment that dynamically remodels at different temporal scales, influencing in turn receptors diffusion and their spatial organization.

---

# Optimal estimates of diffusion coefficient from single-particle trajectories

Carlos Mejia-Monasterio<sup>1</sup>

<sup>1</sup> *Technical University of Madrid*

.....

Experimental methods based on single particle tracking (SPT) are being increasingly employed in the physical and biological sciences, where nanoscale objects are visualized with high temporal and spatial resolution. SPT can probe interactions between a particle and its environment but the price to be paid is the absence of ensemble averaging and a consequent lack of statistics due to a limited number of trajectories. Here I address the question of how to accurately extract the diffusion constant of one single Brownian trajectory, by analysing a class of estimators based on weighted functionals of the square displacement. For a certain choice of the weight function these functionals provide the true ensemble averaged diffusion coefficient, with a precision that increases with the trajectory resolution. Extensions to diffusion on random potentials, fractional Brownian motion and the running maximum of a Brownian trajectory will also be discussed.

---

# Single-shot self-supervised particle tracking

B. Midtvedt<sup>1</sup>, J. Pineda<sup>2</sup>, H. Bachimanchi<sup>3</sup>, D. Midtvedt<sup>4</sup>, G. Volpe<sup>5</sup>

<sup>1</sup> *University of Gothenburg, Department of Physics, benjamin.midtvedt@physics.gu.se*

<sup>2</sup> *University of Gothenburg, Department of Physics, jesus.pineda@physics.gu.se*

<sup>3</sup> *University of Gothenburg, Department of Physics, harsith.bachimanchi@physics.gu.se*

<sup>4</sup> *University of Gothenburg, Department of Physics, daniel.midtvedt@physics.gu.se*

<sup>5</sup> *University of Gothenburg, Department of Physics, giovanni.volpe@physics.gu.se*

.....

The quantitative analysis of statistical measures about the dynamics of particle systems is fundamentally reliant on the ability to acquire high-quality, sub-pixel determinations of the positions of the particles in question. However, in order to attain the best possible results, it is often necessary to develop custom solutions for each experiment. While data-driven approaches have made great strides in overcoming the challenges associated with constructing tracking methods optimized for the data at hand, the current state-of-the-art still almost invariably relies on the ability to synthetically reproduce the system under study.

In this work, we propose a novel deep learning-based method for training a high quality particle tracker directly from the experimental data, bypassing the distributional shift of a synthetic double. The method is based on a combination of two highly successful modern fields of deep learning: self-distillation learning and geometric deep learning. Self-distillation allows us to train the network to understand the data without annotations, while geometric deep learning allows us to exploit symmetries and invariances to guide that understanding. In effect, the method requires no labels, and is able to achieve great results from a single training image. We demonstrate that the method outperforms traditional single-particle trackers in terms of sub-pixel accuracy, as well as achieving almost perfect detection scores in multi-particle datasets. In fact, models trained using the method are found to display highly desirable emergent behaviors when presented with data far outside the training distribution, such as the ability to separate densely packed structures as well as distinguish objects by morphology. We make the method publicly available through the python package DeepTrack, bundled with several scripts and notebooks demonstrating different scenarios. Label-free, single-shot particle tracking enables extremely fast and easy development of high quality analysis pipelines, democratizing customized state-of-the-art methods to researchers without extensive experience in computer vision.

---

# Rapid Fickian yet non-Gaussian Diffusion after subdiffusion in a system of colloidal beads in random light patterns

R. Pastore<sup>1</sup>, A. Ciarlo<sup>2</sup>, G. Pesce<sup>2</sup>, F. Greco<sup>1</sup>, A. Sasso<sup>2</sup>

<sup>1</sup> *Department of Chemical, Materials and Production Engineering, University of Naples Federico II, P.le Tecchio 80, Napoli 80125, Italy, raffaele.pastore@unina.it*

<sup>2</sup> *Department of Physics E. Pancini, University of Naples Federico II, Complesso Universitario Monte S. Angelo, Via Cintia, I-80126, Naples, Italy*

.....

Around a decade ago, ground-breaking experiments on colloidal tracers in complex biological fluids [1, 2] revealed the existence of a novel type of diffusion that is distinct from both standard Brownian motion and anomalous diffusion: it is indeed characterized by the counterintuitive co-existence of a Mean Square Displacement (MSD) increasing linearly in time (Fickian), and by a non-Gaussian displacement distribution. Since then, such a 'Fickian yet non-Gaussian Diffusion' (FnGD) has been found in a wide variety of soft matter systems, but its understanding remains an intriguing open issue [3]. In this talk, I will describe our recent experiments [4, 5] on quasi-2d systems of colloidal beads in water, under the action of a static and spatially random optical force field (speckle pattern), which mimics the heterogeneous energy landscape of soft matter environments, but with much higher control and reproducibility if compared to "real" materials. First, I will demonstrate that this system is indeed an optimal experimental model of FnGD, where this phenomenon can be finely tuned and investigated over an unprecedented range of probabilities and timescales. Next, I will show that a "rapid" FnGD regime, with a diffusivity close to that of free suspension, can originate from earlier subdiffusion. These two regimes appear to be strictly tangled: for instance, we find that, as subdiffusion deepens upon increasing the optical force, deviations from Gaussianity in the FnGD regime becomes larger and more persistent in time. Overall, our results suggest that FnGD may generally be a memory effect of earlier subdiffusive processes. Finally, if time permits, I will hint at a few interesting perspectives to gain deeper insights on FnGD in the present experimental model, by exploiting the tools recently developed in the framework of the AnDi Challenge [6].

## References

- [1] B. Wang, S. M. Anthony, S. C. Bae, and S. Granick, *Proc. Natl. Acad. Sci. U.S.A.* **106**, 15160 (2009).
- [2] B. Wang, J. Kuo, S. C. Bae, and S. Granick, *Nat. Mater.* **11**, 481 (2012).
- [3] R. Metzler, *Biophysical journal* **112**, 413 (2017).
- [4] R. Pastore, A. Ciarlo, G. Pesce, F. Greco, and A. Sasso, *Phys. Rev. Lett.* **126**, 158003 (2021).
- [5] R. Pastore, A. Ciarlo, G. Pesce, A. Sasso, and F. Greco, under review.
- [6] Gorka Muñoz-Gil, et al., *Nat. Comm.* **12**, 6253 (2021)

# Attention-based fingerprinting graph neural network improves object association in particle tracking

Jesus Pineda<sup>1,\*</sup>, Benjamin Midtvedt<sup>1</sup>, Harshith Bachimanchi<sup>1</sup>, Giovanni Volpe<sup>1</sup>, and Carlo Manzo<sup>2</sup>

<sup>1</sup> Department of Physics, University of Gothenburg, Origoavagen 6B, SE-41296 Gothenburg, Sweden

<sup>2</sup> The Quantitative BioImaging lab, Facultat de Ciències i Tecnologia, Universitat de Vic – Universitat Central de Catalunya (UVic-UCC), C. de la Laura,13, 08500 Vic, Spain

\* e-mail: [jesus.pineda@physics.gu.se](mailto:jesus.pineda@physics.gu.se)

.....

