Nanobiotechnology toward Diagnostic Industry: Obstacles and Opportunities

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ABSTRACT

The use of nanotechnology for biotechnology application shows great promise to meet stern demands in personal and clinical medicine, diagnostics and genomic research. In this paper some future potential and opportunities as well as obstacles and fundamental limits that may exist in front of anobiotechnology toward industrialization are discussed.

Keywords: nanobiotechnology, genomics, diagnostics, nanobiosensors, industrialization.

INTRODUCTION

The rigorous demand for diagnostics and medical and genomics research pushes both universities and industry toward a lot of efforts in order to overcome technological and fundamental challenges in biology and the life sciences research and hopefully reach the point to treat effectively some of the severe diseases such as cancer, Parkinson or HIV [1, 2].

Have a deeper look at the biological sciences; it is obviously clear that this field of science is suffered from the lake of fundamental and deep logical analyses that have gone through different possibilities thoroughly and today we have a general database as a referee for research and industry. After several years of on-going research and a lot of governmental and personal funding on such projects worldwide, we still do not have an effective and efficient way to diagnose infection disease or hereditary problems shortly.

These deep and organized analyses have been done in Physics starting from about middle of the eighteen century up to date, which mainly leads to what we call it as engineering sciences or simply engineering. This understanding of Physics rules and basics helps us to model our world with a reasonable accuracy which leads to a good reliability and reproducibility in technology. Engineering could be seen as nothing more than these to-the-point analyses that make it possible to take advantage of Physics in our desired applications, after a proper combination with logic, mathematic and informatics. The great and fast success in invention of integrated circuits followed with break through in IC technology and microelectronics industry is one example of this prefect combination of the physics of semiconductors and the next logical steps toward organizing, mathematical modeling, etc.

Surprisingly you can not similar advances in life science side and such technology with a high accuracy and control on biological applications has not made so far or it is still in early stages of research. While we can go deep to nanometer size resolution in IC technology, we are still challenging pretty difficult with bio-species, for instance proteins which deals in similar or larger size or even more, dealing with cells of human body with bigger size but important in some disease detection and diagnostics. (In some applications you don't even need to go in the details of the cell for treatment of a disease while in some others, you have to deal with the sub-species which makes it harder to overcome).

This difference seems to be due three major reasons; firstly due to very high complexity of the biological science. Secondly, the lake of adequate tools and info structure in the field decrease the speed of growth in the field and as the third reason, we might refer to a big gap between the expert of the fields of engineering and life sciences. Since there are a very high coherence between these reasons, people might combine two of these factors as one or even all as one big reason of high complexity of the nature of biology.

FUNDAMENTAL & HISTORICAL LIMITS

The inherent complex nature of the life sciences, for instance from the building block of life: DNA goes to hundreds of thousands of different types of proteins and other bio-species, makes it difficult to have deep and universal analyses over the field. While you can analyze the property of silicon once and then expect to have similar results from all similar devices made from this semiconductor, you don't have just one or a few numbers of protein types then by having information of those proteins; you would expect to have the information of all proteins or a large number of them. Usually we would not have access to all their behaviors or even couldn't expect a linear or even smooth relation between the functionally of two types with minor differences in their structure, contrary to what you can expect from silicon in transistors. Even though you can usually find some similarities between their functionality and responses, but the differences are huge enough that extracting more information to predict other type's functionality and extrapolating of the results which is very common in engineering is not useful here, all because

of the nature of uniqueness of the bio-species which demands a huge efforts and very large database. Evolution has made each and any part of this world in such a perfect and unique way that expecting one from the other is not trivial.

The other reason behind differences between what we are now in microelectronics (or in better word nanoelectronics) technology and the biological sciences could be seen is the lake of tools and advance instrumental technology for the latter one. The rate of advancement could be seen as an exponential function versus time which slope at any given point depends on the previous moments and the availability of info-structure for new achievements. We are in the great need of a handheld highly integrated device with multiplexing feature which can work as high accuracy, throughput and reliability platform in generating new data in bio-analyses; but one reason can be seen since we don't still have early stages available.

For instance let's have a look at the DNA sequencing research which is one of the essentials for genomics studies, clinical applications, disease detection and discovery, diagnostics, drug discovery and personalized medicine. The revolution that the Sanger method of DNA sequencing [3] and its subsequent array automation [4] continued by the sequencing of human genome and completion of Human Genome Project [5, 6]. Sanger dideoxy DNA sequencing has been the most commonly used method for DNA sequencing so far, particularly in large scale genomic sequencing, but inherent limitations of this method such as cost, throughput and read length and its enzymatic complexity make it impractical to deliver the current needs of DNA sequencing. The Human Genome Project was essentially accomplished by a reduction in the cost of DNA sequencing by three orders of magnitude. It is desired to reduce the cost by another three orders of magnitude to enable profiling of individuals genome. The increase of large scale DNA sequencing projects in recent years shows this search for alternative methods to reduce cost and time [7-11]. Many efforts have been investigated toward achieving a high throughput and low cost assay for DNA sequencing such as high-density parallel sequencing with stepwise enzymatic cleavage and ligation [12, 13], base addition with deprotection steps [14], mass spectroscopy [15-18], sequencing by hybridization [19], micro fluidic device sequencing-by-synthesis [13], nanopore sequencing, polymerase colonies [20-23], and Pyrosequencing [9, 11, 24-28].

