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Mini Review



# Single-Molecule Studies of Small Molecule Drugs through Nanopore Detection

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## Introduction

During the last decades, nanopore single-molecule analysis has shown great potential in detection of DNA [1-3], RNA [4], proteins [5-8], polymers [9], organic molecules [10-11], and chemical reactions [12-13], and has been further extended to high-throughput nucleic acid sequencing. The detection of drug interactions [14] is crucial to evaluate the effect and safety of drugs, and it is also an indispensable part in the process of drug development and clinic treatment [15]. Over the past few years, the nanopore worked as a new platform for the discovery of drug interactions. Nanopore sensor, with the advantages of simple operation, speed and portability, can allow single molecule to pass through.

## Discussion

a) Direct detection of small molecule drugs using nanopore technology

Applied to nanopore, Li-Qun Gu and Hagan Bayley were first to propose stochastic sensing to detect drug molecules, including Promethazine and Imipramine [16]. The paper shows that stochastic sensing of drug molecules can be procured from a-haemolysin by equipping the channel with an internal, non-covalently molecule adapter which mediates channel blocking by the drug molecule. Through hybrid a-hemolysin protein pore and the channel blocking characteristics, another interesting paper was reported by Tudor Luchian [17]. This work can distinguish between antibiotic molecules of different size and charge, belonging to the b-lactam family, including ampicillin, amoxicillin and azlocillin.

b) Detection of nucleic acid-small molecule interactions using nanopore technology

Most studies of interactions between nucleic acid and small molecules has accomplished by monitoring changes in nanopore current patterns of nucleic acids or binding with drug molecules. Yao et al. performed nanopore-based detection of DNA-doxorubicin (Dox) drug interactions using a-HL pores [18]. The DNA-Dox adduct showed a distinctive electronic signal pattern compared to original DNA. In contrast to the hairpin DNA event, DNA-Dox adduct generated prolonged events with a 10-fold longer duration. This result suggests that the nanopore sensor can be used to examine interactions between anticancer drug and DNA, and can be applied to functional analysis and Pharmacological analysis. Recently, our research group investigated DNA shearing action caused by bleomycin, accompanied by detection of bleomycin with high selectivity and ultra-low detection limit [19]. A dumbbell-based DNA probe based on the nanopore current signal was designed, which can produce blockage current signals. however, the addition

of BLM-Fe (II)would make the dumbbell DNA probe undergo an irreversible strand break, resulting and releasing the short-chain oligonucleotide fragment, which lead to the disappearance of the blockage event. Soon afterwards, a new method related to DNA oxaliplatin adduct was proposed [20], which enables real-time monitoring of DNA oxaliplatin condensation process. Specifically, signals with specific current characteristics are observed during this process. Typical high-frequency signals were obtained by recording the resulting designed DNA sequences. Furthermore, the generation of these signals was confirmed to be independent of the homologous adducts. Suggesting that DNA oxaliplatin adducts can serve as potential sensors to detect oxaliplatin lesions and multiple types of molecules.

## Conclusions

Taken together, nanopore could be a promising platform for the ultrasensitive, label-free and single-molecule analysis for drug interactions and screening research. Through nanopore technology, we can accurately and efficiently evaluate drug interactions, providing an important reference for drug development and disease diagnosis and treatment. There are still some challenges and urgent problems to be solved in the application of nanopore technology in drug interaction detection. For example, the preparation method and stability of nanopore need to be further improved to improve the accuracy and reproducibility of detection. Meanwhile, the application of nanopore technology in large-scale screening of drug interactions needs to be further explored. Finally, we suggest that single-molecule-based nanopore applications would be useful for high-throughput screening in drug discovery. In future, nanopore technology open up a new path for single-molecule-level drug discovery, which will provide guidance for drug discovery and pharmacological research.