Particle tracking is essential for imaging-based biological research [1]. This process is generally approached by detecting the particles in each frame of an image sequence and linking their detections and properties over time while maintaining their identities. Standard detection linking algorithms are highly dependent on fine-tuning various user-defined parameters specific to the scenario, to achieve a successful tracking estimation. However, biological systems exhibit highly heterogeneous dynamics that impose analytical challenges to conventional techniques. Dealing with this variability is challenging as there is no single model that fits all solutions [2, 3].

This work introduces a graph-based deep learning method for detection linking, where particle motion and their interactions are geometrically modeled using graph representations. Precisely, we propose an interpretable and adaptive Graph Neural Network (GNN) block, referred to as Fingerprinting Graph Layer, that determines the optimal trajectories and adapts to different biological scenarios given a set of particle detections. Furthermore, the Fingerprinting Graph Layer contains attention-based components that, besides allowing the correct association of the detections and their interactions over time, directly estimate global statistics associated with the trajectories (e.g., the mean square displacement or the anomalous exponent).

We demonstrate that approaching the detection linking from a geometric perspective can pave the way towards a general framework, easily adaptable, that allows exploiting the intrinsic nature of biological system dynamics. The implementation of our method is provided as part of the new release of DeepTrack 2.1, a deep learning framework for microscopy [4].

## References

- [1] Benjamin Midtvedt, Saga Helgadottir, Aykut Argun, Jesus Pineda, Daniel Midtvedt, and Giovanni Volpe, *Quantitative digital microscopy with deep learning*, Applied Physics Reviews **8.1**: 011310 (2021).
- [2] Nicolas Chenouard, Ihor Smal, Fabrice de Chaumont, et al, *Objective comparison of particle tracking methods*. Nat Methods **11**: 281–289 (2014).
- [3] Gorka Muñoz-Gil, Giovanni Volpe, Miguel Angel Garcia-March, et al, *Objective comparison of methods to decode anomalous diffusion*. Nat Commun **12**: 6253 (2021).
- [4] Benjamin Midtvedt, Saga Helgadottir, Aykut Argun, Jesus Pineda, Daniel Midtvedt, and Giovanni Volpe, DeepTrack 2.0, <https://github.com/softmatterlab/DeepTrack-2.0>.

# Step-wise inference of normal and anomalous diffusion properties

B. Requena<sup>1</sup>, M. Lewenstein<sup>1,2</sup>, G. Muñoz-Gil<sup>3</sup>

<sup>1</sup> *ICFO-Institut de Ciències Fotoniques, The Barcelona Institute of Science and Technology, Av. Carl Friedrich Gauss 3, 08860 Castelldefels (Barcelona), Spain*

<sup>2</sup> *ICREA, Pg. Lluís Companys 23, 08010 Barcelona, Spain*

<sup>3</sup> *Institute for Theoretical Physics, University of Innsbruck, Technikerstr. 21a, A-6020 Innsbruck, Austria*

.....

Characterizing diffusion processes is a challenging task of great interest in a wide variety of fields, ranging from biology to economy. Traditional techniques, such as estimating the time-averaged mean square displacement (TAMSD), rely on either several or long observations of the same process, conditions which are rarely met in experiments. In order to overcome this limitation, researchers have proposed several machine learning (ML) models that operate at a single-trajectory level and have motivated the organization of the Anomalous Diffusion (AnDi) challenge. As seen in the AnDi Challenge, characterizing trajectories of processes with time dependent properties is very challenging, yet it may be the most important analysis when dealing with experimental scenarios. These changes at a microscopic level are often tied to important macroscopic dynamics. For example, the change in the diffusive behaviour of a protein inside a cell may trigger a mechanism at full body scale, like an inflammation process. This change can have a wide variety of sources, such as variations in the medium or the interaction with other elements.

One of the main difficulties involved in the analysis of trajectories with changes comes from the uncertainty in the changepoints. In most cases, we do not know, beforehand, where the changepoints will be, how many will there be or, even more, whether there will be any at all. To tackle this problem in the most generic way as possible, in this work, we formalize the characterization of diffusion processes as a prototypical segmentation task in ML. In this framework, we train a ML learning model to make a point-wise prediction of the quantities of interest: diffusion coefficient, anomalous exponent and the theoretical model that best describes the observation. This way, we have an individual prediction for every time-step, which allows us to naturally see changes in any of these quantities and determine the position of the changepoints at the same time that we find a description of the segments.

We build the model using state-of-the-art techniques combining convolutional neural networks with attention mechanisms. The former capture the local properties around every point, while the latter extract information about the long-range correlations. First, we use our protocol to tackle the segmentation task of the AnDi challenge (Task 3 - 2D), obtaining better performance than the best presented models. Then, we take it a step further and train a model to infer the point-wise diffusion coefficient. We test the model with trajectories containing one to four changepoints and diffusion coefficients that span six orders of magnitude. The model successfully finds the changes in diffusion coefficient and even provides a better estimation for each segment than the standard TAMSD applied to the segments alone.

# Automated Optical Tweezers for Multi-Particle Experiments

M. Selin<sup>\*1</sup>, V. Carmona Sosa<sup>2</sup>, A. Maguzzo<sup>3</sup>, R. Di Leonardo<sup>2</sup>, G. Volpe<sup>1</sup>

<sup>1</sup> *University of Gothenburg, Gothenburg, Sweden,*

<sup>2</sup> *Sapienza University of Rome, Rome, Italy,*

<sup>3</sup> *Istituto Processi Chimico-Fisici (CNR-IPCF), Messina, Italy,*

*\*martin.selin@physics.gu.se*

.....

We present a method which can be used for automating single and multi-particle experiments with optical tweezers. By using real-time image analysis our program can autonomously operate our microscope and optical tweezers. This way a large numbers of particles can be controlled as demonstrated in Fig. 1 where 9 particles have been trapped automatically by the program. The flexibility of the method means that it can easily be adapted to different types of particles and experiments, for instance using many particles or particles with unique shapes. Computerized control also allows for using less laser power than when manually operating the system since the program is faster and more accurate in responding to movement by the particles than a human operator.

