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The Progression of Nanomaterials and the Introduction of 3D Nanomaterial Prosthetics

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ABSTRACT
Prosthetics have come a long way, evolving from their first prototypes with limited functionality to advanced computer-based systems integrated with AI and enhanced by nanomaterials. Three dimensional (3D) nanomaterial prosthetics have caught the attention of the medical community and have shown promising revolutionary advancements in prosthetic implants. Nanomaterials have become extremely versatile and applicable in many different health applications, thus researchers have explored the integration of 3D nanomaterials into prosthetics. This review provides a brief overview of the common types of nanomaterials, along with various examples and their properties. Additionally, various examples of nanomaterial prosthetics will be discussed along with any implant implementation concerns. In the end, future research on nanomaterials and prosthetics will be presented. To summarize, this review will provide readers with a brief understanding of nanomaterials and their implementation in prosthetics.
Keywords: Prosthetics, Biomaterials, Nanomaterials, Toxicity, Artificial intelligence

1 INTRODUCTION

In the field of biomedical engineering, designs referred to as prosthetics have been created to replace lost limbs for patients who have suffered accidents. Currently, prosthetics enable patients to regain their functionality, even after the loss of the limb (Karim et al., 2024).

Throughout the better part of a decade, prosthetics have made significant advancements, enhancing the experience for patients (Moisan & Zong-Hao Ma, 2024). With recent advances in the field of nanomaterials, prosthetics have become more precise. Allowing for a more functional, controllable, comfortable, and long lasting experience for its users (Gunasekaran et al., 2024).

During early stages of prosthetics, prosthetics were used for trauma incidents involving amputees that lost limbs during warfare; they were made out of leather, wood, and metal (Raschke, 2022). However, prosthetic implants were too expensive for many amputees to afford and were not widely available in their early days. At the time, prosthetics were not advanced enough to offer proper functionally, so research on prosthetics stagnated. Further advancements in technology made prosthetic research more prevalent.

This literature review aims to investigate and discuss the advancements in prosthodontics through the presentation of various research articles that have been published within the past decade. Moreover, this review will provide an in-depth analysis into the field of 3-dimensional nanomaterial prosthetics and its recent advancements. With relevance to the biomaterial field, the effectiveness of prosthetics for patients can be understood at a molecular level. This review will also provide an overview of the advancements in current research on nanomaterials for prosthetic applications, highlighting existing challenges and necessary developments required for their acceptance and use. The commercial viability will also be discussed to determine whether or not these prosthetic devices will be widely available and affordable to the public. This paper hopes to provide the most up-to-date information about prosthetics to allow for further research to improve the quality of life for patients.

2 BIOMATERIALS

When discussing any implants in the human body, the field of biomaterials needs to be considered. Biomedical engineers need to ensure that implant designs are biocompatible (Kanďárová & Pôbiš, 2024). Around 1976 AD, Dr. Jonathan Cohen defined biomaterials as any materials used for implants, such as materials consisting of plastics, metals, ceramics, and composite materials (Marin et al., 2020). Each of these materials are carefully manufactured

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into implants that are able to withstand the conditions of the human body such as the pH and temperature depending on the location within the body.

Biomaterial concepts like atomic structures, corrosivity and diffusibility are important in determining the effectiveness, and safety of designed implants. It is vital to consider these biomaterial concepts when ensuring an implant is bio-compatible, safe and effective.

Nanomaterials are an important field of research in biomaterials that has attracted the interest of many scientists and engineers worldwide. To be more specific, nanomaterials have notably been integrated into prosthetic designs. This review will further discuss the benefits and limitations of using nanomaterials in prosthetics.

3 ADVANCEMENTS OF PROSTHETIC IMPLANTS

The early days of prosthetics were not successful. Made from materials like leather, wood, and metal, these prosthetics struggled to replicate functional human motion. It was not until later that prosthetics became more popular in the healthcare sector. Starting with the basics, the development of prosthetics can be divided into four key stages.

3.1 Four Industrial Revolutions

The progress of prosthetic devices can be broken up into what is referred to as the four industrial revolutions (Raschke, 2022). These revolutions are a simple way to categorize the advancements in prosthetic implants. As expected, the first industrial revolution contained the start of limb prosthetics in healthcare. The prosthetics were made of leather, wood, and metal. These prosthetics were neither effective nor comfortable, which prevented them from gaining mainstream attention and resulted in a lack of further research and development.

