A mini current amplifier and digitizer for nanopore based DNA and Protein seqeuncing applications

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Abstract—

Nanopore technology offers exciting possibilities for DNA and protein analysis. Recent years have seen a surge in research utilizing synthetic and biological nanopores for DNA and protein sequencing. However, conventional amplifiers used for these applications, like the bulky and expensive Axopatch 200B, hinder widespread adoption. This work presents the development of a low-cost, portable amplifier and signal digitizer. This innovation aims to accelerate research in nanopore-based biomolecule sensing, democratizing access and paving the way for advancements in healthcare research.

I. Introduction

Tiny holes called nanopores, ranging from 1-100 nanometers in size, are emerging as a powerful tool for single-molecule DNA and protein sequencing, making them a popular choice in next-generation sequencing (NGS) techniques. Commercial nanopore sequencers, primarily for DNA sequencing, already exist (https://nanoporetech.com/). However, these biological pores lack stability in extreme temperatures and pH conditions. In contrast, synthetic nanopores, like those drilled into silicon nitride, offer advantages due to their mechanical and chemical robustness, simplifying integration with electronic measurement systems[1].

Research in nanopore-based single-molecule sequencing, particularly in developing countries, is hampered by the difficulty of obtaining sensitive current amplifiers and digitizers for ionic current measurements. Existing systems like the Axopatch 200B or AM2400 are typically bulky, expensive, and complex. Limited technical support infrastructure worldwide further extends repair wait times. The portability of conventional amplifiers also presents a challenge for achieving the healthcare sector's goal of sequencing anywhere. To accelerate research in this area, developing miniaturized versions of current amplifiers and digitizers is crucial

II. Related Work

Nanopore sequencing relies on mapping picoampere (pA) range ionic current signals generated as biomolecules traverse a tiny hole less than 100 nanometers in size[2]. This highly sensitive detection requires meticulous control, as even power line noise or electromagnetic interference from other sources can disrupt experiments, leading to unusable/very noisy data. Researchers typically use the Axopatch 200B amplifier or similar systems (e.g., AM 2400) with a minimum 100 kHz sampling frequency alongside a digitizer to measure the ionic current. A typical experimental setup is shown in Figure 1.

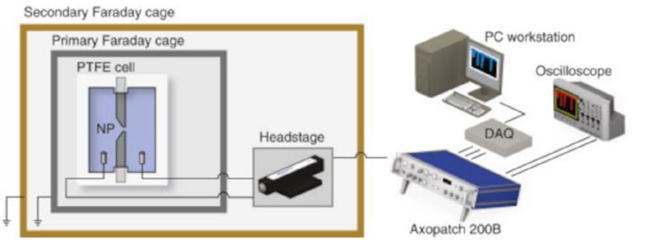

Figure 1: Schematic diagram of typical nanopore sensing experiment[3]

III. Idea for Prototype Development

The electronic part of this measurement system, as shown in figure 1 include head stage, amplifier, and Digital to analog converter. Theas are heavy, occupy large space and complex. An image of amplifier and digitiser is shown in figure 2. As part of this summer school, I would like to develop a simpler and mini-version of the amplifiers and digitiser used for nanopore sensing experiments.

Figure 2: Top : Digitiser, Mid: Axopatch 200B amplifier, Bottom: A faraday cage for sensitive measurements.

IV. Responsible innovation

This innovation promises to significantly democratize and accelerate nanopore research by providing a miniaturized amplifier and digitizer. Its cost-effective design will not only free up valuable lab space but also minimize wait times associated with bulky instruments requiring repairs. The system's simplicity and potential open-source design will foster collaboration and expedite repairs within the research community. Furthermore, its educational value can be harnessed by integrating it with existing electronics curriculums and nanopore research courses[4]. The miniaturized design also contributes to a more sustainable research environment. Overall, the development of this prototype has the potential to become a sustainable champion for advancing nanopore research.

V. Author bio(s) / experiences

Muhammad Sajeer P, is a joint PhD scholar between University of Manchester and Indian Institute of Science, Bangalore. Sajeer's PhD is involved in advancing the field of nanopore-based sensors for single molecular protein sequencing—a groundbreaking technology with the potential to revolutionize healthcare and biotechnology. Holding the position of Senior Research Fellow at the Centre for Nano Science and Engineering, Sajeer applies expertise in micro and nanofabrication, simulation, and programming to design and test various nanodevices and systems.

Google Scholar: https://scholar.google.com/citations?user=MfhfGS0AAAAJ&hl=en&oi=ao

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VI. Refernces

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