## References


1. D Wendell, P Jing, J Geng, V Subramaniam, TJ Lee, et al. (2009) Translocation of double-stranded DNA through membrane-adapted phi29 motor protein nanopores. Nat Nanotechnol 4(11): 765-772.
2. IM Derrington, TZ Butler, MD Collins, E Manrao, M Pavlenok, et al. (2010) Nanopore DNA sequencing with MspA. Proc Natl Acad Sci USA 107(37): 16060-16065.
3. C Wloka, NL Mutter, M Soskine, G Maglia (2016) Alpha-Helical Fragaceatoxin C Nanopore Engineered for Double-Stranded and Single-Stranded Nucleic Acid Analysis. Angew Chem Int Ed Engl 55(40): 12494-12498.
4. Y Wang, X Guan, S Zhang, Y Liu, S Wang, et al. (2021) Structural-profiling of low molecular weight RNAs by nanopore trapping/translocation using Mycobacterium smegmatis porin A. Nat Commun 12(1): 3368.
5. S Zernia, N J van der Heide, NS Galenkamp, G Gouridis, G Maglia (2020) Current Blockades of Proteins inside Nanopores for Real-Time Metabolome Analysis. ACS Nano 14(2): 2296-2307.
6. H Brinkerhoff, ASW Kang, J Liu, A Aksimentiev, C Dekker (2021) Multiple rereads of single proteins at single-amino acid resolution using nanopores. Science 374(6574): 1509-1513.
7. S Yan, J Zhang, Y Wang, W Guo, S Zhang, et al. (2021) Single Molecule Ratcheting Motion of Peptides in a Mycobacterium smegmatis Porin A (MspA) Nanopore. Nano Lett 21(15): 6703-6710.
8. FLR Lucas, RCA Versloot, L Yakovlieva, MTC Walvoort, G Maglia (2021) Protein identification by nanopore peptide profiling. Nat Commun 12(1): 5795.
9. M Boukhet, NF Konig, AA Ouahabi, G Baaken, JF Lutz, et al. (2017) Translocation of Precision Polymers through Biological Nanopores. Macromol Rapid Commun 38(24): 1700680.
10. HC Wu, H Bayley (2008) Single-molecule detection of nitrogen mustards by covalent reaction within a protein nanopore. J Am Chem Soc 130(21): 6813-6819.
11. T Diederichs, K Ahmad, JR Burns, QH Nguyen, ZS Siwy (2021) Principles of Small-Molecule Transport through Synthetic Nanopores. ACS nano 15(10): 16194-16206.
12. J Cao, S Zhang, J Zhang, S Wang, W Jia, et al. (2021) A Single-Molecule Observation of Dichloroaurate(I) Binding to an Engineered Mycobacterium smegmatis porin A (MspA) Nanopore. Anal Chem 93(3): 1529-1536.
13. J Cao, W Jia, J Zhang, X Xu, S Yan, et al. (2019) Giant single molecule chemistry events observed from a tetrachloroaurate(III) embedded Mycobacterium smegmatis porin A nanopore. Nat Commun 10(1): 5668.
14. R Stahlmann, H Lode (2000) Chapter 14 – Safety Overview: Toxicity, Adverse Effects, and Drug Interactions. The quinolones Pp. 397-453.
15. P Prabhakar, AM Kayastha (1994) Mechanism of DNA-drug interactions. Appl Biochem Biotechnol 47(1): 39-55.
16. LQ Gu, O Braha, S Conlan (1999) Stochastic sensing of organic analytes by a pore-forming protein containing a molecular adapter. Nature 398(6729): 686-690.
17. A Asandei, A Apetrei, T Luchian (2011) Uni-molecular detection and quantification of selected β-lactam antibiotics with a hybrid α-hemolysin protein pore. J Mol Recognit 24(2): 199-207.
18. F Yao, J Duan, Y Wang, Y Zhang, Y Guo, et al. (2015) Nanopore Single-Molecule Analysis of DNA–Doxorubicin Interactions. Anal Chem 87(1): 338-342.
19. T Li, XX Li, XY Li, L Yang, HL Wang (2021) Nanopore single-molecule detection of bleomycin via dumbbell DNA scission. Microchem J 170(7): 106738.
20. T Li, W Lu, H Tian,Y Cao, QQ He, et al. (2023) Identification and Characterization of DNA–Oxaliplatin Adducts through α-hemolysin Nanopores. Anal Chem 95(30): 11201-11210.