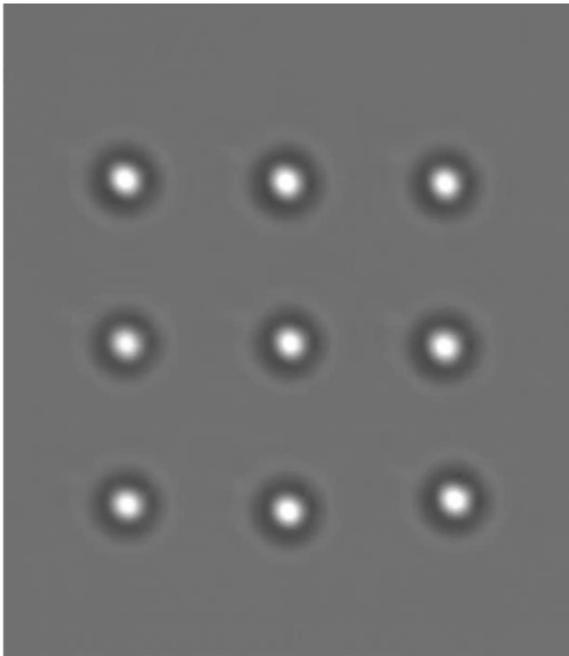


Figure 1: 9 particles which have been trapped by the program without manual intervention.

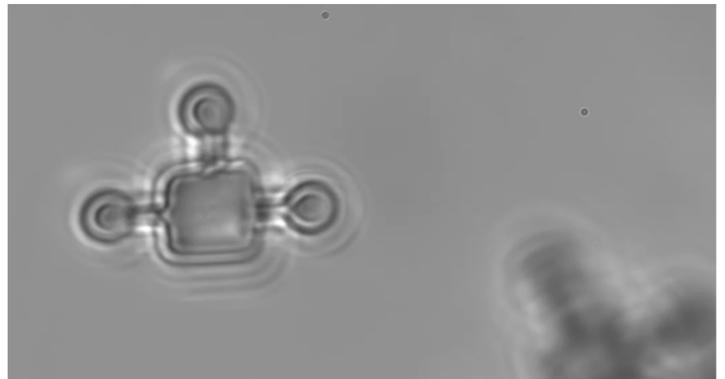


Figure 2: Custom made microprobe trapped in 3d with four traps, one per handle and one for the body in the center. The traps are generated by a holographic optical tweezers and enable us to control both position and orientation of the probes.

As a first application we are working on using the system for measurements of critical Casimir forces between two custom made microprobes as function of temperature and distance, see Fig. 2 for example of one of these microprobes trapped. By trapping two microprobes and bringing them close together we aim to measure critical Casimir forces between flat surfaces.

# Feature-based approach to classification of anomalous diffusion

J. Szwabiński

*Faculty of Pure and Applied Mathematics, Wrocław University of Science and Technology, Wrocław, Poland*  
*janusz.szwabinski@pwr.edu.pl*

.....

The most popular method to identify the class of a single-particle tracking trajectory is based on the mean-square displacement (MSD). However, due to its known limitations, several other approaches have been already proposed. With the recent advances in algorithms and the developments of modern hardware, there is a growing interest in machine learning approach to classification of diffusion modes. Among the available algorithms, deep neural networks seem to be of particular importance as they already constitute the state-of-the-art classification methods in many domains. However, the traditional feature-based methods may be still worth considering, since they are usually easier to interpret and work better on small data.

In this talk, a feature-based algorithm will be adopted to the problem of trajectory classification. Different sets of features and their impact on the performance of the classifier will be discussed. The resulting models will then be applied to real data for G protein-coupled receptors and G proteins. Their results will be compared to recent statistical methods going beyond MSD.

## References

- [1] H. Loch-Olszewska, J. Szwabiński, Impact of Feature Choice on Machine Learning Classification of Fractional Anomalous Diffusion, *Entropy* 22(12), 1436, (2020)
- [2] J. Janczura, P. Kowalek, H. Loch-Olszewska, J. Szwabiński and A. Weron, Classification of particle trajectories in living cells: Machine learning versus statistical testing hypothesis for fractional anomalous diffusion, *Phys. Rev. E* 102, 032402 (2020)
- [3] P. Kowalek, H. Loch-Olszewska, J. Szwabiński, Classification of diffusion modes in single-particle tracking data: Feature-based versus deep-learning approach, *Phys. Rev. E* 100, 032410 (2019)

# Machine learning and minimal particle-based interaction model of experimentally tunable transcription factor condensates

Juan Andres Torreno-Pina<sup>1,2</sup>, G. Munoz-Gil<sup>1</sup>, C. Romero-Aristizabal<sup>2</sup>, N. Mateos<sup>1</sup>, L.I. de Llobet-Cucalon<sup>2</sup>, M. Beato<sup>2,3</sup>, M. Lewenstein<sup>1,4</sup>, M. F. Garcia-Parajo<sup>1,4</sup>

<sup>1</sup> *ICFO-Institut de Ciències Fotoniques, The Barcelona Institute for Science and Technology (BIST), 08860 Barcelona, Spain.*

<sup>2</sup> *Centre de Regulació Genòmica (CRG), The Barcelona Institute of Science and Technology (BIST), Dr. Aiguader 88, Barcelona, Spain.*

<sup>3</sup> *Universitat Pompeu Fabra (UPF), Barcelona, Spain.*

<sup>4</sup> *ICREA, Pg. Lluís Companys 23, Barcelona, Spain*

.....

