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Design and Computer Simulations of 2D MeX2 (Me=transition metal) Nanopores for DNA and Protein Detection and Analysis

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Three main results: (1) an analysis based on the current threshold to extract and characterize meaningful sensing events from ionic current time series computed from molecular dynamics. (2) A mechanism of translocation was established, for which side chains of each amino acid are oriented parallel to the electric field when they are translocating through the pore and perpendicular otherwise. (3) A new procedure based on the permutation entropy algorithm was detailed
to identify protein sequence motifs related to ionic current drop speed.

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ACHIEVEMENTS IN 2020

- Maria Daniela Pérez Barrios defended her thesis at the Université de Bourgogne in Dijon the **7 January 2020**. The PhD manuscript was approved and published (Ref. 1).

- During the 6 months extension (January to July 2020), we pursued the simulations of protein translocation and protein sequencing using MoS_2 2-D materials using molecular dynamics simulations (MD).
  We are the first to apply the so-called permutation entropy analysis to the ionic current time series in a nanopore 2D membrane. This approach was initiated with a master student (Aniket Rath) committed on the grant in 2019. In particular, we analyzed the current fluctuations simulated by MD for the translocation of short (6 amino acids) peptides which are motifs of alpha-synuclein, a key protein in Parkinson Disease.
  We published this work in Nanoscale in October 2020 (Ref. 2).
  Three main results were brought by this study.
  - First, we presented an analysis based on the current threshold to extract and characterize meaningful sensing events from ionic current time series computed from MD.
  - Second, a mechanism of translocation was established, for which side chains of each amino acid are oriented parallel to the electric field when they are translocating through the pore and perpendicular otherwise.
  - Third, a new procedure based on the permutation entropy (PE) algorithm was detailed to identify protein sequence motifs related to ionic current drop speed. PE is a technique used to quantify the complexity of a given time series and it allows the detection of regular patterns. Here, PE patterns were associated with protein sequence motifs composed of 1, 2 or 3 amino acids. Finally, we demonstrated that this very promising procedure allows the detection of biological mutations and could be tested experimentally, despite the fact that reconstructing the sequence information remains unachievable at this time.

- Simulations of model (TAT) peptides were continued. The collection of TAT translocation events simulated by MD will be compared to conductance data when available.

PUBLICATIONS IN 2020

1. M. D. Barrios-Pérez, « Design and Computer Simulations of 2D MeX2 (Me=transition metal) Nanopores for DNA and Protein Detection and Analysis", PhD thesis (2020)

2. Nanopore sensing of single-biomolecules: a new procedure to identify protein sequence motifs from molecular dynamics, Adrien Nicolaï, Aniket Rath, Patrice Delarue and Patrick Senet, Nanoscale,12: 22743 (2020)

Remark: due to COVID-19, we were not allowed to attend conferences in 2020.

PUBLICATIONS (2017-2020)

1. M. D. Barrios-Pérez, « Design and Computer Simulations of 2D MeX2 (Me=transition metal) Nanopores for DNA and Protein Detection and Analysis", PhD thesis (2020)

2. Nanopore sensing of single-biomolecules: a new procedure to identify protein sequence motifs from molecular dynamics, Adrien Nicolaï, Aniket Rath, Patrice Delarue and Patrick Senet, Nanoscale,12: 22743 (2020)

3. Molecular Dynamics Investigation of Poly-Lysine Peptide Translocation through MoS2 Nanopores, A. Nicolai, M. D. Barrios-Perez, P. Delarue, V. Meunier, M. Drndić, P. Senet, The Journal of Physical Chemistry B 123, 2342-2353 (2019)

4. Improved model of ionic transport in 2-D MoS2 membranes with sub-5 nm pores, M. D. Barrios-Pérez, A. Nicolai, P. Delarue, V. Meunier, M. Drndić, P. Senet, Applied Physics Letters 114, 023107 (2019)

5. Angstrom-Size Defect Creation and Ionic Transport through Pores in Single-Layer MoS2, J. Priyanka Thiruraman, K. Fujisawa, G. Danda, P. M. Das, T. Zhang, A. Bolotsky, N. Perea-López, A. Nicolaï, P. Senet, M. Terrones, M. Drndić, Nano Letters 18, 1651–1659 (2018)

6. Computational investigation of the ionic conductance through molybdenum disulfide (MoS2) nanopores, Maria Daniela Barrios Perez, Patrick Senet, Vincent Meunier, Adrien Nicolai, WSEAS Transactions on Circuits and Systems, 16, 35-44 (2017)

COMMUNICATIONS (2017-2020)

1. "Computational Investigation of MoS2 Solid-State Nanopores for Peptide Translocation". M. D. Barrios, A. Nicolaï , P. Delarue, V. Meunier, M. Drndic,
P. Senet, JED 2019: Carnot-Pasteur Doctoral School days, Dijon, 11-12/06/2019 (France) (talk)

