

# Integration of Long-Read Whole Genome Sequencing in Graduate Curriculum of Diagnostic Genetics and Genomics

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## Purpose of the Project

- Two tracks in Diagnostic Genetics and Genomics (DGG) master's program at SHP: Molecular Genetics and Genomics (MGG) and Cytogenetics and Cytogenomics (CGG)
- Overarching goal of DGG-MGG: to train technologists/scientists with expertise in high capacity data generation (wet lab) and bioinformatic/computational analyses (dry lab)
- To serve one of the institution's core values, *Discovery*, we strive to introduce cutting-edge technologies to maintain our program at the forefront of graduate education.
- The current project aims to incorporate the innovative Nanopore sequencing technology [1] into our curriculum.

## Rationale for Integration into Curriculum

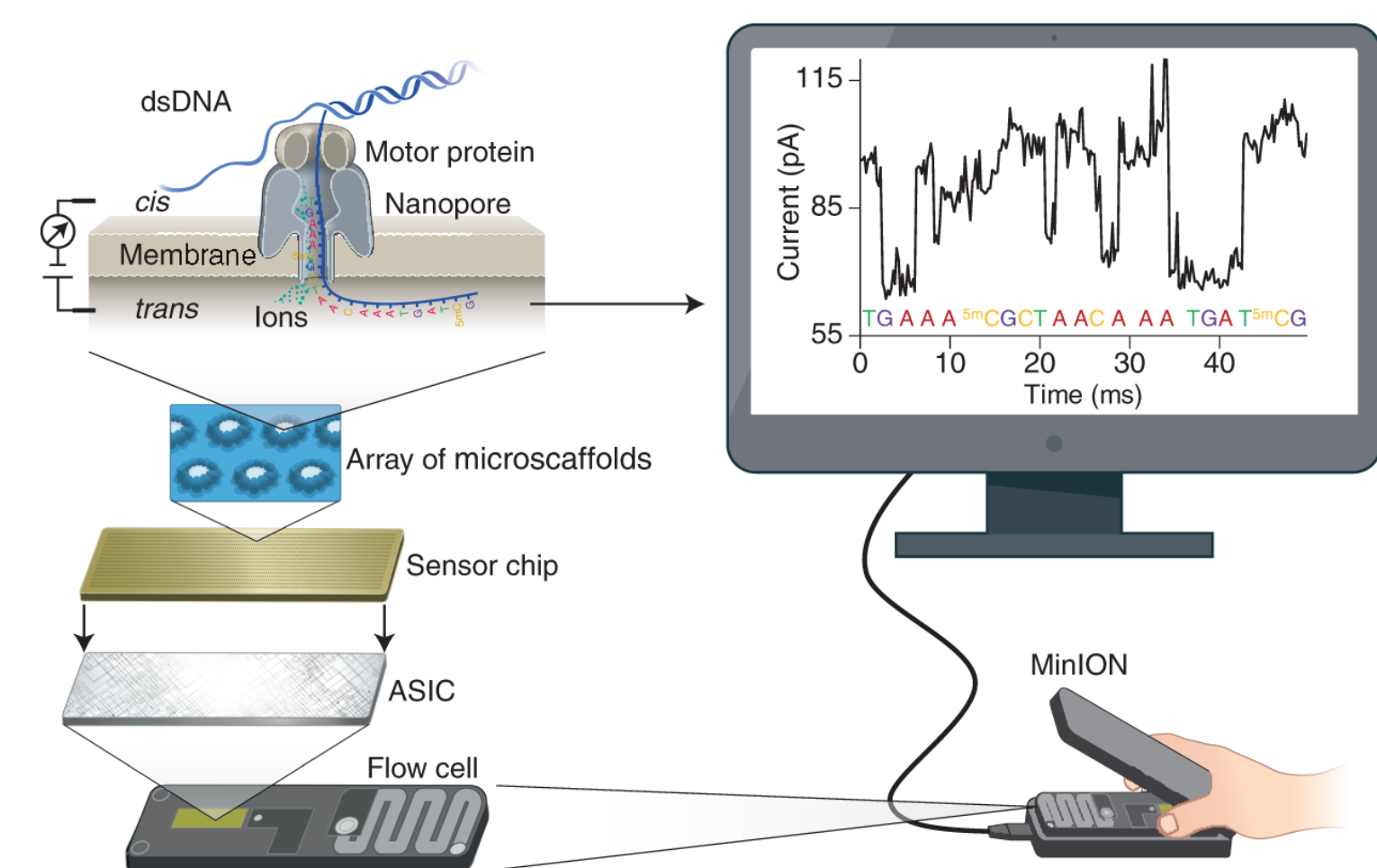
- The existing MGG core curriculum deploys first-generation sequencing (Sanger method) and next-generation sequencing (NGS, Illumina platform) for the first-year students' training.
- Third-generation sequencing (TGS) offers high speed and long sequence reads and is increasingly being used in genomic studies [2] as well as pathogen surveillance [3].
- Benefits of including the emerging TGS technology in the core curriculum: (a) expand our sequencing platforms; (b) supplement and help fill the gaps in genome assemblies made from short reads generated by NGS
- MinION (launched in 2015), along with the associated MinIT (2018), is a portable TGS device from Oxford Nanopore Technologies (ONT) that is readily meeting our teaching need.