Phase separation is emerging as key physical principle governing the spatiotemporal organization of different molecular components inside living cells. Such a phenomenon gives rise to the emergence of so called biomolecular condensates that play important roles in the regulation of multiple biological functions, including gene transcription and chromatin architecture. Given its relevance in cell biology, these findings have triggered renewed interest from the physical community aiming to model and theoretically predict biomolecular condensation in living systems. Yet, most models developed so far rely on specific descriptions of equilibrium systems which are difficult to adapt to the living cell. Here we propose a theoretical model, where phase separation is explained by means of interaction probabilities between particles. With minimum model requirements, particle condensates emerge above a critical interaction probability and grow following Brownian Motion Coalescence. By introducing a particle escape probability from condensates, we successfully describe arrested growth of condensates in time. We tested the model predictions with single molecule experiments of tunable transcription factor condensates in the nucleus of living cells. Moreover, we exploited a machine learning architecture to retrieve the anomalous diffusion behavior of individual transcription factors inside and outside condensates. We find that the fraction of molecules associated to condensates preferentially exhibit fractional Brownian motion, whereas outside condensates, diffusion is essentially Brownian but heterogeneous. Overall, our results show that phase separation, condensate sizes, mobility parameters and diffusion behavior quantified by single molecule data analysis and machine learning are fully recapitulated by our model. Our combined theoretical and experimental approach provides a general framework to address at the single molecule level phase separation in living cells and in other soft matter-based interacting system

# Model-free analysis of biomolecule dynamics with simulation-based inference

H. Verdier<sup>1, 2</sup>, F. Laurent<sup>1</sup>, C. L. Vestergaard<sup>1</sup>, J.-B. Masson<sup>1</sup>

<sup>1</sup> Institut Pasteur, Université de Paris, USR 3756 (C3BI/DBC) & Neuroscience department CNRS UMR 3751, Decision and Bayesian Computation lab, F-75015 Paris, France

<sup>2</sup> Histopathology and Bio-Imaging Group, Sanofi R&D, Vitry-sur-Seine, France

.....

Photo-activated localization microscopy (PALM) enables high-resolution recording of single proteins trajectories in live cells, thus providing precious probes of small-scale properties of biomolecules environment. A diversity of dynamics has been observed and analysis schemes tailored to specific biological systems have been developed to quantitatively characterize the motion, notably using estimators developed on model random walks [1], such as fractional Brownian motion, continuous time random walk etc...

Yet, in most cellular environments, the complex interplay of multiple interactions leads to random walks that don't necessarily match a unique canonical model. We propose an amortised inference scheme that allows quantitative and statistical analysis of experimental biomolecule recordings without requiring model identification.

The first step of our approach [2] is to associate to each biomolecule trajectory, no matter its scale or its length, a fixed-size vector of learnt features. We developed a graph neural network for this purpose trained on simulated trajectories whose properties (including measurement noise) can be adapted to the specificities of the observed system and can include a large set of canonical random walks. Features describing trajectories are learnt by the neural network and thus capture more information than conventional estimators do, especially on short trajectories. We have shown that these feature space can be leveraged to infer subdiffusive parameters with linear complexity (regarding trajectory size) for fractional Brownian motion[3]. Coupled to a new approach to Approximate Bayesian Computation[4] (ABC) the posterior distribution of parameters of interest can be assessed.

We demonstrate our approach by mapping the spatial evolution of the alpha-synuclein random walks and show that we can detect pharmacologically induced differences in receptors motion. This work paves the way to single molecule pharmacology.

## References

- [1] Metzler R, Jeon JH, Cherstvy AG, Barkai E. *Anomalous diffusion models and their properties: non-stationarity, non-ergodicity, and ageing at the centenary of single particle tracking* Physical Chemistry Chemical Physics. 2014;16(44):24128-64.
- [2] Verdier H, Duval M, Laurent F, Casse A, Vestergaard CL, Masson JB. *Learning physical properties of anomalous random walks using graph neural networks* Journal of Physics A: Mathematical and Theoretical. 2021 May 14;54(23):234001.
- [3] Verdier H, Laurent F, Vestergaard CL, Masson JB. *Near optimal amortised inference of fractional Brownian motion with linear complexity* (In review)
- [4] Stefan T. Radev, Ulf K. Mertens, Andreass Voss, Lynton Ardizzone, Ullrich Köthe, *BayesFlow: Learning complex stochastic models with invertible neural networks*, arXiv 2003.06281, 2020

# Unravelling the origins of anomalous diffusion: from molecules to migrating storks

Ohad Vilk<sup>1,2</sup>, Erez Aghion<sup>3</sup>, Tal Avgar<sup>4</sup>, Carsten Beta<sup>5</sup>, Oliver Nagel<sup>5</sup>, Adal Sabri<sup>6</sup>, Raphael Sarfati<sup>7</sup>, Daniel K. Schwartz<sup>7</sup>, Matthias Weiss<sup>6</sup>, Diego Krapf<sup>8</sup>, Ran Nathan<sup>2</sup>, Ralf Metzler<sup>5</sup>, Michael Assaf<sup>1,5</sup>

<sup>1</sup>*Racah Institute of Physics, The Hebrew University of Jerusalem, Jerusalem, Israel*

<sup>2</sup>*Movement Ecology Lab, Department of Ecology, Evolution and Behavior, Alexander Silberman Institute of Life Sciences, Faculty of Science, The Hebrew University of Jerusalem, Jerusalem, Israel*

<sup>3</sup>*Departments of Physics and Chemistry, University of Massachusetts Boston, MA 02125, USA*

<sup>4</sup>*Wildlife Space-Use Ecology Lab, Department of Wildland Resources and Ecology Center, Utah State University, Logan, UT 84332, USA*

<sup>5</sup>*Institute of Physics and Astronomy, University of Potsdam, Potsdam 14476, Germany*

<sup>6</sup>*Experimental Physics I, University of Bayreuth, D-95440 Bayreuth, Germany*

<sup>7</sup>*Department of Chemical and Biological Engineering, University of Colorado Boulder, Boulder, CO 80309, USA*

<sup>8</sup>*Department of Electrical and Computer Engineering, and School of Biomedical Engineering, Colorado State University, Fort Collins, CO 80523, USA*

.....

Anomalous diffusion or, more generally, anomalous transport, with nonlinear dependence of the mean-squared displacement on the measurement time, is ubiquitous in nature. It has been observed in processes ranging from microscopic movement of molecules to macroscopic, large-scale paths of migrating birds. Using data from multiple empirical systems, spanning 12 orders of magnitude in length and 8 orders of magnitude in time, we employ a method to detect the individual underlying origins of anomalous diffusion and transport in the data. This method decomposes anomalous transport into three primary effects: long-range correlations ("Joseph effect"), fat-tailed probability density of increments ("Noah effect"), and non-stationarity ("Moses effect"). We show that such a decomposition of real-life data allows to infer nontrivial behavioral predictions, and to resolve open questions in the fields of single particle cell tracking and movement ecology.

---

Abstracts

Posters

---

# Spatiotemporal Dynamics of Endoplasmic Reticulum-Golgi Membrane Contact Sites in Transport Carrier Biogenesis

J. Angulo-Capel<sup>1</sup>, R. Pons<sup>1</sup>, M. F. Garcia-Parajo<sup>1,2</sup>, F. Campelo<sup>1</sup>

<sup>1</sup> *ICFO-Institut de Ciències Fotoniques, The Barcelona Institute of Science and Technology, Barcelona, Spain*

<sup>2</sup> *ICREA-Institució Catalana de Recerca i Estudis Avançats, Barcelona, Spain*

.....