2. "Identifying Patterns in Time Series Data", A. Nicolaï, A. Rath, P. Delarue, P. Senet, International Conference on Advanced Nanotechnology and Nanomaterials, Crowne Plaza Dubai -Deira, 20-21/11/2019 – UAE (talk)

3. "Improved Model of Ionic Conductivity in 2D MoS_2 nanoporous membranes", M. D. Barrios Pérez, A. Nicolaï, P. Delarue, V. Meunier, M. Drndic, P. Senet, SF Nano, C Nano, joint meeting 2019, Dijon, 10-12/12/2019 (France) (Poster)

4. "Identifying Patterns in Time Series Data: Application to Biological Peptide Translocation through single-layer MoS2 Nanopores", A. Nicolaï, M. D. Barrios Pérez, A. Guzzo, P. Delarue & P. Senet, SF Nano, C Nano, joint meeting 2019, Dijon, 10-12/12/2019 (France) (Poster)

5. "Monitoring the translocation of single polypeptides through MoS_2 nanopores from ionic current fluctuations, lessons from all-atom molecular dynamics simulations", P. Senet, Maria Daniela Barrios Perez, Patrice Delarue, Vincent Meunier, Adrien Nicolaï, GrapheneforUS, New York (USA). 22-23/02/2018

6. "Modeling of the ionic conductivity and biomolecule translocation through sub-5 nm MoS_2 nanopores using all-atom MD simulations", M. D. Barrios, A. Nicolaï, P. Delarue, V. Meunier, M. Drndic, P. Senet, Carnot-Pasteur PhD School days ,12/06/2018, Besançon (France).

7. "Computational investigation of MoS_2 solid-state nanopores for peptide translocation", M. D. Barrios, A. Nicolaï, P. Delarue, V. Meunier, M. Drndic, P. Senet, Fall Symposium RPI, 07/12/2018, Troy (USA).

8. "Modeling the ionic conductivity and biomolecule translocation through solid-state MoS_2 nanopores", M. D. Barrios, P. Delarue, V. Meunier, M. Drndic, P. Senet, A. Nicolaï, 2018 MRS Fall Meeting, 25-30/11/2018, Boston (USA)

9. "Computational investigation of the translocation of single polypeptide through MoS2 nanopores from ionic conductance dynamics", Maria Daniela Barrios Perez, Patrick Senet, Vincent Meunier, Adrien Nicolai¨, Deciphering complex energy landscape and kinetic network from single molecules to cells : a new challenge to make theories meet experiments, Dijon (France), 3-8 September 2017

10. "Computational investigation of the ionic conductance and peptide translocation through nanopores of MoS2 membranes", Maria Daniela Barrios Perez, Adrien Nicolai¨, Patrice Delarue, Vincent Meunier, Patrick Senet , JED 2017: Carnot-Pasteur PhD School days, Université de Bourgogne, Dijon, France. 18-19 May 2017.

11. "Computational investigation of the ionic conductance and peptide translocation through nanopores of MoS2 membranes", Maria Daniela Barrios Perez, Adrien Nicolai¨, Patrice Delarue, Vincent Meunier, Patrick Senet , XI RCTGE Conference (Journées de Chimie Théorique du Grand Est). Université de Franche-Comté, Besançon, France. 8-9 June 2017.

12. "Computational investigation of the performances of MoS2 nanopores for biological peptide sequencing", Maria Daniela Barrios Perez, Patrick Senet, Vincent Meunier, Adrien Nicolai¨, XXVI International Materials Research Congress, Cancun Mexico. Symposium A. Nanoscience and Nanotechnology. Session A.6 Micro-Nanofabrication of Biomedical Devices—BioMEMS-NEMS, Lab-on-a- Chip and Organ-on-a-Chip, 20-25 August 2017

13. "Computational investigation of the ionic conductance and peptide translocation through nanopores of MoS2 membranes", Maria Daniela Barrios Perez, Adrien Nicolai¨, Patrice Delarue,Vincent Meunier, Patrick Senet, HeteroNanoCarb17 Conference (Advances and applications in carbon related nanomaterials: From pure to doped structures including heteroatom layers). Centro de Ciencias de Benasque Pedro Pascual. Benasque, Spain, 11-15 December 2017

14. "Computational investigation of the ionic conductance and peptide translocation through nanopores of MoS2 membranes", Maria Daniela Barrios Perez, Adrien Nicolai¨, Patrice Delarue, Vincent Meunier, Patrick Senet , 20th GGMM Conference (Groupe de Graphisme et Modélisation Moléculaire). Université de Reims Champagne-Ardenne, Reims, France. 9-11 May 2017.