The subsequent industrial revolutions consisted of technological advancements such as the storage of electrical activity, the invention of processors and computers, and the integration of biological systems with digital and electrical systems through the field of biomedical engineering (Raschke, 2022). These innovative developments led scientists and engineers to resume prosthetic limb research.

With all the technological discoveries and innovations, it has allowed for prosthetic devices to become more widely accepted and utilized. Since then, prosthetics implants have continued to improve and are now more commonly used in healthcare to enhance a patients' quality of life.

3.2 Challenges in Development

Everything that is designed and implemented has to go through multiple stages of testing before it can be considered safe and useful. In the field of prosthodontics, the complex nature and handling of prosthetics means that designs must undergo testing.

Two of the biggest challenges in designing and developing prosthetic limbs are the comfortability and functionality (Kulkarni et al., 2024). As it can be expected, it has been a challenge for engineers and physicians to create prosthetics that can restore the full range of motion and functionality that patients once had, along with providing the proper sensory feedback. On top of this, the prosthetics also need to be designed in such a way that maximizes the biocompatibility to reduce infections, potential damage to the prosthetic, and rejection from the body overall. While much progress has been made to overcome these challenges and limitations, there is still much more that needs to be done.

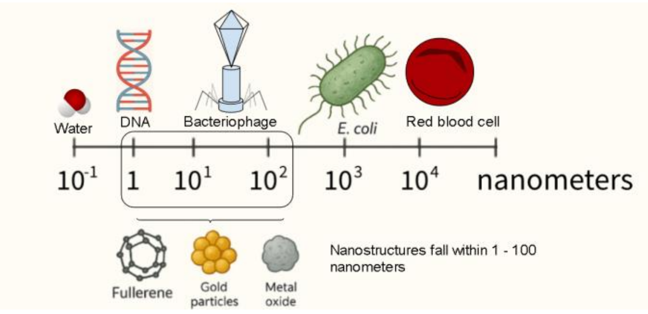

Figure 1: Size comparison of nanostructures and nanoscale biomolecules.
Adapted from (Saallah and Lenggoro, 2018), KONA Powder and Particle Journal, under CC BY 4.0 license.

4 NANOMATERIALS

Nanomaterials have gained a lot of notoriety when it comes to the designing of prosthetics. In recent years, nanomaterials are considered to have a key role in overcoming past limitations, and to revolutionize development of prosthetic devices (Karim et al., 2024).

Nanomaterials are classified as a type of material that in one dimension (width, depth/diameter, or length) has a unit length of under 100 nanometers (Sajid, 2022). Nanomaterials have a large variety of forms that are beneficial in the field of biomedical engineering, commonly classified into: organics; inorganics; carbon based nanoparticles (Ealia & Saravanakumar, 2017).

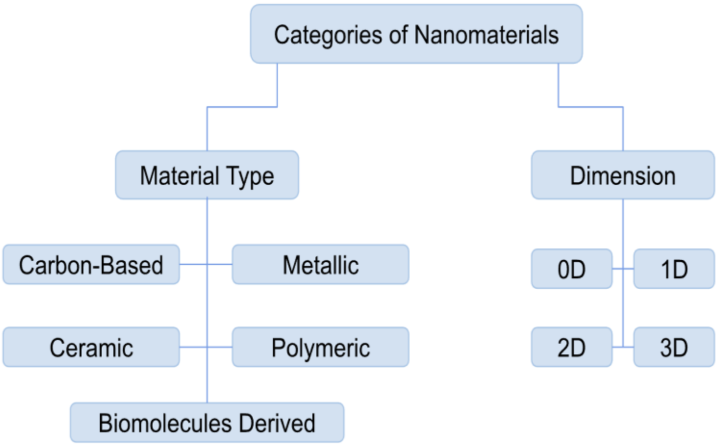

Figure 2: Categories of Nanomaterials.

4.1 Categories of Nanomaterials

There is a broad variety of nanomaterials due to their versatility. Therefore, they can be categorized in multiple ways. Nanomaterials can be classified by the type of material they are made of (Sajid, 2022). Some examples include but not limited to,

I. Carbon-based nanomaterials
II. Metallic nanomaterials
III. Ceramic-based nanomaterials
IV. Polymeric nanomaterials
V. Biomolecules derived nanomaterials

Another way to classify nanomaterials is based on their number of dimensions (Mekuye, 2023). Nanomaterials have four possible dimensions; 0D, 1D, 2D, and 3D. Each dimension refers to the number of axes in which they are not confined to the nanoscale.

