Medical Technologies Journal, Volume: 1, Issue: 3, July –September 2017, Pages: 62-75.
DOI: https://doi.org/10.26415/2572-004X-vol1iss3p62-75

Recent Advances of Mechanical Engineering Applications in Medicine and Biology

Type of article: review

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Abstract

Background: Mechanics is an area of science dealing with the behavior of physical bodies (solids and fluids) undergoing action of forces, it comprised of statics, kinetics, and kinematics. The advances and research in Applied Mechanics has wide application in almost fields of study including medicine and biology. In this paper, the relationship between mechanical engineering and medicine and biological sciences is investigated based on its application in these two sacred fields. Some emergent mechanical techniques applied in medical sciences and practices are presented.
Methods: Emerging applications of mechanical engineering in medical and biological sciences are presented and investigated including: biomechanics, nanomechanics and computational fluid dynamics (CFD).
Results: This review article presents some recent advances of mechanical engineering applications in medicine and biology. Specifically, this work focuses on three major subjects of interests:

- Biomechanics that is increasingly being recognized as an important application of mechanical fundamentals in biomedical and biological sciences and practices, biomechanics can play a crucial role in both injury prevention as well as performance enhancement of living systems.
- Novel techniques of nanomechanics including: Carbon nanotubes applications in therapy, DNA recognition, immunology, and antiviral resistance. Nanorobotics that combines between nanotechnology, mechanics and new biomaterials to design and develop nanorobots based bacteria and biochips; these nanoscale robots can be involved in biomedical applications, particularly for the treatment of cancer, cerebral aneurysm treatment, kidney stones removal surgery, treatment of pathology, elimination of defected parts in the DNA structure, and some other treatments to save human lives.
- Computational fluid dynamics (CFD) tools that contribute on the understanding of blood flows, human organs dynamics and surgical options simulation.

Conclusion: Recent advances of mechanical applications in medicine and biology are carried out in this review, such as biomechanics, nanomechanics and computational fluid dynamics (CFD). As perspectives, mechanical scholars and engineers can involve these cited applications in their researches to solve many problems and issues that doctors and biologists cannot.
Keywords: Biomechanics, Nanorobotics, Medicine, Biology, Biomedical engineering.

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Received: July 28, 2017, Accepted: September 27, 2017, English editing: September 27, 2017, Published: September 28, 2017.
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1. Introduction

As applied physics, the modern mechanical engineering which permeates almost all the core Engineering or rather scientific disciplines, has proven its reliability to be involved in resolution of complex problems in several disciplines even medicine and biology.
Why does mechanics serve for medical technologies and biological sciences?
Mechanical engineering is a broad engineering subject with a range of activities and functions that derives its breadth from the need to design and manufacture medical technologies from small individual parts and devices to large systems that can be involved in almost every aspect of technology. It covers topics related to energy,

fluid mechanics and dynamics, robotics, solid mechanics, heat transfer, design and manufacturing, maintenance and control. This diverse background helps mechanical engineers and scholars to define, orient the future of technology, and play a critical role in solving global issues and challenges of many areas of interest outside mechanical technologies. Medicine and biological sciences have been adopted by mechanical principles and theories such as fundamental role in orthopedics, immunology, or the absolute reliance of mass transport and diffusivity equations on pharmacokinetics and pharmacodynamics for understanding cardiovascular physiology and pathology. Currently, the meeting between mechanical engineering and medicine oversteps than what were unimaginable until recent times, because of the integration of novel disciplines and novel techniques. We can cite many topics and emergent issues including engineering mechanisms, processes, bio-sensors and bio-devices in medicine, biology and healthcare, where the mechanics is the main player and the key for problem-solving. Following are some topics that connect mechanics with medicine and biology:

- Biofluid Mechanics, Biorheology, Blood Flow dynamics
- Hemodynamics using Computational Fluid Dynamics (CFD).
- Biomaterials and Biosensing
- Cellular, Subcellular, Genetic, Epigenetic, or Molecular Biomechanics
- Medical Nanoelectro-mechanical Systems (NEMS)
- Medical Robotics.
- Reproductive and Urogynecological Mechanics.
- Muscle/Neuromuscular/Musculoskeletal Mechanics and Engineering.
- NEMS/MEMS, Microfluidics.
- Mechanobiology and healthcare
- Computational Biomechanics/Physiological Modelling
- Clinical Biomechanics.
- Cellular and Tissue Mechanics/Engineering.
- Cardiovascular/Cardiac Mechanics.
- Cardiovascular Systems Engineering.
- Bio-Nanotechnology and Clinical Application.
- Biomedical Signal Processing Techniques
- Artificial Organs, Biomechanics of Organs.
- Medical Instrumentation and BioSensors.
- Respiratory System Engineering.
- Bioheat Transfer and Mass Transport, Nano Heat Transfer.
- Human Movement and Animal Locomotion.
- Implant Design and Mechanics.
- Sports Medical Mechanics, Joint Mechanics.
- Therapeutic Physics and Rehabilitation Engineering.

2. Biomechanics applications

Biomechanics is the application of mechanical principles in the study of living organisms including their kinematics (description of motion) and kinetics (actions of forces associated with motion), it views the human body as a collection of levers, made of bones which are moved by its muscles. In sport and exercise, where mechanics can be involved to analyze the performance of athletes based on their interaction with the equipment. [1]. Figure.1 presents a case study of a knee joint simulated via Ansys.

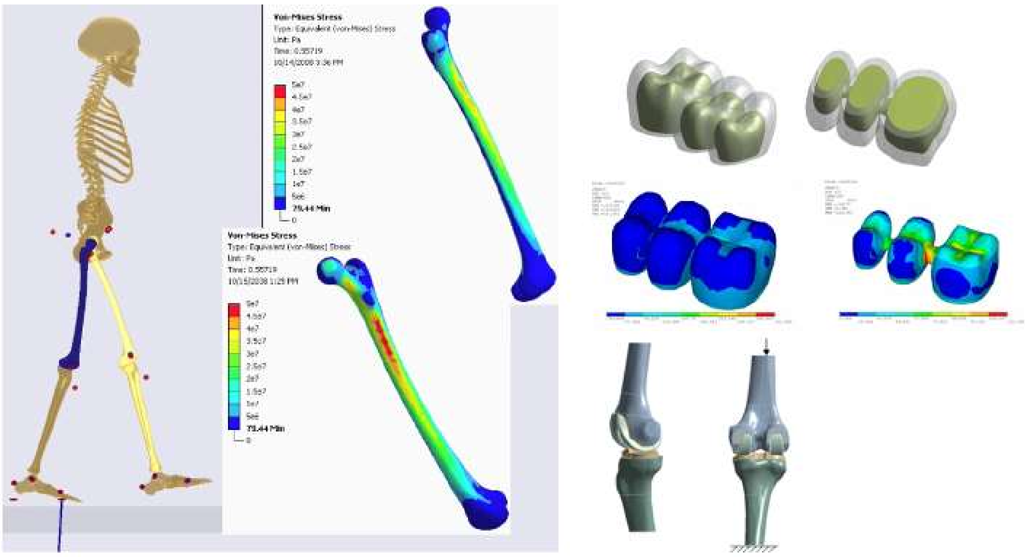

Figure.1 Musculoskeletal model coupled with ANSYS allows simulation of femur stresses during gait, residual viscoelastic stresses in a partial denture, knee joint geometry for wear simulation. [2]

According to the scale in which the study or the application is done, we can distinguish between biomechanics and mechanobiology. Biomechanics is more related to the scale of body segments, interaction with the surrounding environment, etc. On the other hand, Mechanobiology is concerned more with the level of cells, it focuses on the physical forces behavior and transfer in cell or tissue mechanics.

3. Nanomechanics applications:

Nanotechnology is the understanding the behavior of matter at infinitesimal dimensions called nanometers (a nanometer is one-billionth of a meter; a human hair is about 75000 nanometers in diameter), where incredible properties enable emergent applications. Considering combination between nanoscale science, engineering and technology, nanotechnology covers sensing, imaging, measuring, manufacturing, control and manipulating nanoscale matter. In mechanics, the integration of nanotechnology is focused on three main topics including: nanostructures (carbon nanotubes), nanofluids and microfluidics, and nanorobotics. In following, we present the application of these nanomechanics topics in medicine and biology.