The Golgi apparatus is a fundamental cellular organelle that processes newly synthesized molecules and distributes them to other cell compartments or outside of the cell. This transport out of the Golgi is carried out by small, membrane-bound structures, termed transport carriers. Understanding how these carriers form at the Golgi is therefore of an utmost importance in cell biology. However, and despite its relevance, it still remains as a poorly understood process due to its complexity. In my research, I aim to elucidate the role of the so-called endoplasmic reticulum (ER)-Golgi membrane contact sites (MCS). MCS are a newly identified communication mode between cellular compartments, and we have evidence to suggest that they are key for the regulation of Golgi-derived carrier formation.

Contrary to classical biochemical research approaches, I do not seek to identify new elements of the molecular machinery involved in the process, but to functionally place the already known players in time and space. To that end, I use single molecule tracking (SMT) to characterize and analyze the dynamics of single proteins within the Golgi, as well as in their journey out of this organelle. This technique allows tracking of single molecules with a temporal resolution of milliseconds, and a spatial resolution of nanometers. The simultaneous visualization of these molecules together with the ER-Golgi MCS structures will serve to understand how ER-Golgi MCS are involved in the steps leading to carrier biogenesis.

# ConvTransformer: A Parallel Architecture for Characterization of Anomalous Diffusion

N. Firbas<sup>1</sup>, J.A. Conejero<sup>2</sup>, M.A. Garcia-March<sup>2</sup>

<sup>1</sup> *Department of Biological Sciences, National University of Singapore, 21 Lower Kent Ridge Rd, Singapore 119077. [Nicolas.Firbas@gmail.com](mailto:Nicolas.Firbas@gmail.com)*

<sup>2</sup> *Instituto Universitario de Matemática Pura y Aplicada, Universitat Politècnica de València, Valencia, Spain. [aconejero@upv.es](mailto:aconejero@upv.es)*

<sup>3</sup> *Instituto Universitario de Matemática Pura y Aplicada, Universitat Politècnica de València, Valencia, Spain. [garciamarchma@gmail.com](mailto:garciamarchma@gmail.com)*

.....

It is clear from the results of the 2020 Anomalous Diffusion Challenge (AnDi Challenge) that machine learning based models outperform conventional statistical methods at characterization of anomalous diffusion[1]. Of the 5 models that placed in the top 3 across Task 1 (inference of the anomalous diffusion exponent  $\alpha$ ) and Task 2 (classification of the underlying anomalous diffusion model), all of them incorporate machine learning and 3/5 of them use recurrent neural networks (RNNs) [5], either conventional RNNs or long-short term memory networks (LSTMs)[6]. Following Vaswani et al.'s 2017 landmark paper *Attention is all you need*[3], Transformers have overtaken recurrent neural networks in the realm of Natural Language Processing (NLP) [2]. Drawing a parallel between the sequential nature of languages and single particle trajectories, we propose a new neural network architecture, called Convolutional Transformer (ConvTransformer), for the aforementioned Tasks 1 and 2 of the AnDi Challenge. Based off our (Team NOA's) prior success with a convolutional bilayered LSTM as well as that of UPV-MAT [3], we reused our two layer CNN and supplanted the LSTM [6] with a Transformer encoding block. This yields a sizable performance improvement in the F1-Score from 0.788 to 0.844 when benchmarking with the AnDi interactive tool<sup>1</sup>, highlighting the potential of the Transformer encoding block. However, the principal advantage of our ConvTransformer is that, unlike methods that depend on recurrence, it is fully parallelizable and performs well at short trajectory lengths, which are the most important for experimental researchers.

## References

- [1] Muñoz-Gil, G., Volpe, G., Garcia-March, M.A. et al., *Objective comparison of methods to decode anomalous diffusion*. Nature Communications 12, 6253 (2021). <https://doi.org/10.1038/s41467-021-26320-w>
- [2] Wolf, T., Debut, L., Sanh, V. et al., *Huggingface's transformers: State-of-the-art natural language processing*, ArXiv (2020).
- [3] Vaswani, A., Shazeer, N., Parmar, N. et al., *Attention is all you need*, ArXiv (2017).
- [4] Garibo i Orts, O., Baez-Bosca, A., Garcia-March, M.A., Conejero J.A., *Efficient recurrent neural network methods for anomalously diffusing single particle short and noisy trajectories*, Journal of Physics A: Mathematical and Theoretical (2021). doi: 10.1088/1751-8121/ac3707/meta
- [5] Rumelhart, D. E., Hinton, G. E., and Williams, R. J., *Learning representations by back-propagating errors*, Nature (1986), 323(6088):533-536 .
- [6] Hochreiter, S., Schmidhuber, J., *"Long short-term memory"*. Neural Computation (1997). 9 (8): 1735–1780. doi:10.1162/neco.1997.9.8.1735. PMID 9377276. S2CID 1915014.

---

<sup>1</sup><http://andi-challenge.org/interactive-tool/>

# Classification of anomalously diffusing trajectories using Gramian Angular Fields

Òscar Garibo-i-Orts<sup>2</sup>, M.A. García-March<sup>1</sup>, and J. Alberto Conejero<sup>1</sup>

<sup>2</sup> *Valencian Research Institute for Artificial Intelligence, Universitat Politècnica de València, Spain, osgaor@upv.es* <sup>1</sup> *Instituto Universitario de Matemática Pura y Aplicada, Universitat Politècnica de València, Spain, garciamarch@mat.upv.es, aconejero@upv.es*

.....

Anomalous diffusion is all around, from ultra-cold atoms and telomeres in the nucleus of cells to moisture transport in cement-based materials. Identifying the underlying method with high confidence is important since much information can be inferred about the system dynamics. Classification using raw trajectories and statistics extracted from them have been broadly used under the AnDi Challenge scope [1]., proving that the shorter the trajectory, the harder to classify.

We present a data-driven method based on Gramian Angular Fields to represent each 1D trajectory as an image, with Polar Ordinate coordinates system. Here, each point of the plane is determined by its distance to a reference point and the angle from a reference direction. Mathematics of the Gramian Angular Field is intrinsically linked to the inner product and the corresponding Gram Matrix, which preserves the temporal dependency. Gramian Angular Fields were initially proposed in [2] for encoding time series as images and thus being able to classify them using deep learning techniques developed in the computer vision field.