## Educational Goal and Performance Objectives

- Goal:** Students in the MGG teaching lab will demonstrate an understanding of the principle of Nanopore sequencing to be applied in hands-on practice by generating and analyzing bacterial whole genome sequencing (WGS) data and presenting results.
- Objectives:**
  1. Explain the concept of Nanopore sequencing and elaborate how it works (*intellectual skill*)
  2. Prepare libraries for WGS using MinION and perform sequencing (*psychomotor skill*)
  3. Analyze sequencing data using bioinformatic tools (*intellectual & psychomotor*)
  4. Summarize data from both wet and dry labs and present results in groups (*cognitive & social*)

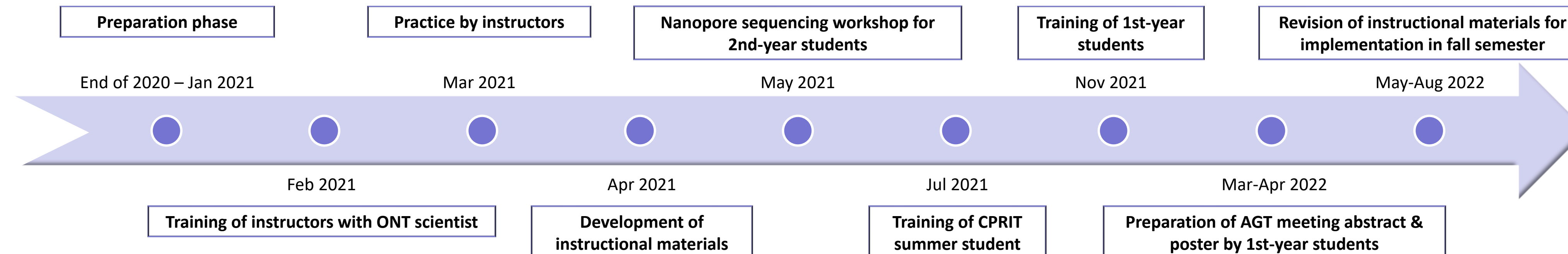
## Background of Nanopore Sequencing

- Concept and mechanism
- Video <https://nanoporetech.com/applications/dna-nanopore-sequencing>



**Figure 1. Principle of Nanopore sequencing (only MinION device shown) [1]**

- Advantages over Illumina-based NGS platform [4]
  - a. Long read (> 5k bp), high speed (1 bp/ns), and real-time base calling
  - b. Fluorescent tag-free detection of bases
  - c. Less sensitive to temperature throughout sequencing; reliable outcome
  - d. Shortened hands-on time



**Figure 2. Project timeline**

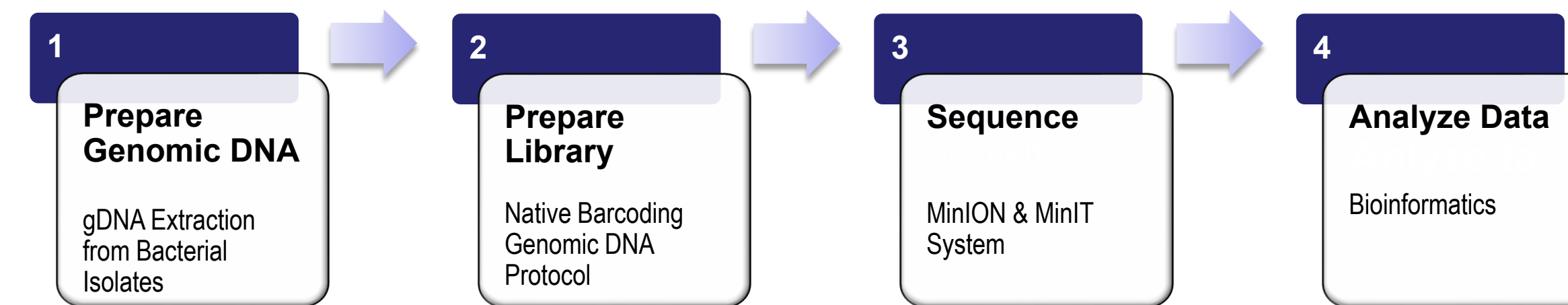
## Instructional Strategies and Materials

The design of instruction is based on the Constructivist learning theory using active learning approaches [5,6]. Students are ensured to apply their new learning through concept application. The focus of instructional activities is on learner engagement, group work (collaboration), and critical thinking skills.