For zero dimension nanomaterials, the zero indicates that none of the axes are of a macroscale, hence the length, width, and height of 0D nanomaterials are all within the length dimensions associated with the nanoscale (Mekuye, 2023). It could also be expressed with length variables as x, y, and z.

The one dimension nanomaterials have one dimension that is not of the nanoscale. This could either be x, y, or z. The same goes for two dimensions and three dimensions where two coordinates are not of the nanoscale, and three coordinates are not of the nanoscale respectively. It is important to note while some of these lengths in bulk materials extend beyond the nanoscale, they are not necessarily confined to it; the individual components that make the material are still small within the nanometer range (the materials are composed of individual nanoparticles).

To summarize, nanomaterials are categorized based on the materials they are made of along with their dimensionality, and various combinations can lead to different resulting materials that can be used for various purposes. The types of materials that are used are arguably more important than the dimensions when it comes to biocompatibility and implementing nanomaterials in prosthetics.

4.2 Carbon-based Nanomaterials

Carbon-based nanomaterials have become popular within recent years due to the many different forms that carbon can take (Maiti et al., 2019). These types of carbon-based nanomaterials have many biomedical applications, making them good candidates for use in prosthetic implants.

Some of the recent carbon-based nanomaterials that have grabbed the attention of scientists and engineers are carbon nanotubes (CNTs), graphene, and nanodots (Sajid, 2022). The graphene and nanodots may also be referred to as graphene oxides (GO) and graphene quantum dots (GQDs) respectively. Each of these materials have applications in biosensors, drug delivery, and cancer therapy. In this review, the focus will be more on biosensors in relation to prosthetics.

Carbon nanotubes have high aspect ratios, conductivity, chemical stability sensitivity, and electron transfer rates, making CNTs a clear candidate for biosensors in prosthetics (Maiti et al., 2019). CNTs typically have one length dimension that is not of the nanoscale (Sajid, 2022). This indicates that CNTs are one dimensional (1D) nanomaterials. CNTs work to immobilize biomolecules on their surfaces which enhances any recognition and signal transductions.

Graphene oxides are able to interact with probes along with the transduction of specific responses towards target molecules. The transduction process is achieved through fluorescence, Raman scattering and electrochemical reactions (Maiti et al., 2019). This is the basis in which GOs are able to act as biosensors. This makes them another good candidate for prosthetics. Graphene is considered to be an one-atom thick sheet of carbon atoms (Sajid, 2022). This means that two dimensions are not of the nanoscale, indicating that graphene is a 2D nanomaterial.

Finally, the graphene quantum dots act in a similar way to GOs, as the basis for their photoluminescence and electrical chemiluminescence. Due to these properties, GQDs can be used for sensing bio-macromolecules (Maiti et al., 2019). GQDs are zero dimensional carbon particles which means that all of its dimensions are confined to the nanoscale (Sajid, 2022). This property allows GQDs to have the potential to be modified into many different structures for various applications.

As useful and advanced as carbon-based nanomaterials are, carbon-based nanomaterials have been shown to have numerous cellular toxicity effects which hinders their progress in health care implementation (Madannejad et al, 2019). Some of the toxic effects that carbon-based nanomaterials have shown are:

- neurotoxicity
- hepatotoxicity
- nephrotoxicity
- immunotoxicity
- cardiotoxicity
- genotoxicity and epigenetic toxicity
- dermatotoxicity
- carcinogenicity

As it can be seen, more research needs to be done in order to either negate or remove these effects of carbon-based nanomaterials. Until then, this may not be a suitable option without putting patients in danger.

4.3 Metallic Nanomaterials

Metallic nanomaterials are one of the strongest candidates to use for prosthetics as they are typically used to enhance biosensors (Wang et al., 2022).

A lot of the metals that are commonly used are titanium dioxide, iron(II, III) oxide, manganese dioxide, zinc oxide, cobalt(II, III) oxide, gold, silver, platinum, and palladium.

Numerous of these metals have also been shown to have an antimicrobial effect (Sajid, 2022). These metals will have the ability to act as alternative antibacterial agents which will be useful to prevent complications when implanting a prosthetic device.

