

Synthesis of Digital Polymers for Nanopore Sequencing

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Mots-clés : sequence-controlled polymers, nanopore sequencing, solid-phase synthesis

Résumé :

Since the emergence of life, biological macromolecules like DNA and RNA have been storing the genetic information of all living organisms. Recently, scientists have shown that data can also be stored in sequence-defined synthetic polymers.^[1] In particular, our group has demonstrated the efficiency of this concept by synthesizing sequence-defined poly(phosphodiester)s through stepwise automated phosphoramidite chemistry.^[2] These macromolecules are made up of two, or more, monomer alphabets (such as 0 and 1) enabling digital encryption.

However, so far, these polymers can only be decoded by tandem mass spectrometry.^[3] Although this method is quite effective, it requires large instrument setups. Therefore, it is essential to explore alternative sequencing methods for digital polymers such as nanopores. This advanced technology, typically used for accurately reading DNA sequences, works by detecting distinct ionic current signatures produced by different monomers as they pass through a nanopore (Fig. 1.a).^{[4],[5]} For this reason, a new alphabet of monomers was synthesized to improve current fluctuations to be decoded more efficiently (Fig. 1.b). Compared to conventional 0 and 1 monomers, these new monomers of different molecular properties such as the length of the repeating unit, rigidity of the main chain, and the bulkiness of the side chain influence the interactions between the polymers in solution and the pore.^[6] As a consequence, distinctive ionic current signal can be induced and the time of the translocation of the polymer can be increased for nanopore sequencing.

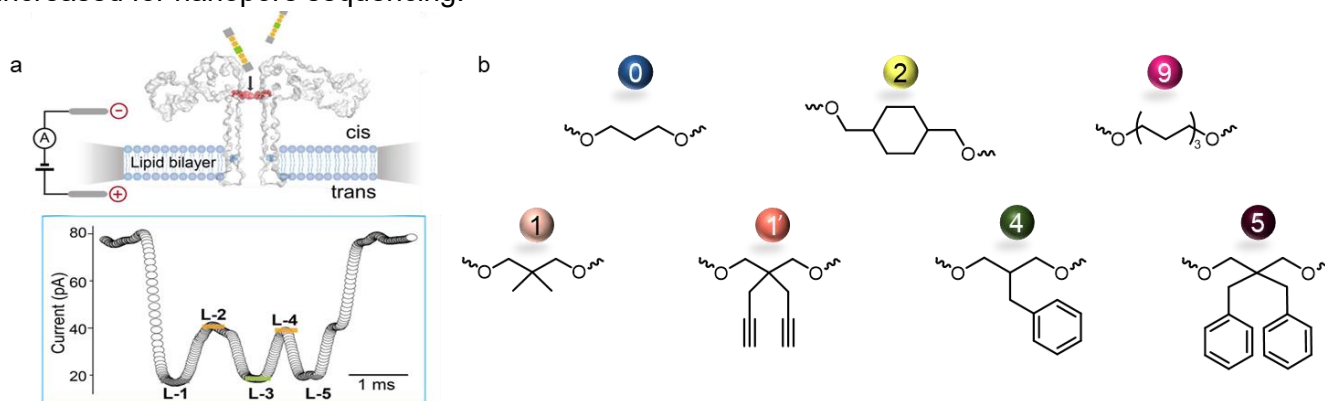


Figure 1 – (a) Illustration of single-channel recording setup using an aerolysin pore and raw current trace measurement of a translocating synthetic polymer. (b) The alphabet of monomers synthesized and used in this work.

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