In this work, we have focused on short, noisy trajectories whose length varies from 10 to 50.

We have analyzed the response of the most widely used image classification models (Resnet, xception, inception, and mobilenet). We have also compared the results with other models based on recurrent neural networks, such as the ones we developed in our participation in the AnDi Challenge [3].

## References

- [1] G. Muñoz-Gil, G. Volpe, G., M.A. Garcia-March, et al. *Objective comparison of methods to decode anomalous diffusion*. Nature Communications. DOI: 10.1038/S41467-021-26320-W (November 2021).
- [2] Z. Wang, T. Oates. *Imaging Time-series to improve classification and imputation*. In Proceedings of the 17th International Conference on Artificial Intelligence, Las Vegas, NV, USA pp. 3939-3945. (July 2015)
- [3] Ó. Garibo-i-Orts, A. Baeza-Bosca, M.A. Garcia-March, and J. Alberto Conejero. *Efficient recurrent neural network methods for anomalously diffusing single particle short and noisy trajectories*. Journal of Physics A: Mathematical and Theoretical. DOI:10.1088/1751-8121/AC3707 (November 2021).

# The actin machinery of dendritic cells regulates Siglec-1 nanoclustering and determines the capture and trafficking of HIV-1 into the virus-containing compartment

E. Gutierrez-Martinez<sup>1</sup>, S. Benet<sup>2</sup>, N. Mateos<sup>1</sup>, J. A. Nieto-Garai<sup>3</sup>, M. Lorizate<sup>3</sup>, C. Manzo<sup>5</sup>, K. Borgman<sup>6</sup>, F. Campelo<sup>1</sup>, N. Izquierdo-Useros<sup>2</sup>, J. Martinez-Picado<sup>2,7</sup>, M. Garcia-Parajo<sup>1,7</sup>

<sup>1</sup> ICFO-Institut de Ciències Fotoniques, The Barcelona Institute of Science and Technology, Castelldefels 08860 (Barcelona), Spain.

<sup>2</sup> IrsiCaixa AIDS Research Institute, Department of Retrovirology, Badalona 08916, Spain.

<sup>3</sup> Instituto Biofísica (UPV/EHU, CSIC) University of the Basque Country, Leioa E-48940, Spain.

<sup>4</sup> Department of Biochemistry and Molecular Biology Faculty of Science and Technology, University of the Basque Country, Leioa E-48940, Spain.

<sup>5</sup> Facultat de Ciències i Tecnologia, Universitat de Vic-Universitat Central de Catalunya, Vic 08500, Spain.

<sup>6</sup> Institut Curie, PSL Research University, Sorbonne Université, CNRS UMR3664, Nuclear Dynamics Unit, F-75005, Paris, France.

<sup>7</sup> ICREA-Institució Catalana de Recerca i Estudis Avançats, Barcelona 08010, Spain.

.....

The immunoglobulin-like lectin receptor CD169 (siglec-1) mediates the capture of HIV by dendritic cells (DC) through the binding to sialylated ligands, however the mechanisms by which in activated DCs this interaction results in a much more efficient capture as compared to resting DCs are poorly understood. Here we show that DC activation leads to a change in the steady-state nanoscale organization of siglec-1 receptors, forming small nanoclusters that enhance the avidity of siglec-1 receptors to limiting concentrations of gangliosides. We also show that this basal nanoclustering occurs at specific regions of the plasma membrane where siglec-1 diffusion is constrained by Rho-ROCK activation and formin-dependent actin polymerization. Finally, we show that siglec-1 nanoclusters increase in size after the initial binding to either HIV viral particles or liposomes carrying gangliosides. HIV-induced siglec-1 clustering is accompanied by global acting rearrangements characterized by a drop in RhoA activity, which allow the final accumulation of viral particles in single sac-like compartment at the plasma membrane of activated DCs.

---

# Simulations of Fluorescence Fluctuation Spectroscopy Measurements of Molecular Diffusion in Biomembranes

Agnes Koerfer<sup>1</sup>, Francesco Reina<sup>2</sup>, Christian Eggeling<sup>1,2,3</sup>

<sup>1</sup> *Friedrich-Schiller University Jena*

<sup>2</sup> *Institut für Photonische Technologien*

<sup>3</sup> *Medical Research Council Oxford*

.....

The complexity of the organization and the functions of cell membranes has been of interest for a long time, especially every interaction of the cell with a partner or its environment is actually an interaction with its cell membrane. Therefore, to understand processes like signalling, infection, fusion and fission better it is crucial to study the organization and dynamical behaviour of the membrane molecules. By observing the diffusion of the membrane molecules such as lipids and proteins we can study their interactions and hence function during different cellular processes. Here, we present a novel, versatile and open accessible program based on Python for simulating molecular membrane diffusion. There have been different approaches to describe the complex trajectories of the membrane molecules and divide them into different diffusion modes. The main three ones which we have simulated in our project are Brownian diffusion, compartmentalized or hop diffusion (with transient confinement in larger areas which are given by an underlying meshwork) and trap diffusion (with transient slowdowns due to environmental influences). A Voronoi transformation on a uniform random distribution of seed points is performed for compartmentalized and trapping diffusion simulations to construct, respectively, the underlying network of distinct boundaries and random distributed trapping sites. We are setting up a simulation toolbox not only for the different diffusion modes but also for a variety of fluorescence fluctuation microscopy techniques such as point, scanning and image correlation spectroscopy. The ultimate goal is to have an easy simulation software to help understand the dynamic data obtained in living cells.

---

# The role of shear forces in LFA-1 activation and dynamics

L. Lau<sup>1</sup>, R. Huo<sup>1</sup>, M. García-Parajo<sup>1</sup>

<sup>1</sup> ICFO, Av. Carl Friedrich Gauss, 3, 08860 Castelldefels, Barcelona - SPAIN, [lukas.lau@icfo.eu](mailto:lukas.lau@icfo.eu)

.....

Integrin transmembrane receptors on the cell surface are key players in a multitude of different cellular contacts and adhesions. They mediate force transmission over the cell membrane, e.g. from an integrin ligand to the intracellular actin network. The interaction of integrin LFA-1 (Lymphocyte function-associated antigen 1) with its ligand ICAM-1 (Intercellular adhesion molecule 1) is known to play a prominent role in the immune response [1]. It is crucial for the adhesion and arrest of leukocytes on the blood vessel wall, as they are recruited as first responders to a site of infection. Force-dependent properties of this binding have been shown lately on LFA-1 and other integrins. Their ligand affinity was shown to be regulated by mechano-sensitive inside-out and outside-in signalling cascade. As the three conformation states of LFA-1 correspond to three respective ligand affinities, force must be a driver of conformational state transitions. We investigate how the flow-derived shear forces acting on the entire leukocyte affect the molecule conformation ensemble by examining their dynamics. This is done by following the molecular diffusion via Single Particle Tracking [2].