Due to the wide variety of metals that can be used, it becomes hard to clarify whether or not metallic nanomaterials pose a threat to a patient's cellular health since each material can have its own effect. For example, gold has had conflicting research that suggests it may be biocompatible with little toxicity worries, but some other research has found gold's physicochemical properties could be toxic (Sengul & Asmatulu, 2020).

Some other metals such as cobalt and titanium dioxide have been determined to be potentially carcinogenic and have the ability to damage DNA. Unless there are specific metals that have no negative effects, it is difficult to say metallic nanomaterials are a safe option for prosthetic implants.

4.4 Ceramic-based Nanomaterials

Another common type of nanomaterial are ceramic-based nanomaterials. Ceramic-based nanomaterials are generally non-metallic inorganic materials with various forms (John et al., 2023). Due to their size within the nanoscale, they have a high hardness and an increased resistance to heat and corrosion. These properties allow ceramic-based nanomaterials to have many applications in biomedical fields; within the field of prosthetics, ceramic-based nanoparticles play a significant role in orthopedics.

Similarly to metallic nanomaterials, ceramics have a wide range of effects (John et al., 2023). Some ceramic nanomaterials have no inherent toxicity, but have other effects such as increasing the calcium content in the body through calcium phosphate nanoparticles. Some other ceramic nanomaterials can cause cytotoxicities such as mesoporous silica, but otherwise the effects do not seem as severe as carbon-based and metallic nanomaterials.

4.5 Polymeric Nanomaterials

Another class of nanomaterials are called polymeric nanomaterials. These materials have been observed to have the potential to address some of the challenges in medicine, with one of the most important being the enhancement of therapeutic effects (Yoon, 2023).

Polymeric nanomaterials have a significantly high surface area to volume ratio, thus able to act as good optical, thermal, and electrical sensors (Sajid, 2022). They have also been shown to be useful as nanoparticulate probes for improving diagnostic and therapeutic techniques (Yoon, 2023).

Polymeric materials, commonly used for drug delivery, are made of biodegradable and biocompatible polymers. As a result, they are preferable over other nanomaterials due to their controllable biodegradability and biological safety to the environment (Sajid, 2022).

While polymeric nanomaterials have high biodegradability and biological safety, they are not completely toxic-free. Polymeric nanomaterials have been linked to potentially cause cytotoxicity and genotoxicity (Sairam et al., 2023). This makes it clear that while polymeric nanomaterials have various benefits, they still need to be used carefully in biomedical applications due to their potential toxicity effect in the human body. Polymeric materials typically have at least one dimension in the range of 1 to 1000 nm which makes them highly modifiable. This allows them to be in the form of any of the dimensions listed earlier, thus making them a good candidate to use in 3D nanomaterial prosthetics.

4.6 Biomolecules Derived Nanomaterials

The final common category of nanomaterials are biomolecule-derived nanomaterials. These are nanomaterials that are created from biomolecules such as proteins, lipids, polysaccharides, nucleic acids, and more (Sajid, 2022).

These types of nanomaterials have always been insignificant compared to the others but in recent years, they have gained a lot of attention due to their increasing applications of biocompatibility and biodegradability. These new types of materials could revolutionize the field of biomaterials.

An important area of research for biomolecule-derived nanomaterials is the combination of biomolecules with other inorganic materials such as metal and polymers (Saallah and Lenggoro, 2018). Organic molecules may also be combined with molecule-derived nanomaterials to create composite nanomaterials. Combinations of different types of nanomaterials can possibly lead to overcoming many limitations that were once a problem.

Some of the problems that arise from biomolecules-derived nanomaterials are degradation and possible rejection from the body causing an immune response (Datta et al., 2020). Certain chemical modifications can overcome these limitations, but further research is required to ensure the safety of biomedical devices implanted when using these materials.

Biomolecules-derived nanomaterials arguably are the most diverse and useful as they can be combined with all other nanomaterials discussed earlier, leading to composite nanomaterials. This could potentially lead to many of the benefits of the previously discussed nanomaterials to be combined, which may encourage the use of nanomaterials in prosthetics even more.

