Literature Review

Zaki Salma

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1 Abstract

Since the Covid-19 pandemic had first surfaced in late 2019, the diagnosis of the virus has proved to be a crucial factor in its containment and an area of great interest within the scientific community as a result of the inherent difficulty in detecting the pathogen (long incubation time, high case to case variation in patient symptoms), as well as its life-saving practical applications.

This paper serves to catalogue the various techniques in physics that have played an important role in the identification of this betacoronavirus.

2 Introduction

The endeavors into the detection of the COVID-19 virus by the Physics community roughly falls into three main subsections of research: X-ray Crystallography, X-ray Imaging and Cryo-Electron Microscopy (Cyro-EM).

2.1 X-ray Crystallography

X-ray crystallography is a method by which the structure of a crystalline substance can be unveiled. The general basis of the technique is to shine a beam of X-rays, generally produced from some form of a synchrotron, at the desired crystal, the X-rays then diffract off of layers in the crystal. Measuring the angles and intensities of these diffracted beams is used to produce a 3D map of the electron density in the crystal, from which the positions of the atoms in the crystal can be inferred.

In the context of structural biology, the first X-ray diffraction image of a biological molecule was recorded in 1934 by Bernal and Dorothy Crowfoot. While some proteins naturally exhibit a crystalline structure, more often than not the diffraction of X-rays off of single biological molecules produces only very faint signals, consequently, the samples are generally first crystallised by protein crystallisation methods.

A research team led by Zihe Rao **et al.** at ShanghaiTech University determined the structure of the virus's main protease using X-ray crystallography at the Shanghai Synchrotron Radiation Facility. [6]

2.2 X-ray Imaging

X-ray imaging or more specifically chest radiography is commonly used for diagnosis of lung problems such as pneumonia and lung cancer, it produces a projection radiograph of the chest of the patient which can in turn, be used for diagnosis.Joanne Cleverley**et al.**[4] goes into detail on how changes on a radiograph can indicate the prescence of Covid-19 pneumonia. This procedure can be extended and with the use of machine learning (ML) and neural networks. Boran Sekeroglu **et al.**[2] used deep convolutional neural networks in the detection of the virus through limited image based data of chest x-rays with a 98.50% mean accuracy. Other literature on the use of ML by Tej Bahadur Chandra**et al.**[5] present an automatic covid screening system (ACoS), emphasising the importance automatic detection as opposed to slow manual diagnosis due to limited availability of experts. These automatic systems however, require further work and improved reliability for clinical approval.

2.3 Cryo-Electron Microscopy

Some draw backs of using X-ray crystallography is that the sample needs to first be crystallised. For some biomolecules, crystallising can be very difficult and so using the crystallography methods can prove to be quite challenging. In these cases it is often more advantageous to use the Cryo-Electron Microscopy (Cyro-EM) technique in which a solution containing the biomolecule is placed onto a thin layered grid. The same is then flash-frozen and then imaged an electron microscope. This technique also only uses a small ammount of the sample however due to the high levels of noise associated with using low electron doses to reduce radiation damage, only relatively low resolutions are attainable .

2.4 Other

Nicolas Shiaelis **et al.**[3]

References

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