## References

- [1] Brandon L Walling, Minsoo Kim, *LFA-1 in T Cell Migration and Differentiation*, Frontiers in Immunology (2018).
- [2] Carlo Manzo, Maria F Garcia-Parajo, *A review of progress in single particle tracking: from methods to biophysical insights*, Reports on Progress in Physics (2015).

# The role of glycosylations on integrin $\alpha 5 \beta 1$ diffusion in the plasma membrane

S. Masó<sup>1</sup>, M. Cullell-Dalmau<sup>1</sup>, M. Masoliver-Prieto<sup>1</sup>, J. Bertran<sup>2</sup>, C. Manzo<sup>1</sup>

<sup>1</sup> *the Quantitative BioImaging (QuBI) Lab, Facultat de Ciències i Tecnologia, Universitat de Vic - Universitat Central de Catalunya (UVic-UCC). C. de la Laura, 13 - 08500 Vic (Barcelona) - Spain*  
*sergi.maso.orriols@uvic.cat*

<sup>2</sup> *Bioinformàtica i Estadística Mèdica (BEM), Facultat de Ciències i Tecnologia, Universitat de Vic - Universitat Central de Catalunya (UVic-UCC). C. de la Laura, 13 - 08500 Vic (Barcelona) - Spain*

.....

Glycosylation is a common post-translational modification in membrane proteins with impact on their function. Despite a deep knowledge on the mechanisms of glycosylation, little is known about its impact on the dynamics of proteins at the membrane. HeLa cells wearing glycosylation mutations in the  $\alpha 5 \beta 1$  protein have altered proliferation and migration rates [1]. The subunit  $\alpha 5$  is a type I membrane glycoprotein that, together with the  $\beta 1$  chain forms an integrin that functions as a fibronectin receptor, participating in cell-matrix adhesion and cell signaling. We have performed single particle tracking in the mentioned HeLa cells to assess the impact of glycosylation on  $\alpha 5 \beta 1$  lateral diffusion in the membrane. Our experiments confirm the role played by  $\alpha 5$  glycosylation in cell proliferation and migration [1] and reveal different interactions and diffusion features associated with glycosylation. We are currently broadening our analyses and widening the palette of techniques to learn about changes in protein-protein interactions associated with the observed phenotype.

## References

- [1] Q. Hang, T. Isaji, S. Hou, Y. Zhou, T. Fukuda, and J. Gu, *A Key Regulator of Cell Adhesion: Identification and Characterization of Important N-Glycosylation Sites on Integrin  $\alpha 5$  for Cell Migration*, *Molecular and cellular biology* **37**(9): e00558-16 (2017).

# Spatiotemporal Organization of Integrin Receptors and Adaptor Proteins Inside Focal Adhesions

N. Salvat<sup>1</sup>, S. Keary<sup>1</sup>, N. Mateos<sup>1</sup>, C. Manzo<sup>2</sup>, M. Garcia-Parajo<sup>1,3</sup>

<sup>1</sup> *ICFO-Institut de Ciències Fotoniques, The Barcelona Institute of Science and Technology, Castelldefels 08860 (Barcelona), Spain.*

<sup>2</sup> *Facultat de Ciències i Tecnologia, Universitat de Vic-Universitat Central de Catalunya, Vic 08500, Spain.*

<sup>3</sup> *Institució Catalana de Recerca i Estudis Avançats (ICREA), Barcelona 08010, Spain*

.....

Adhesion complexes are protein platforms found in the plasma membrane through which cells interact with the extracellular matrix (ECM) and sense external stimuli. Within these macromolecular structures, integrin proteins act as the main linkers between the ECM and the actin cytoskeleton of the cell through adaptor proteins that bind to the integrins cytoplasmic tails. Integrins  $\alpha_5\beta_1$  and  $\alpha_V\beta_3$  are enriched within adhesion complexes but their specific role in converting mechanical cues into biochemical signals is still elusive. Integrins diffuse along the plasma membrane experiencing multiple arrestment cycles that correlate with their different activation states. Moreover, adaptor proteins are also constantly recruited and recycled underneath the plasma membrane. To quantify the dynamics of integrins  $\alpha_5\beta_1$  and  $\alpha_V\beta_3$ , and detect possible synergistic effects and cross-talk, as well as transient interactions and recruitment of adaptor proteins we have implemented a multi-colour single particle tracking (SPT) strategy working under total internal reflection geometry. We will report on the labelling strategies used for extended and simultaneous SPT of both integrins, as well as labelling of the adaptor partners paxillin and vinculin, compatible with single molecule live cell imaging. We will show our analysis pipeline to detect transient interactions between different integrins inside focal adhesions and correlation of these interactions with potential changes in the activation state of both integrins. Finally, we will show preliminary single molecule data aiming at establishing the temporal scales involved in integrin activation and vinculin recruitment.

---

# Bayesian Deep Learning for error estimation in anomalous diffusion analysis

Henrik Seckler<sup>1</sup>

<sup>1</sup> *Institute of Physics & Astronomy, University of Potsdam, Karl-Liebknecht-Str 24/25, D-14476 Potsdam-Golm, Germany, hseckler@uni-potsdam.de*

.....

During the *AnDi-Challenge* many participants have developed Machine Learning techniques to classify the diffusion model and infer the anomalous exponent from single particle anomalous diffusion trajectories.<sup>[1]</sup> While these methods have proven very successful, they lack an estimation of the certainty/expected error of the given information, that other methods can provide (e.g. Bayesian Inference). This work aims to bridge this gap by using what is known as *Bayesian Deep Learning*<sup>[2]</sup> to provide a machine learning prediction together with an estimation of the expected error of this prediction. The poster will serve as a short introduction into the used "Stochastic Weight Averaging - Gaussian" (*SWAG*)<sup>[2]</sup> technique, as well as present some results obtained from applying *SWAG* to the generated trajectories of the *AnDi-Challenge* data set.