3.1. Carbon nanotubes:

Carbon nanotubes (CNTs) [3] are nanoscale structures made of pure carbon that are long and thin and shaped like tubes, these molecules are same sized and structured in chemical boding and aligned by Van der Walls forces into ropes, the length of CNTs can reach some millimeters while its diameter in on the order of some nanometers. In reference to the number of structured walls, we can distinguish single walled nanotubes (SWCNTs) shown in Figure.2, and multi-walled nanotubes (MWNTs) depending upon the walls number.

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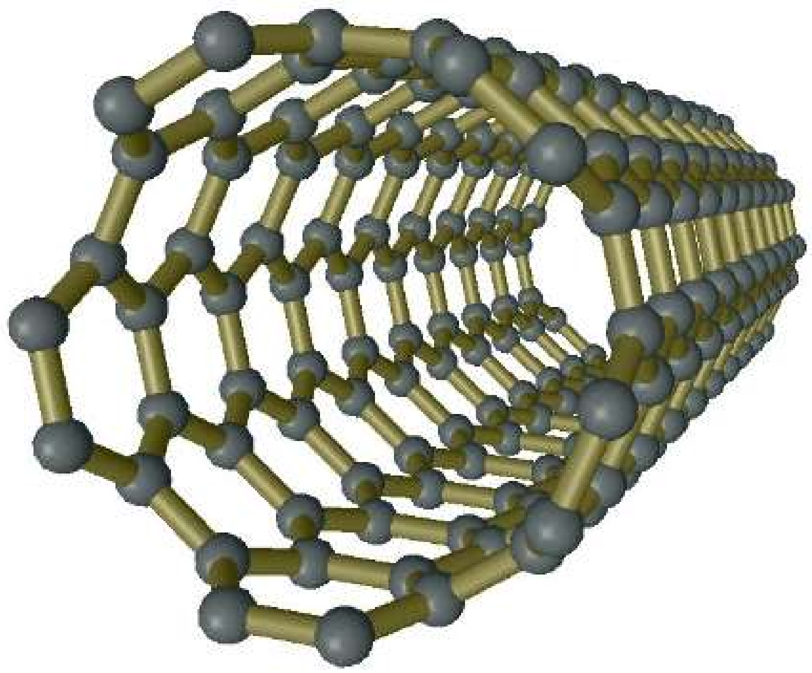

Figure.2 CNT molecular diagram

In addition to spherical bucky-balls, nanotubes are also members of the fullerene structural family, named nanotubes from their long length and hollow structure formed by the turning of single atom thick sheets of a matter called graphene, which is extracted from graphite. The importance of CNT's are their exceptional electrical, mechanical [4], optical and chemical properties. The use of CNT's in medicine and biology is presented as following:

3.1.1. The application of carbon nanotubes in cancer therapy

Cancer belongs to the most complicated diseases in the world. According to the WHO, the cancer is considered one of the main causes of morbidity and mortality worldwide, with approximately 14 million cases in 2012 [5]. Anticancer drugs like Chemotherapy or Radiotherapy often have physiological, biochemical and cellular toxic side effects. Several methods in many fields have been objected to reduce this problem, among them, Carbon Nanotubes (CNTs). They have unique mechanical properties that open a way for many therapeuticsto strongly minimize their side effects. Many Centers for Cancer Research focus to discover new drugs originating from Carbon Nanotubes.

3.1.2. The anticancer agent taxoid with a cleavable linker

Taxoid is a chemotherapeutic agent to block proliferating cancer cells. CNTs have been explored as a tool in nanocarriers for the exploration of novel drugs. There are large varieties of nanoscale drug delivery vectors like single-walled carbon nanotubes (SWCNTs). As CNTs are needle-like shape, they have been involved in injection and integration into target cells [6], CNTs are combined to the anticancer agent taxoid as a cleavable linker [7]. In order to ensure the target cell, the drug is transported via endocytosis and released in the cell. Microtubules interact with the drug as evaluated by flow cytometry thus formatting a stable microtubule-taxoid complex. [7].