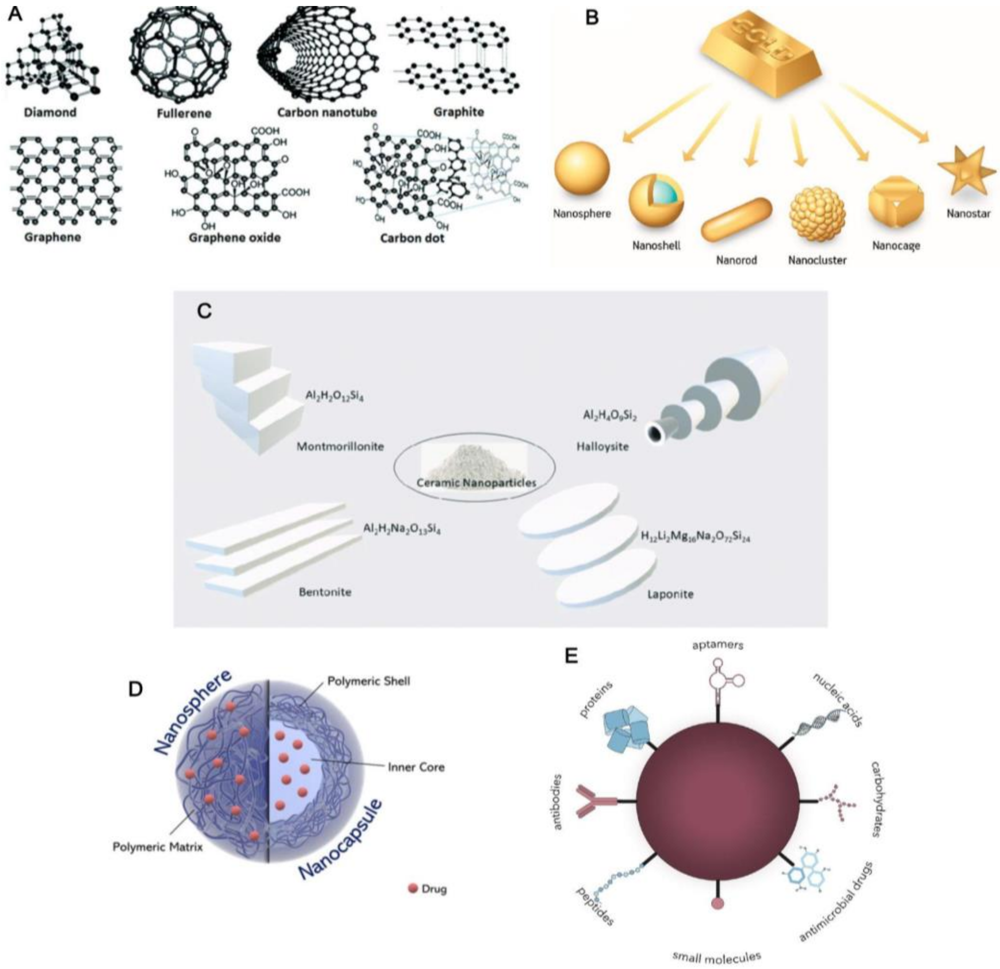

Figure 3: Example of common nanomaterials: (A) Various carbon-based nanomaterials. Reused under CC BY 3.0 license (Yan et al., 2016): (B) Various metallic nanomaterials made from gold. Reused under CC BY 4.0 license (Freitas de Freitas, 2018): (C) Examples of ceramic nanomaterials. Reused with consent from (Mobaraki et al., 2022): (D) Structure of common polymeric nanomaterial used for drug delivery. Reused under CC BY 4.0 license (Gagliardi et al., 2021): (E) Common biomolecules used for nanomaterials. Reused with consent from (Spirescu et al., 2021).

5 3D NANOMATERIAL PROSTHETICS

In recent years, research in prosthetic limbs has exponentially increased. One such area is the use of three-dimensional nanomaterials to design prosthetics (Karim et al., 2024). Recent research in this new area for prosthetics can revolutionize the rehabilitation for people who have lost their limbs due to accidents or trauma. This new research may help improve the performance of implants and overcome past limitations.

5.1 Types of Prosthetics and Potential Nanomaterial Candidates

Recall that there were two ways to categorize nanomaterials; the material they are made of, and the dimensions. In this article, only the 3D nanomaterials will be considered.

Recall that every type of nanomaterial discussed in this article has a variety of effects. Depending on the effects, some may be desirable while others not so much. However, the preference of one nanomaterial over another is also dependent on the type of tissue or limb that is being replaced.