- Pre-instruction assignment
- Lecture before wet lab
- Hands-on experiment
- Individual & collaborative lab notes
- Bioinformatic analysis
- Student presentations

## Implementation

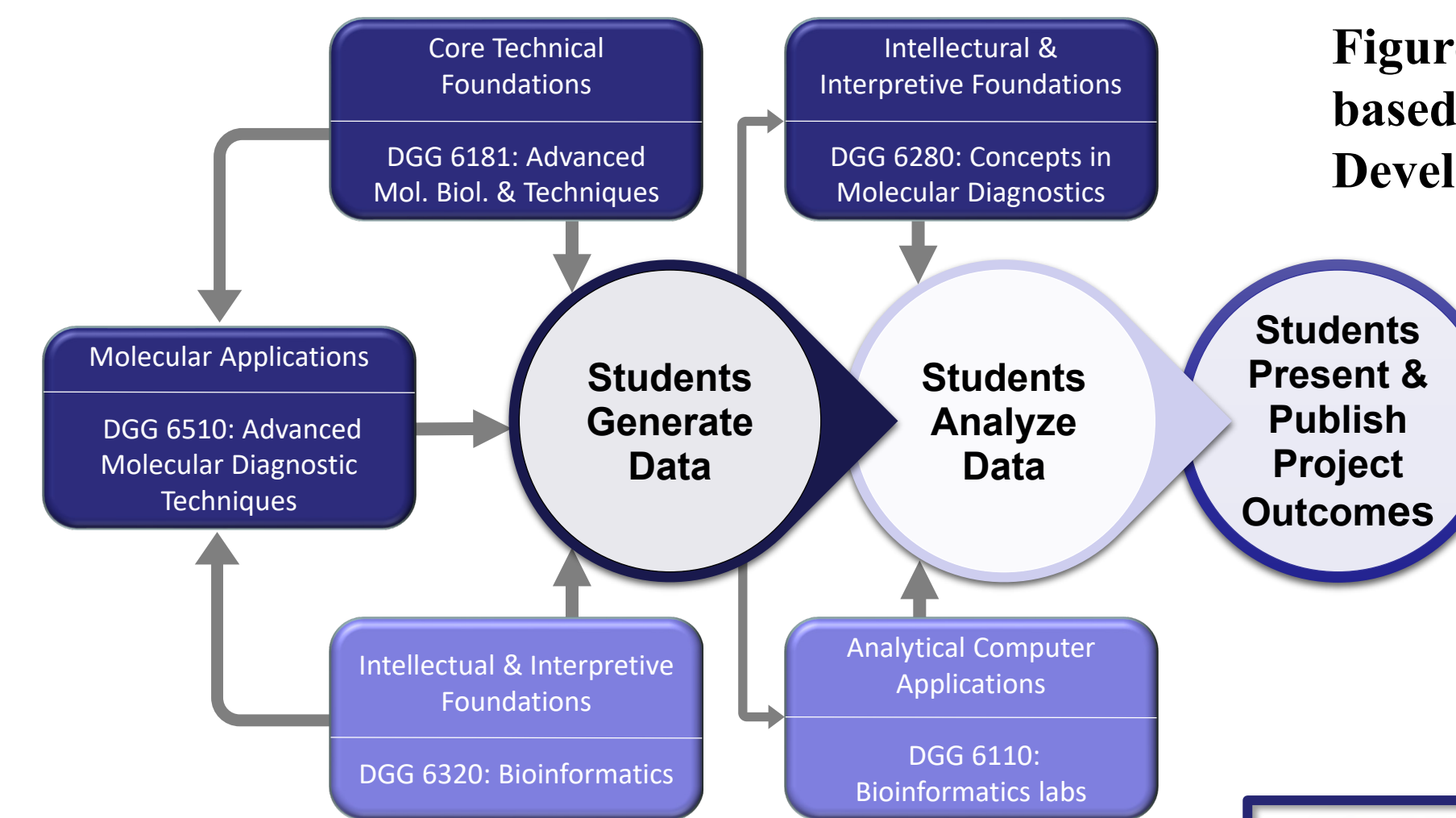
- Timeline of project phases (Fig. 2): staff training, instructional design, single/group student trainings
- Program coordination among DGG courses (Fig. 3): scheduling in alignment with Nanopore sequencing need
- Lecture (Fig. 4) followed by wet lab (Fig. 5, Fig. 6, and [video in PDF Attachments](#)) and dry lab (Fig. 7)