3.1.3. Target drug delivery for cancer therapy

One of the novel applications of CNTs is drug delivery called also smart drug delivery, a method of high recognition of cancer cells or cancer tissues [7] in order to deliver medication with high precision. It is efficient for the lymphatic system; metastases of certain cancers can be effectively inhibited [8] for subcutaneous injection. Adsorption on the PAA-CNT surface [9] is possible through co-precipitation of Fe3O4-based magnetic nanoparticles, polyacrylic acid (PAA) can be added to CNTs to become highly hydraulic.

3.1.4. The "longboat" anticancer system

In this application, CNTS are used for cancer treatment based on a functionalized SWNT attached to a complex of cisplatin and folic acid derivative via covalent or noncovalent bonding to comprise the "longboat" which has been reported to be taken up by cancer cells via endocytosis; then, the release of the drug and its interaction with the DNA. Targeted single-wall carbon nanotube-mediated Pt(IV) prodrug delivery is using folate as a homing device [10]

3.1.5. The application of carbon nanotubes in cancer immunotherapy as a vaccine

Nanotechnology has advanced in theoretical and practical research in all fields of biomedicine. Recently, the application of Nanotechnology in Immunotherapy has opened another choice for the treatment of cancer, which was evaluated as an anticancer drug by using CNTs. Carbon nanotube antibodies are used to recognize and target tumor cells. Many works have been done to show the possibility the anticancer immune reaction increase of tumor cell by using CNTs as delivery media. Ruggiero et al [11] have reduced the tumor volume by creating complexes of tumor neovascular-targeting antibody E4G10 to SWCNTs using radiometal-ion chelates and improved median survival time relative to control [12]. Fan et al [13] haveconfirmed that intracranial CNT–CpG therapy blocked subcutaneous melanomas. Recently, Fadel et al [14] attached antigens to bundled CNTs (CNT–polymer composite). This CNT complex was conjugated with polymer NPs containing magnetite with T-cell growth factor IL-2. The results proved that T-cells denied the tumor growth.

3.1.6. Stimulation of immune system

Using oxidized Multiwall Carbon Nanotubes (MWCNT), the immune system activity increased in a hepatocarcinoma tumor-bearing mice model. After injection of CNTs the activities of immune cells were stimulated by activation and stimulation of phagocytosis of macrophagesand promotion of inflammatory cytokines secreted due to the activation of the complement system [15].

3.1.7. Using complex specific IgG responses for antigen stimulation

Villa et al. [16] have demonstrated that SWCNTs can activate humoral immune responses. There are studies about the possibility of enhancement of immune responses by using SWCNTs as antigen carriers. A complex of a number of peptides (0.4 mmol/g) and SWCNTs was created and internalized into professional APCs . This created specific IgG responses against the peptide,

3.1.8. T-cell (Treg)-specific receptors

A group of researchers provides a foundation for innovative immunotherapy against cancer; they investigated in vivo the selective internalization of Polyethylene Glycol-modified SWCNTs (PEG–SWCNTs) to be drived by ligands against T-cell (Treg)-specific receptors in the tumor microenvironment. Whereas, PEG–SWCNTs with glucocorticoid-induced TNFR-related receptor GITR ligands were internalized by Treg through receptor-mediated endocytosis and conveyed into the cytoplasm/nucleus cytoplasm and nucleus ex vivo and in vivo [17].

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3.1.9. Vaccine

Creation of vaccine at the stimulation of immunity against a tumor cell employs the association of MWCNTs to tumor lysate protein. An efficient tumor curing and a cellular antitumor immune reaction is improved [15] in an H22 liver cancer-bearing mice. The antitumor immune reaction response was specific. The antibody delivery system in immunotherapy was ensured by CNTs that can be used to promote new antitumor immunotherapies.

3.1.10. The application of carbon nanotubes in infection therapy

The gradual emergence of resistant bacteria is occurring worldwide have enhanced medicine and saved many people-threatening bacterial infections [18]. In the past, pharmaceutical antibiotics have been used as a strategy to combat resistant bacteria. Currently, the use of innovative antimicrobial agents [19] for infection therapy has been answered by CNTs that serve as novel antibiotics for the treatment of these infections.