One such important prosthetic is neural materials. These types of prosthetics would require the use of biosensors such as nerve sensors in order to recover a patient's sensory functions. Nerve sensors can be manufactured from nanomaterials using carbon-based nanomaterials, metallic nanomaterials, and composite nanomaterials such as metal-polymer mixes (Tan et al., 2022). Many of the materials listed here are able to act as sensors and detect even subtle movements such as skin epidermal movement. This could improve the functionality of the prosthesis and help the patient regain their mobility. Many of the materials listed are also stable, stretchable, have high sensitivity, have low consumption, and more.

Another important prosthesis is for the skin. Nanomaterials that can be used for skin prosthetics are common carbon-based, metallic, and composites (Tan et al., 2022). Carbon-based nanomaterials are good for creating "electronic skin" (e-skin) which is a good imitator. Due to the strain sensitivity, the e-skin can have a wide range of tensile and compressive stimuli. The metallic nanomaterials are able to aid in physical flexibility and various metals such as zinc oxide nanorods can also measure the temperature. As for the composite nanomaterials, they can imitate the look of human skin including all the structures and the mechanical and tensile properties. As for the nails, if the prosthetic is for the hand, some composite materials such as silane and keratin derivatives can be used to imitate the nail.

Finally, another important use of nanomaterials in prosthetics is to replace bone material. Skeletal material is typically used in prosthetics for support which means high rigidity and may be particularly heavy (Tan et al., 2022). For bone materials, the preferable nanomaterials are polymeric nanomaterials like fibre nanomaterials, metallic nanomaterials, and composite materials. The important aspect of any nanomaterials used for bones is that they should have extremely high hardness, a good weight, and a lot of toughness to properly represent the bone. A commonly used material is Agave fibre with its unique features of high biodegradability and strong mechanical properties. Agave fibre is then commonly used as a socket joint. Metallic and composite materials such as Ti-Ta have high strength and ductilities, and low modulus with exceptional biocompatibility. This type of composite is used for bearing applications.

All in all, it can be seen that every nanomaterial that was listed earlier in this article has been shown to be incredibly useful for many different prosthetic applications. Each one provides their own unique benefits and has their own purpose in such implants. In terms of 3D nanomaterial prosthetics, every nanomaterial listed in Table 1 could play a role in this new area of research.

Table 1: Potential Candidates for 3D Nanomaterial Prosthetics.

Nanomaterial	Benefits	Limitations	References
Carbon-Based	Many biomedical applications such as biosensors, drug delivery, and cancer treatment.	Various dangerous toxicity effects along with carcinogenicity.	(Sajid, 2022; Maiti et al., 2019; Madannejad et al, 2019)
Metallic	Can act as very good biosensors and various metals can be used. Can possess an antimicrobial effect as well.	Many metals can be carcinogens and damage DNA.	(Wang et al., 2022; Sajid, 2022; Sengul & Asmatulu, 2020)
Ceramic-Based	High hardness and increased resistance to heat and corrosion.	Many ceramics may have negative effects and are cytotoxic.	(John et al., 2023)
Polymeric	Good for sensors and improving therapeutic techniques. Good controllability for biodegradability and biological safety.	Potential cytotoxicity and genotoxicity effects.	(Yoon, 2023; Sajid, 2022; Sairam et al., 2023)
Biomolecules Derived	Good controllability for biodegradability and biological safety. Useful to combine with other types of nanomaterials.	Degradation and potential rejection from the body.	(Sajid, 2022; Saallah and Lenggoro, 2018; Datta et al., 2020)

5.2 Biocompatibility in Nanomaterials

Biocompatibility has been defined in various ways depending on the context and focus of different studies. There are five main definitions of biocompatibility, stated down below.

I. Dorland's dictionary: Not having any toxic or harmful effects.
II. Williams dictionary: Works without causing bodily harm.
III. Williams on biomaterials: Safely performs its intended function without any undesired effects while achieving the best possible responses.
IV. ASTM: Biocompatibility is assessed as how the localized tissue reacts to a new implant material in comparison to a known safe control material.
V. International dictionary of medicine and biology: Coexisting without causing deleterious changes.