## References

- [1] Muñoz-Gil, G., Volpe, G., Garcia-March, M.A. et al. *Objective comparison of methods to decode anomalous diffusion*. Nat Commun 12, 6253 (2021).
- [2] W. Maddox, P. Izmailov, T. Garipov, D. Vetrov, A.G. Wilson: *A simple baseline for bayesian uncertainty in deep learning*. Advances in Neural Information Processing Systems (2019)

# A deep-learning based network for quantitative analysis of Single Particle diffusion on compartmentalized surfaces

B. Vogler<sup>1</sup>, F. Reina<sup>1,2</sup>, A. Koerfer<sup>1,2</sup>, C. Eggeling<sup>1,2,3</sup>

<sup>1</sup> *Institute of applied Optics and Biophysics (IaOB), Philosophenweg 7, 07743 Jena*

<sup>2</sup> *Leibniz Institute of Photonic Technologies (Leibniz-IPHT), Albert-Einstein-Straße 9, 07745 Jena*

<sup>3</sup> *MRC Human Immunology Unit, Radcliffe Department of Medicine, University of Oxford*

.....

Diffusion of single lipids on cellular and model lipid membranes is a topic of continuous interest in modern Biophysics. New developments in Single Particle Tracking, brought forward by recent advancements in microscopy as MINFLUX and Interferometric Scattering Microscopy have unlocked the possibility of collecting extremely long ( $10^3$ - $10^4$  localizations) particle trajectories at kHz frame-rates in 2D and 3D.

One of the most accepted models to describe the cellular membrane is the picket-fence model, whereby the membrane, formed by the cellular cytoskeleton as a series of semi-permeable compartments, can transiently confine the diffusing molecules. The problem we tackle in this work consists of determining the diffusion modes underlying the molecule movement in this compartmentalized environment. We propose an analysis pathway based on a multi-layered analysis program which is capable of identifying the diffusion modes of the trajectories, and of extracting relevant physical parameters, such as the characteristic compartment size and the confinement strength felt by the tracked particle.

First of all, our model uses a neural network trained on a combination of criteria based on time sensitive topology and displacement angle distributions to differentiate flow- and super- from Brownian or anomalous diffusion.

Currently, we train the model to recognize trajectories and infer best fitting parameters to gain insights into the global scale of each track. We look for parameters such as the hopping probability, confinement size and local diffusion coefficient to threshold between different modes of anomalous diffusion. Following that we aim to classify the trajectories by their diffusion mode and characteristic physical parameters.

Bringing the analysis tool to experimental data gathered by MINFLUX or iSCAT systems will be tackled in the near future. By combining the analysis of several trajectories of particles moving inside a set field-of-view, we further aim at generating diffusion mode maps, highlighting areas of heterogeneous diffusion.

## List of Participants

- Enrique Abad, University of Extremadura
- Jessica Angulo, ICFO-The Institute of Photonic Sciences
- Aykut Argan, University of Gothenburg
- Harshith Bachimanchi, University of Gothenburg
- Joan Bertran, UVic-UCC
- Stefano Bo, Max Planck Institute for the Physics of Complex Systems
- Felix Campelo, ICFO-The Institute of Photonic Sciences
- Eric Cereceda-López, Universitat de Barcelona
- J. Alberto Conejero, IUMPA - Universitat Politècnica de València
- Marta Cullell-Dalmau, UVic-UCC
- Alexandre Dauphin, ICFO-The Institute of Photonic Sciences
- Daniel del Pozo Bueno, Universitat de Barcelona
- Gabriel Fernández Fernández, ICFO-The Institute of Photonic Sciences
- Nicolas Firbas, National University of Singapore
- Miguel Angel Garcia-March, IUMPA - Universitat Politècnica de València
- Maria Garcia-Parajo, ICFO-The Institute of Photonic Sciences
- Óscar Garibo i Orts, IUMPA/VRAIN - Universitat Politècnica de València
- Alessia Gentili, University College London
- Enric Gutiérrez Martínez, ICFO-The Institute of Photonic Sciences
- Ediz Herkert, ICFO-The Institute of Photonic Sciences
- Zihan Huang, School of Physics and Electronics, Hunan University
- H el ene Kabbech, Erasmus MC
- Sarah Keary, ICFO-The Institute of Photonic Sciences
- Christian Knapp, ICFO-The Institute of Photonic Sciences
- Agnes Koerfer, Friedrich Schiller University Jena
- Patrycja Kowalek, Wroc law University of Science and Technology
- Diego Krapf, Colorado State University, USA

- Lukas Lau, ICFO-The Institute of Photonic Sciences
- Maciej Lewenstein, ICFO-The Institute of Photonic Sciences
- Carlo Manzo, UVic-UCC
- Sergi Masó Orriols, UVic-UCC
- Montse Masoliver, UVic-UCC
- Jean-Baptiste Masson, Institut Pasteur
- Nicolas Mateos, ICFO-The Institute of Photonic Sciences
- Carlos Mejia-Monasterio, Technical University of Madrid
- Ralf Metzler, University of Potsdam
- Benjamin Midtvedt, University of Gothenburg
- Gorka Muñoz-Gil, Institute for Theoretical Physics, University of Innsbruck
- Jhoan Sebastian Ortiz Giron, UPF
- Raffaele Pastore, University of Naples Federico II
- Jesús Pineda, University of Gothenburg
- Borja Requena, ICFO-The Institute of Photonic Sciences
- Felix Ritort, Universitat de Barcelona
- Carolina Rodríguez-Gallo, Universitat de Barcelona
- Natalia Salvat, ICFO-The Institute of Photonic Sciences
- Henrik Seckler, University of Potsdam
- Martin Selin, University of Gothenburg
- Jelena Stanisavljevic, ICFO-The Institute of Photonic Sciences
- Janusz Szwabiński, Wrocław University of Science and Technology
- Pietro Tierno, Universitat de Barcelona
- Juan Andres Torreño Piña, ICFO-The Institute of Photonic Sciences
- Hippolyte Verdier, Institut Pasteur
- Ohad Vilks, Hebrew University of Jerusalem
- Bela Vogler, Institute of applied Optics and Biophysics (IaOB)
- Giorgio Volpe, University College London
- Giovanni Volpe, University of Gothenburg

## List of Online Participants

- Ashwin Balakrishnan, University of Würzburg
- Marc Botifoll, ICN2
- María Florencia Carusela, Univ. Nac. Gral Sarmiento
- Onur Inam, Gazi University
- Amy Moores, University of Oxford
- Farzaneh Nazari, Department of Physics, Yazd University
- Ihor Smal, Erasmus MC - University Medical Center Rotterdam
- Arturo Vesga, Centro Nacional de Biotecnología (CNB-CSIC)