3.1.11. Application of carbon nanotubes for attacking antibacterial resistance drugs

The carbon nanotubes have been evaluated for infection therapy to attack multi drug resistant bacteria [20]. The effect of benign ε-polylysine/silver nanoparticle, nanocomposite (EPL-g-butyl@AgNPs) with polyvalent and synergistic antibacterial is reported to understand the antibacterial mechanism of AgNPs-based nanocomposites, and devrlop an efficient antibacterial agents for clinical applications.

3.1.12. Application of carbon nanotubes for attacking fungi

Functionalized CNTs have been studied like the antifungal amphotericin. After crating, a complex with association of CNTs and amphotericin B this was transported it into mammalian cells. This conjugate has reduced the antifungal toxicity [21]. Combination of the antimicrobial agent Pazufloxacin mediated with amino-MWCNT demonstrated a high adsorption and will be applied to experimental assays for infection treatment [22].

3.1.13. Application of carbon nanotubes for attacking antiviral resistance

Wang et al. [23] have evaluated the adsorption behavior of the antiviral drugs oseltamivir (OE) and its metabolites (i.e., oseltamivir carboxylate (OC) on CNTs, three types of CNTs are used including SWCNTs, MWCNTs and carboxylated SWCNT (SWCNT-COOH). The comparison of the adsorption on different CNTs shows that SWCNTs-COOH plays a key role during the adsorption process. The adsorptive mechanism of hydrophobic interaction electrostatic interaction, Van der Walls force and H-bonding were suggested as the contributing factors for OE and OC adsorption on CNTs. Especially, to affirm the contribution of electrostatic interaction; the changes of adsorption partition performance (Kd) of OE and OC on CNTs were evaluated by varying pH from 2 to 11 and the importance of isoelectric point (pHIEP) of CNTs on OE and OC adsorption was addressed.

3.1.14. Carbon Nanotubes for Gene Therapy by DNA Delivery

Gene therapy by DNA Delivery using CNTs has spread out. Curently around 4000 genetic disorders are identified. Almost if not most of them are hereditary and caused by mutations [24]. Gene therapy is regarded as a new technique that deal with several incurable morbus, such as cancer and other genetic disorders [25]. The use of carbon nanotubes substitution of mutated genesis targeting at acquainting DNA molecule into the cell nucleus. Whereby a broaden range of therapeutically active nucleic acids, including plasmid DNA (pDNA), small -interfering RNA (si

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RNA) , antisene oligo Deoscy Nucleotides (ODNs) , and aptamers, have experiense at the posttranscriptional or translational levels Kun Him [12]. Ramos -Perez [26.] designed the surface modification of carbon nanotubes (CNTs) to permit the formation of a complex between these potential carriers with DNA. Procedures were developed to prepare transfection vectors through the modification of MWCNTs. These procedures composed of divisions determined the reduction of CNTs length, to rise the dipersability of CNTs and finally for a surface modification to attach through electrostatic interaction DNA to the CNTs. Several f-CNTs have been studied to deliver p DNA using amine groups, polyethylenemine hybrids, cationic, glycopolymers, and ethylenediamine. Singh et al [27] underseek the optimization of f-CNTs as Gene delivery vehicles, including ammonium- funti onalized MWCNTs (MWCNTs-NH3+, SWCNTs - NH3+) and lysine functionalized SWCNTs (SWCNTs–lysine–NH3+), with pDNA resulting in a complex formation between f-CNTs and DNA. Pantarotto et al [28] offered an ammonium-functionalized SWCNTs with pDNA to reduce cytotoxicity. The gene expression level by f-CNT-based DNA delivery was tenfold higher.

3.2. Nanorobotics:

Nanorobotics has been widely known as an emerging field developing small machines and devices in the scale of some micrometers involved in nanobiotechnology, using specific materials to build what called nanorobts. These nanorobots (nanobots) are applied in microbiology as an effective strategy by enabling propulsive potential by attaching them to magnetotactic bacteria (magnetococcus, magnetospirillum, magnetotacticum and magnetospirillum magneticum [29]) . Using the application of magnetic field [30] to guide these bacteria to follow a desired direction (Target cells). Another application for these micro/nanodevices as smart sensors [31] to collect information. In surgery and medical treatments, microdevices has brought many in clinical procedures for heart and intracranial surgery [32-34], pervasive medicine [35, 36], and medical procedures [37, 38]. Figure.3 shows a nanorobot with a human embryo.