The second reason of not having good and sensitive tools that put us today in a slow slop points in the exponential graph could be consider due to the third reason of lake of good and effective communication between professionals of the two fields. While engineers have no clue about what people in biological research needs to measure and detect, the biology experts don't have enough information on the current state-of-the-art technology which can go deep to nanometer with very high precision [29] and the some possibilities and opportunities which may already exist for solving their own research challenges and (the application of engineering in biology which is so called as Bioengineering, extra to the potentials of collaboration on using bio-species in engineering applications.

THE NICHE AND THE ROLE OF NANOBIOTECHNOLOGY

As mentioned above, one of the reasons because of the gap between engineers and biologist could be considered as the very complex nature of bio-species, which makes it difficult and almost impossible to overcome on challenges with classical engineering tools and methods. Here is the place that nanotechnology appears as a useful pill for this pain. This gap has been shrunken in the recent years to some extend, but still a lot of time and efforts is needed to let engineers and biologist can have a good image of the other ones need and the potential ability in solving that problem.

Nowadays, we are hearing more and more about nanotechnology and the promises of its role to improve human life. Thousands of research projects worldwide are on going on nanoscale science and technology and in the recent years the number of companies started in this field shows that nanotechnology has been one of the most fast-growing fields in the industry in the recent years.

Special aspects of nanoscale devices, high sensitivity, high integration and multiplexing potential make nanotechnology as a candidate for solving unknown facts in life science studies and low speed detection and discovery theme in medical research and industry. This mixture of nanotechnology and biotechnology that with the aim of nanotechnology, we try to overcome medical and biological challenges is so called as nanobiotechnology (e.g. NanoBioFET Sensors including Nanowire Field Effect Transistor for bacteria and virus detection antibody-antigen interaction detection, etc [29-34, 49], and CNTFET or Carbon Nanotube Field Effect Transistor [35-47] and Nanopore sensor for protein detection or DNA Sequencing [20-23, 48, 50]) where the use of bio-species helps on nanotechnology and engineering side (e.g. DNA-based memory [52], DNA markers for RFID technology or Molecular Electronics). This need to have a high sensitivity and accuracy device in the integrated platform is to the point that some market analysts rank nanobiotechnology as the highest potential market in the next decade.

More attention to the first case which is related to Bio-sensor or nanobiotechnology, we can see a lot of research and efforts specially starting the new century are on-going around the world. Nano-devices may get characterized in four different categories of carbon Nanotubes, Nanowires, Nanocrystals or Quantum Dots (QD), and nanopores.

The early papers in each of these fields claims to have a good signal to noise ratio (SNR) for detection of a bio-species such as a protein, bacteria, or virus return back to at least about six or seven years now [42, 49] and many papers in well known journals such as nature, science and

Proceeding of National Academy of Science, USA have been published; [31-33, 40-42, 47, and 50]; but interestingly enough we can not see a full coherence between the results claimed about different devices and neither still haven had these devices as commercial products in the real world for clinical or personal use.

CONCLUSION

Biosensing devices should be ideally real-time, multiplexed, sensitive and specific. While no single device thus far have demonstrated superiority with respect to all these qualities, many of the upcoming nanomaterial-based sensors described above appear to be promising and could potentially deliver real-time, multiplexed detections while achieving similar if not better sensitivity and specificity than conventional methods.

The development of these novel nanosensors is currently at its infancy and it is unclear which nanomaterials would be more useful than others as sensors for certain bio-detection. This uncertainty is further compounded by conflicting reports in the literature on the sensitivity of various nanosensors. In one instance, one group of investigators claims that nanotube-based FETs have greater sensitivity than nanowire-based FETs, whereas the other group suggests the opposite [38, 47]. Such discrepancy calls for the need to perform more studies on reproducibility to compare and contrast the performance of various nanosensors under the same experimental setting.

In the other hand, more clinically relevant samples such as sputum, body fluidic and would help the results to get closer to accurate ones that you might expect form the sensor in the real world instead of using purified samples which are not always available. (Some examples of this issue are the blood might contain hemoglobin that could interfere with light emission from quantum dots and if acidic could affect antibody-pathogen binding on either nanowires or nanotubes. High ionic strength of serum could also potentially hinder electrical detection by nanowires.)

Although the nanobiotechnology is still in early development, but addressing these issues would be helpful and beneficial for further development and definitely further testing under more stringent conditions plus development of devices to have higher SNR would be finally needed to see the real effects of high-efficient nanodevices in our clinical and personal medicine.

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