# Post-Doc Position in Physical-Chemistry / Biophysics

## Single Pore Sensing for miRNA Screening and Sequencing

The principle of Nucleic Acids (NA) sequencing by the “single pore sensing” method is shown on Figure 1. An external imposed electric field (blue arrows on Fig.1a) forces a single NA strand through a transmembrane transport protein (in red) *i.e.* a natural nanopore open in a membrane (in green). The real-time NA sequencing method consists in measuring the time dependence of the ionic current of the buffer salt (typically KCl) going through the nanopore. During the translocation process, the related signal is controlled by the sequential transient interactions of the NA bases (T, C, G, A) with the interior channel of the transmembrane protein. The duration of the resulting ionic current blockades and the associated magnitude of the current pulses (Fig.1b), the so-called Electrical Resistive Pulses, are a direct coding of the succession of bases going through the pore: the NA sequence. An artist animated view of this process can be found in reference [1].

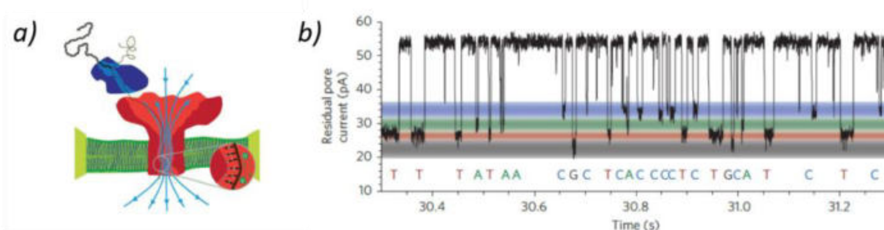


***Figure 1.*** *“Single pore sensing” based NA sequencing trough a biological nanopore. From F. Montel, médecine/sciences, 34, 161 (2018).*

miRNA (RiboNucleic Acid) are short noncoding RNA (≃20 nucleotides) regulating gene expression. As their concentration level is correlated with various pathologies including cancers, they are identified as potential biomarkers. In a regular single pore sensing technique, the translocation speed being of the order of 400 bases per seconds, sequences as short as the miRNA ones cannot be detected. As a consequence, effective methods to identify miRNA in the blood stream remain scarce and biologists face a need for sufficiently selective and sensitive detection methods.

In this framework, the present project addresses the screening then sequencing of miRNA by the use of an original single pore sensing strategy *i)* on a synthetic porous membrane *ii)* filled with a specific electrolyte, good solvent of RNA, and to improve sensitivity, *iii)* showing no conduction noise under confinement. We have a dual objective: first to achieve miRNA screening (see an example in *[2])* using a single pore synthetic membrane. Then we will evaluate the miRNA sequencing potential through a α-hemolysin (HL), a canonic transport protein, functionalized membrane.

Altogether, this study proposes a paradigm change in the fast-growing field of NA screening/sequencing and targets potential technological outcomes. The project is funded by the call “Instrumentation” of the CEA “Programme Transverse de Compétences” and by the CEA “Focus Biomarqueurs”. The employer will be CEA. The position duration is 12 months renewable once.

The Home Laboratory will be Laboratoire Léon Brillouin (UMR 12 CEA-CNRS, Saclay, France) but the work will be developed at IRIG/SyMMES at CEA Grenoble (France) with travels to Saclay and Marseille (France). Please send a letter of motivation and CV at Jean-Marc.Zanotti@cea.fr.

**Keywords:** Nucleic Acid, Single Pore Sensing, Biophysics, Biochemistry, Membrane, Polymer Synthesis, Electrolyte Conductivity, Nanometric Confinement, Microscopy (AFM, SEM, TEM), Focus Ion Beam, NMR, SANS/SAXS, Neutron Spectroscopy, Tip Enhanced Raman Scattering, Magnetic Tweezers.

*[1]* https://nanoporetech.com/support/how-it-works

*[2] Discrimination of α-Thrombin and γ-Thrombin Using Aptamer-Functionalized Nanopore Sensing, L. Reynaud, L. A. Bouchet-Spinelli, J.-M. Janot, A. Buhot, S. Balme and C. Raillon, Anal. Chem. 93:7889–7897 (2021).*