**Figure 5. Nanopore sequencing lab workflow**



**Figure 6. Students perform Nanopore sequencing on MinION**



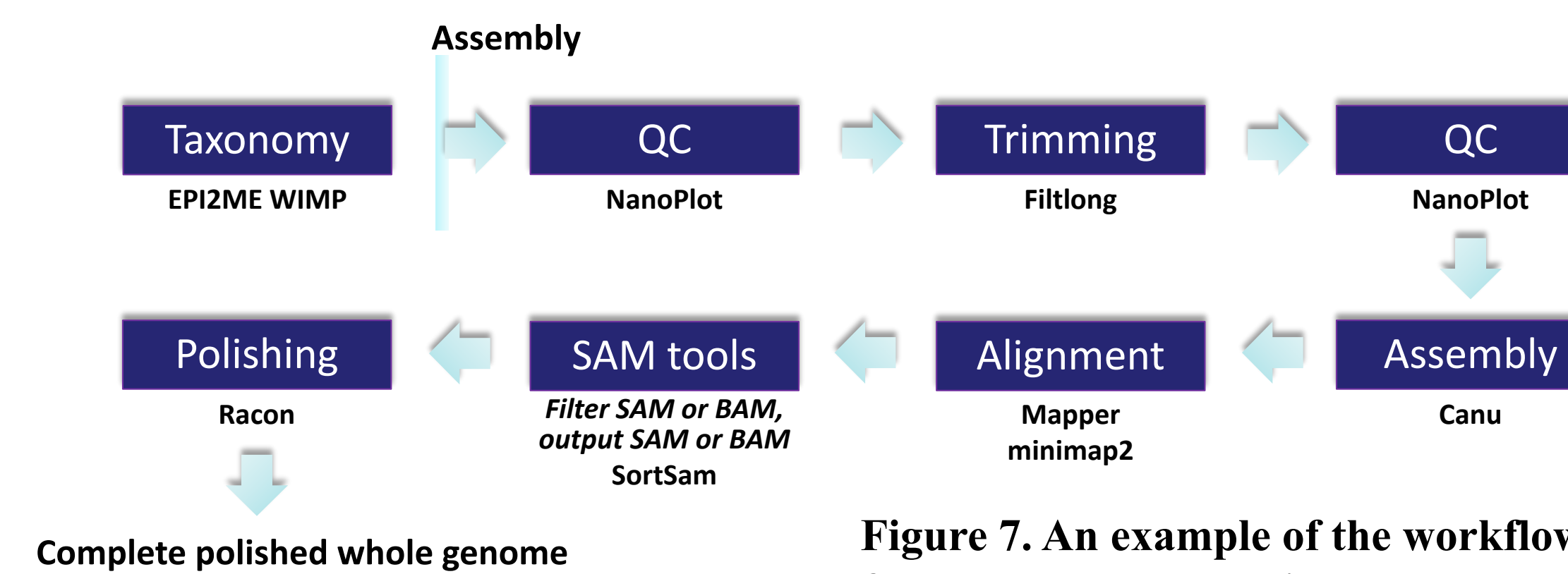
**Figure 3. An overview of the Project-based Integrated Core Curriculum Development Initiative (PICCDIn).**

Five core courses are taught in the entering fall semester. The first eight weeks are devoted to laying down solid foundations in theories, techniques and interpretive skills. In the next eight weeks, students perform a supervised project geared toward real-time, real-world problem solving using cutting-edge genomic technology.