The use of nanorobots in medicine has been widely emerged and impacted; the injection of nanorobots in human body has been carried on for several purpose such as, imaging, sensoring, measuring, cleaning up, surgery and delivering differentiated stem cells… Nonetheless, the future hides surprises to us, maybe in few years nanorobots will replace our organs as they wear out.

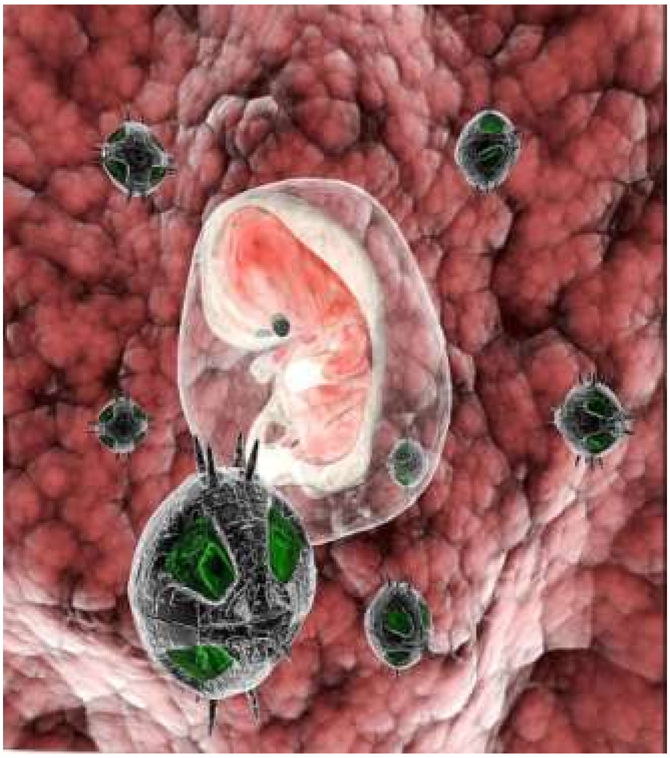

Figure.3 Nanorobots with human embryo by Christian Darkin [39]

Drug delivery is also ensured by using specific nanorobots called Pharmacytes, where the dosage of drug is loaded in to its payload. Pharmacytes ensure the precision in transport of drug delivery to specific cellular targets [40].

Currently, research is focused to design a nanorobot dubbed as respirocyte. The function of the microrobot is linked with the bloodstream physiology. First, collecting oxygen as it passes through the respiratory system via blood circulation system. Second, collecting carbon dioxide from tissues for release into the lungs. Then, metabolizing glucose to power its own functions [41]; The application of nanorobotics in Hemostasis is an emerging smart process involving several steps with a number of promoters and inhibitors balancing thrombosis and fibrinolysis [42].

In neurosurgery, in order to reduce the average of mortality, nanorobots are used in diverse ways for screening for a new aneurysm or closer monitoring of an identified aneurysm. In this issue, Cacalcanti et al. [43] have proposed a novel design for an intravascular nanorobot with the specific property to detect aneurysm formation by detecting the increase of nitric oxide synthase protein levels within the affected blood vessel.

3.3. Nanofluids:

Nanofluid is a fluid mixing nanoscale solid particles, called nanoparticles. The use of nanofluids and dispersant nanoparticles in biology is widely investigated [44]. These fluids are engineered colloidal suspensions of nanoparticles in a base fluid. The aim purpose to use these nanosolids is to benefits from its thermal properties for heat and mass transfer, or electrical and magnetic properties for power transmission or sensing. Nanoparticles which are commonly used in nanofluids are made from numerous materials such as oxide ceramics (Al_2O_3,CuO) [45]. In recent years, Most of the application of nanofluids in biomedicine were fluorescent biological labels [46], drug and gene delivery [47], bio detection of pathogens [48], detection of proteins [49], probing of DNA structure [50] and tissue engineering

[51]. Nanoparticles are on the way to become an extensive field of interest worldwide. The nanoscale has several properties and varieties like size, shape, and diverse components to permit explorations for biomedical applications. Currently, intensive research is done to be applied for the implantation of tissues or the search for cancer therapeutics.