The Dorland definition is contrasted with the William's Dictionary, as it does not address any positive interactions between the body and materials. The second William's definition is a more precise definition of the first, acknowledging that the same materials may have different demands depending on the application. The ASTM contrasts William's definition, as it only focuses on the host's local tissue responses; thus, taking a more comparative approach rather than considering functionality and performance.

Given these perspectives, this study adopts a working definition of biocompatibility as the international dictionary's version of biocompatibility; aligning with the focus of nanomaterial-based prosthetics.

Several studies have shown that certain nanomaterials have been found to correlate with several biological properties. These properties include: anti-inflammatory, antimicrobial, moisture absorbing and retention, and colloidal (Khan et al., 2015; Kushwaha et al., 2022; Mihai et al., 2019). Such properties are essential for prosthetic implants, for which materials directly interact with biological tissues; nanomaterial-based prosthetics have high contact surface area and unique chemical properties. To summarize, antimicrobial and anti-infection properties, and improved wearing and durability are key factors for biocompatibility, as explained by the previously adopted definition. Current studies have focused on antimicrobial properties of nanomaterials and bio-film, focusing on reduction of infection chances (Sahoo et al., 2022).

If a biomaterial is not biocompatible, rapid issues may occur such as the triggering of an immune response, inflammation, toxicity, rejection, which could lead to further issues such as irreversible cell injury, ultimately resulting complete cell death through apoptosis or necrosis (Aljabali et al., 2023; Bahadar et al., 2016).

Therefore, it is significant to ensure biocompatibility with nanomaterial-based prosthetics to help minimize adverse effects, enhancing integration with the body, improving longevity and performance of prosthetics.

Conversely, several challenges have been identified concerning the biological properties of nanomaterials and their correlation with specific nanomaterial features (Kyriakides et al., 2021). These features include size, functionalization, protein binding tendency, composition, surface charge and shape.

5.3 Concerns Regarding Nanoparticles for Prosthetic Devices

In healthcare and medicine, it is widely recognized that anything beneficial to a patient's recovery often comes with potential downsides. For example, medication typically has side effects for its users. Nanomaterial prosthetics are no exception.

The use of nanoparticles in devices has been subject to criticism. According to some toxicology reports and literature, such as reports done by Hasan at al. (2018), it is reported that some nanoparticles cause damage to surrounding tissue, raising safety concerns. Such concerns include the accumulation and secretion of elements from implanted prosthetics. Due to wear caused by repetitive motions over time, materials may degrade, leading to the release of potentially harmful nanoparticles. Specific nanoparticles such as metal oxides, carbon-based, silver, are all examples of materials that bring concerning health and safety risks (Bahadar et al., 2016). These can lead to reactive oxygen species causing oxidative stress. As nanoparticles are increasingly introduced into the fields of biomedicine and biotechnology, it is essential to consider long-term effects. The long-term effects of nanoparticles on human tissue are not well understood, and is a topic that needs more research for further understanding (Najahi-Missaoui et al., 2020).

Furthermore, while nanomaterials have initial beneficial effects on prosthetic wear resistance and durability, several issues have been found in the incorporation of nanoparticles in materials (Mitrano et al., 2015; Pfohl et al., 2022; Saharudin et al., 2016). These concerns include the degradation of nanoplastic fragments. Considering the previously mentioned health risks of nanomaterials, it can be concluded that nanoparticles used to reinforce prosthetics may degrade over time. This degradation is caused by wear from repetitive and external stresses, such as exposure to liquid media, sunlight, abrasion, and others. (Mitrano et al., 2015; Saharudin et al., 2016). This can lead to the release of potentially harmful particles into the body.

Overall, studies highlight the necessity for research on the long-term effects of nanomaterials on the mechanical integrity of prosthetics and nanoparticles, as well as the health implications of exposure.

5.4 Benefits of Nanomaterials in Prosthetics and Osseointegration

In the field of prosthodontics and bone scaffolding, osseointegration is the process in which bone cells grow onto the surface of an implant, increasing stability and security within the human body; thus allowing implants to successfully function similarly as bone (Jayesh & Dhinakarsamy, 2015). Within the field of prosthodontics, bone integration is essential for ensuring that dental implants are compatible with teeth (Pandey et al., 2022).

Building bone is possible due to the bone matrix, which is primarily composed of collagen fibers and mineral calcium apatite, serving as a scaffold. The scaffold allows cells to: attach to other cells in the matrix, communicate with other cells, play an important role in cell growth (in the case of osseointegration, osteoblasts and other bone-building cells), cell movement, and specific cell functions (Hasegawa, 2018).