## Outline

1. The Third-Generation Sequencing
2. Nanopore Sequencing Platform
3. Devices: Focusing on MinION
4. Control Software: MinKNOW
5. MinION Flow Cell
6. Library Preparation
7. Monitoring of MinION sequencing
8. Nanopore Sequencing Data Analysis
9. Applications of Nanopore Sequencing

**Figure 4. An outline of Nanopore sequencing lecture**



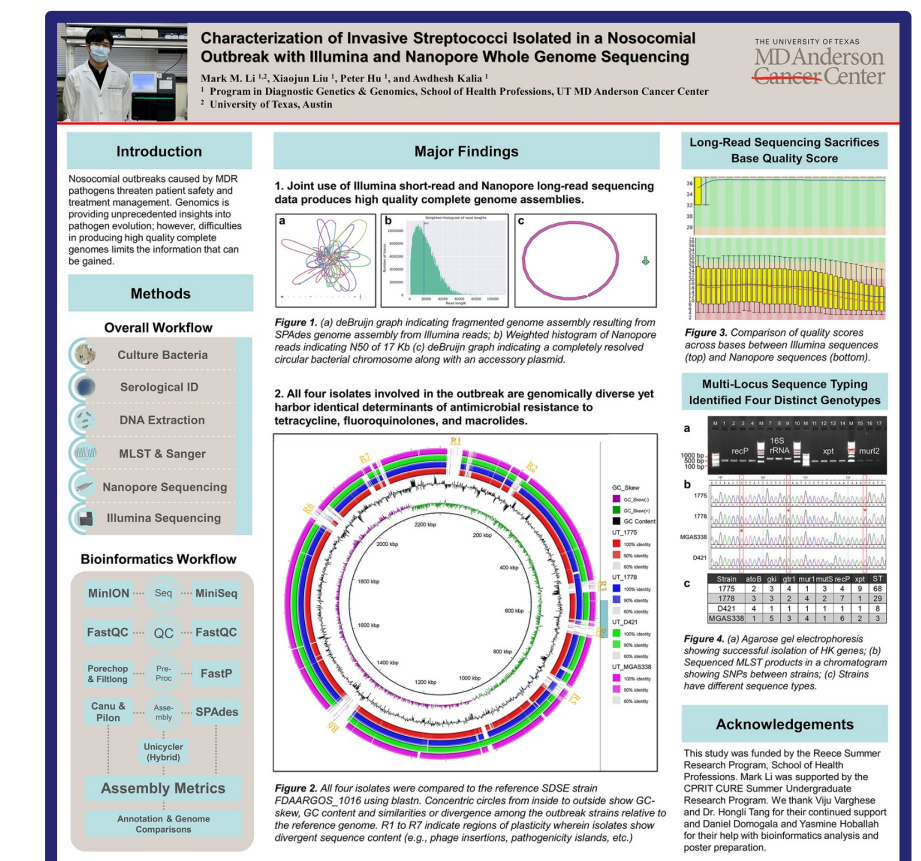
**Figure 7. An example of the workflow for Nanopore sequencing data analysis**

## Evaluation of Educational Outcome

- Student lab notes and group presentation (Fig. 8) upon completion of instruction
- CPRIT summer student's abstract and poster (Fig. 9)
- Current first-year students' abstract (submitted to Association of Genetic Technologists annual joint meeting) and poster (to do in April-May 2022)



**Figure 8. Student presentations in 2021 fall semester**



**Figure 9. 2021 CPRIT summer student's poster, also seen in a screencast in PDF Attachments**

## Conclusions and Implications

- We have successfully adopted Nanopore sequencing technology (MinION) and implemented instruction in the teaching lab for master's students specialized in Molecular Diagnostics.
- This project has introduced novel, state-of-the-art sequencing technology into the DGG training program and increased the depth of the teaching curriculum.
- This practice of teaching long-read sequencing of whole genomes benefit DGG students in that they get exposed to the most advanced technology and prepared for future positions as technologists in the molecular diagnostics field.
- The favorable learning outcomes of this practice warrant replication and improvement in the near future. Besides implementation in the upcoming fall semester, we will seek opportunities to host workshops on Nanopore sequencing and help educate the educators.

## References

- [1] Wang, et al., Nanopore sequencing technology, bioinformatics and applications. Nature Biotech., 2021, 39, 1348–1365. <https://www.nature.com/articles/s41587-021-01108-x.pdf>
- [2] Bold Predictions for Human Genomics by 2030: Session 1. National Human Genome Research Institute, 2021. <https://www.youtube.com/watch?v=fOLIXSu5k14&t=11s>
- [3] González-Recio, et al., Sequencing of SARS-CoV-2 genome using different nanopore chemistries. Applied Microbiol. & Biotech., 2021, 105:3225–3234. <https://doi.org/10.1007/s00253-021-11250-w>
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- [6] Bonwell & Eison, Active Learning: Creating Excitement in the Classroom. 1991 ASHE-ERIC Higher Education Reports. <https://files.eric.ed.gov/fulltext/ED336049.pdf>

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