

Smartphone apps for portable DNA sequencing and data analysis

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Abstract

The following entails recent advancements in portable DNA sequencing and aims to answer some questions about the same.

Introduction

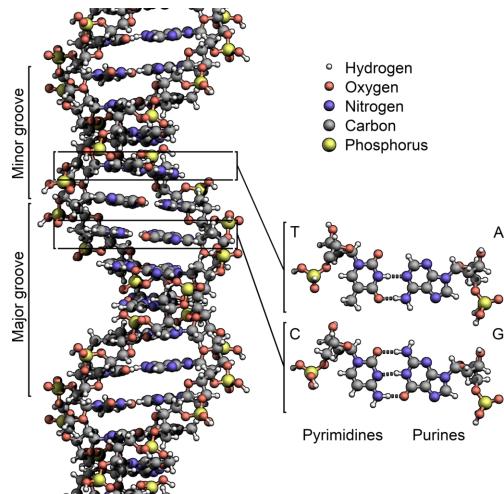
First, we will look at some basic biology concepts and answer some questions to better understand DNA sequencing:

What is DNA sequencing?

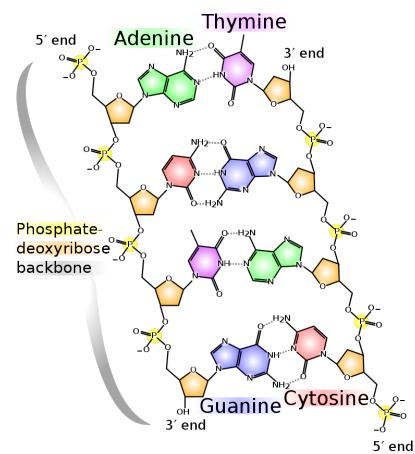
DNA determines what proteins are synthesized and so, they play an important role in determining how an organism behaves and looks like (determines its characteristics and also characteristics of its offspring). How are these instructions stored? They are stored as a long sequence of 4 chemicals/letters (Adenine → A, Thymine → T, Cytosine → C, and Guanine → G). DNA sequencing is the process of determining the order of these 4 chemicals, given a strand of DNA.

How is DNA sequenced? ("Shotgun Sequencing")

DNA is a very long sequence of A's, T's, C's, and G's. So, the strand is first broken (how?) into smaller strands. The smaller strands are then sequenced individually (If you can sequence a shorter strand why not a longer one; and how long of a strand CAN you sequence?). Then, we create thousands of copies of each small strand (to easily identify them?). These small strands are then individually sequenced using enzymes and the four molecules; A, C, G, and T (look into mechanism). Now, somehow using the aforementioned enzymes and molecules we attain the sequences of these individual strands, these small sequences are stitched together using computers (is this where data analysis plays a major role?) to give us *the sequence of the entire genome*.



(a) 3D model of helical structure of DNA



(b) Demonstrates size of DNA

Figure 1: Structure of double-stranded DNA for reference

Portable DNA Sequencing

There are a variety of sequencing methods, we will be looking into "Nanopore Sequencing". This method is, by far, the most portable. There are other sequencers (Illumina HiSeq 2500 sequencer and BGI MGISEQ-2000RS sequencer for instance) that use fairly small machines (possibility of miniturization?) and other sequencing methods, but our current state of technology does not allow miniturization (yet!).

Nanopore Sequencing

Since we have established that: right now, nanopore sequencing is the most portable form of sequencing; we will first look at what nanopore sequencing is. It is best explained by (as we will see later) the current pioneer in nanopore technology, Oxford Nanopore Technologies:

"Nanopore sequencing is a unique, scalable technology that enables direct, real-time analysis of long DNA or RNA fragments. It works by monitoring changes to an electrical current as nucleic acids are passed through a protein nanopore. The resulting signal is decoded to provide the specific DNA or RNA sequence." [7]

So, nanopore sequencing involves passing a single-stranded DNA molecule through a "protein nanopore" and measuring changes in electric current to determine the base pair. This makes sense because we know that atoms are around 10^{-10}m in diameter, so for a single strand of DNA (which is around 8-10 atoms wide) we have a width of $\approx 10^{-9}\text{m} = 1\text{nm}$; hence nanopore! The devices used are surprisingly small, they are **really** small. [8]



(a) Fongle



(b) MinION

Figure 2: The Fongle and MinION can be used for portable analysis



(a) GridION



(b) PromethION

Figure 3: GridION and PromethION can be used for flexible, high-throughput benchtop sequencing



(a) SmidgION



(b) Plongle

Figure 4: SmidgION and Plongle are under development and are excitingly small

Smartphone apps

DNA sequencing	DNA data analysis
MinKNOW	GenoPo, iGenomics

MinKNOW

What mobile apps are available in this space?

Oxford Nanopore Technologies has their very own app: **MinKNOW**. As far as nanopore DNA sequencing is concerned, there are no other prominent apps (explained later).

When were they developed?

MinKNOW is a general application that existed for a while (since at least 2015) but the mobile app was formally released on **November 25th, 2020**. [9]

What features do they offer?

As stated in ONT's website:

"It carries out several core tasks, including:

- **Data acquisition**
- **Real-time analysis and feedback**
- **Local basecalling**
- **Data streaming**
- **Progressive unblocking**
 - Increased data yield of a flow cell
 - Active voltage control → improved signal consistency during a run.

- whilst providing device control including **selecting the run parameters, sample identification and tracking**, and ensuring that the platform chemistry is performing correctly to run the samples." [9] [10]

It also enables users to **run group experiments** and **view/export metrics to a PDF**. Essentially, the app helps manage their devices, we shall also discuss complementary apps, iGenomics and GenoPo.

Which apps are used most frequently by consumers?

MinKNOW basically dominates every other app (if any) as far as nanopore sequencing goes. This is mostly due to the availability of their own native devices, enabling them to modify their app as per device upgrades. Consumers are likely to use MinKNOW if they own a, say, MinION. Similar to how Android users likely use Google Chrome. Besides, sources indicate that they have patented the technology \Rightarrow nanopore sequencing is intellectual property of ONT (for now?). [11]

Are there any advantages and limitations of these tools?

Advantages:

- With new device rollouts, ONT can simply update MinKNOW to accomodate new devices.

Limitations:

- As of now, ONT does not compete with anyone when it comes to nanopore sequencing (a little with Illumina [12]). This indicates that there is not as much a desire to release new technology.

iGenomics and GenoPo

What mobile apps are available in this space?

When were they developed?

What features do they offer?

Which apps are used most frequently by consumers?

Are there any advantages and limitations of these tools?

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