It is aimed at augmenting the chance of compatibility and acceptance of implanted tissues, to reduce the chances of rejection as well as to stimulate the production of osteoblasts by creating nano-sized features on the surface of e hip or knee prostheses. A 3D analysis based on optical "bar coding" of polymer particles in solution, is limited only by the number of unique tags one can reliably produce and detect.

Single quantum dots of compound semiconductors were successfully used as a replacement of organic dyes in various bio-tagging applications. A precise control of quantum dot ratios has been achieved. The selection of nanoparticles used in those experiments had 6 different colors as well as 10 intensities. It is enough to encode over 1 million combinations [52].

An Italian group presented a study with the application of nanoparticles in cell therapy for myocardial infarction treatment and heart regeneration. They focused on the traditional approach to deliver cells at the damaged site [53]. Another group seeks to develop antibodies using conjugated fluorescent dye-doped silica nanoparticles (FDS-NPs) for the rapid detection of Salmonella spp. [54].

Costescu et al. [55] aim to evaluate nanoparticles (Ag:Hap-NPs) for their antibacterial and antifungal activities, using pure silver-doped nanocrystalline hydroxyapatite nanoparticles.

4. Computational Fluid Dynamics:

Computational Fluid Dynamics is an engineering tool that connects mechanics to mathematics and software programming to execute simulation performing how a fluid (liquid or gas) flows based on Navier-Stokes equations which are the main mathematical formulation modelling all phenomena of fluid mechanics. The solution of these equations is elaborated by implementing structured and unstructured meshes using numerical methods such as (finite volume method, and finite element method). CFD has been around since the early 20th century as a tool analyzing air flows around cars, aircraft and performing the cooling systems of data centers and electronic chips. CFD softwares like Ansys, Solidworks, Openfoam, ADINA… are playing a key role in medecine andbiology, where researchers create virtual reconstructions of different human organs [56], surgical options [57] and blood flow [58] system, combining fluid dynamics results with a simplified model of the human body such as the vascular (figure.4) and pulmonary systems. Simulations can actually predict blood flow distribution across the arteries (figure.5) and energy losses at the possible surgical connections.

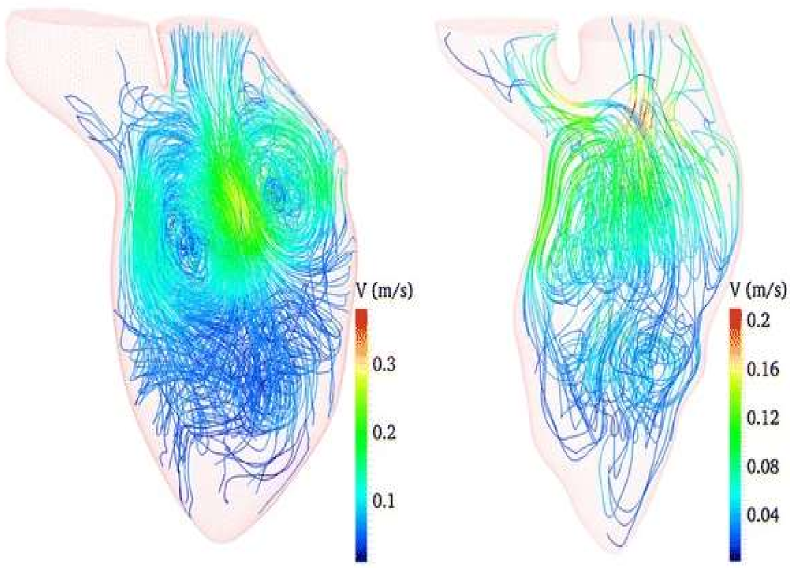

Figure.4 Exemple of CFD simulation of heart blood flow [59]

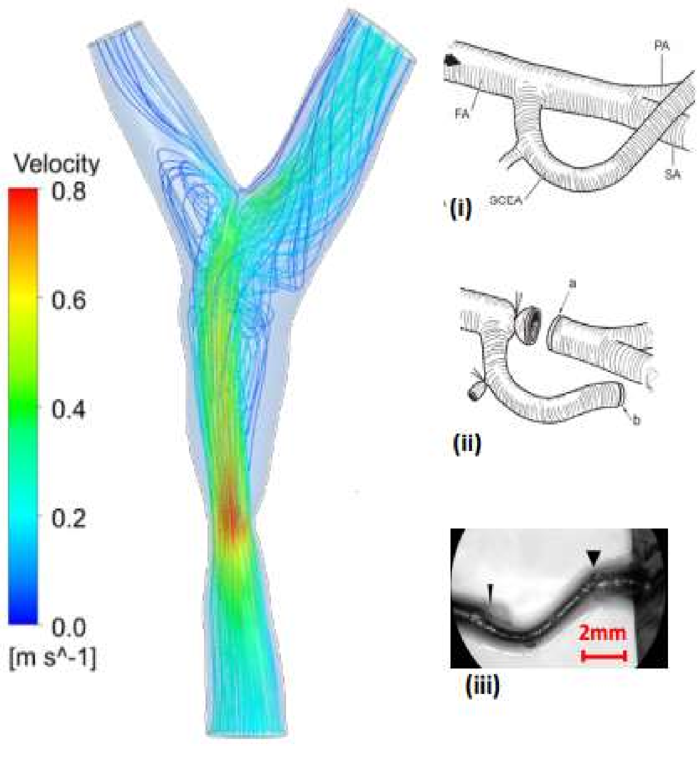

Figure.5 Exemple of CFD simulation of arterial microanastomoses [60]: (i) anatomy of the sdistal femoral artery, (ii) view prior to anastomosing, (iii) a completed anasotomosis,

5. Evaluation and Discussion of presented applications:

The objectives of this study are to critically evaluate these technologies, promote them as emerging areas of research and development for mechanical engineers and scholars, and built a real partnership between medicine, biology and mechanics.
In this review, some recent advances of mechanical engineering applications have been presented summarized in three main topics:

- Biomechanics, which ranges from the inner working of cell to the moving forces that acts on limbs, this field of study is the most investigated by mechanical engineers and scholars among other mechanical technologies. In recent years, many efforts have been devoted to enhance biomechanical research and innovation to advance the field of tissue engineering a well as sport biomechanics and bio mechanobiology.
- Nanomechanics that studies the nanoscale machinery and fluidics, is one of the emerging topics in science and technology in the last decade. Research and development in this field focuses on the introduction of nanorobotics in surgery and medical treatment. Researches done by physicians in this field need to be more audacious and creative. Nanomaterials based CNT's are expected to play an important role in medicine and biology improving the way we live by biological diagnostics using biosensors to recognize molecules and organs, the mechanical, optical, thermal, electrical and chemical properties of CNT's make them in addition to silicon nanowires the building materials for DNA delivery and proteins sensing. Therefore, research in this field is very promising for mechanical scholars.
- CFD tools to execute some simulations for blood flows, cardiovascular pumping and inertia, surgical procedure and external effect on human body. Because of the experimental data are not available, CFD simulation are more theoretic, the collaboration between medical scientists and physicians is required to conduct real-time simulations and achieve coherent results.

Mechanical engineers and scholars can refer to this review to have an overview about the recent advances of mechanical application in medicine and biology, and try to orient their studies to this issue.

6. Concluding Remarks:

This paper gives an overview to describe and understand some applications of mechanical engineering and sciences in medicine and biological sciences, diverse mechanical topics and technics have been presented including biomechanics, nanomechanics and computational fluid dynamics, these applications have proven that mechanics has a determinant role in almost emergent findings and inventions in medicine and biology.
As perspectives, as a mechanical scholar conducting researchers in nanomechanics and thermal engineering, some case studies in medicine and biology will be elaborated including CFD simulations, nanofluids and carbon nanotubes applications in collaboration with biologist and biomedical scholars.

7. Declaration of conflicts

No conflict to declare.

8. Authors' biography

No biography

9. References

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