Within implants, nanotechnology offers unique advantages compared to traditional materials. The advantageous properties include primarily their size and surface, as well as the ability to enhance certain biological interactions. Some benefits include improved osseointegration, increased surface area for greater interaction, enhanced mechanical properties, antibacterial properties, and bioactive coatings (Li et al., 2024; Raymond et al., 2024; Wu et al., 2020; Yeo, 2019).

Research studies, such as ones done by Farjaminejad (2024) show that inorganic nanoparticles, such as ceramic, carbon-based, and metal nanoparticles are promising for advancements in implants (Farjaminejad et al., 2024). This results from the biocompatibility of certain nanoparticles and how they interact with biological tissues. For example, ceramic nano hydroxyapatite (Nano-HA) acts similar to bone components, while metallic nanoparticles like gold nanoparticles, offers strength, durability and low toxicity. As mentioned in Farjaminejad's research, various nanostructures are capable of mimicking the extracellular matrix (ECM), playing a crucial role for bone building. Furthermore, these nanoparticles demonstrate improvements in mechanical properties, and rapid cell proliferation, as well as restricting osteoclasts from breaking down bone.

Overall, bone integration is essential for implants to bond with bone and function properly. Nanomaterials have the potential to enhance osseointegration, improve mechanical properties, and promote bone regeneration, making them excellent candidates for implants.

5.5 Benefits of Nanomaterials in Soft Tissue Integration

Within the field of biomedical engineering, soft tissue integration is a fundamental aspect of implants in orthopedic and prosthetic reconstruction. It refers to the process by which soft tissue (such as skin, ears, breasts) adhere and interact with implant surfaces, forming stable and functional connections. Integration is important for preventing infection, mechanical stability, and enhancing comfort and function (Sharma et al., 2024). Moreover, as nanotechnologies continue to improve implant surface properties, it shows the capability of enhancing cellular adhesion, protein absorption, and compatibility, leading to faster healing and stable tissue attachment.

Nanomaterials play various roles in prosthetic development, such as coatings to improve adhesion to soft tissues, reducing irritation, and overall improving comfort. Specific nanomaterials such as hydrogel-based nanomaterials, help create biocompatible interfaces between the prosthetic and residual limb (Elkhoury et al., 2019). The advantages of nanoparticles include their size, which help to mimic tissue and maintain cell architecture. Electrical conductivity of nano-hydrogels induce cell-to-cell signaling, which is important for cell proliferation and functionality. Other physical properties help to replicate and tune mechanical ability of soft tissue, including elasticity; mechanical ability is important in determining wear resistance, load bearing capacity, and structural support (Angelopoulou, 2024).

Furthermore, nanostructured coatings have additional features such as resistance to water (moisture-wicking), odor, heat (friction), stains, UV-protection, and aforementioned antimicrobial properties (Syduzzaman et al., 2023). This enhances comfort and durability by extending the lifespan of implants and reducing skin irritation caused from heat and moisture (Voegeli, 2020). Overall, soft tissue integration is a critical factor for the success of implants. Advances in nanomaterials, particularly hydrogel-based nanomaterials, enhance the process of cellular adhesion and biocompatibility.

5.6 Increasing Wear Resistance and Durability with Nanomaterial Science

Ensuring there are no complications in prosthetic devices is crucial in improving patient health. Experimental studies done by Haberg (2023) say that preventing complications reduces the need for revision surgeries, and enhances the quality of life. More specifically, Hagberg's studies state that wear resistance and durability are factors in ensuring reliability of implants, reducing mechanical complications and resulting infection (Hagberg et al., 2023). Implants are often subjected to repeated mechanical stress and friction from all directions during motion (Tak et al., 2023). Advances in nanomaterial science offer new advancements in orthopedic implants, enhancing structural integrity and surface properties of materials (Liang, 2024). By incorporating nanomaterials, researchers can develop prosthetics that are longer-lasting and more effective.

Used nanomaterials that help to improve prosthetics include nanostructured ceramics, diamond-like carbon (DLC), and titanium-based nanocomposites (Gautam et al., 2022; Ramezani & Ripin, 2023). Wear resistance, a critical factor in longevity of implants, is important for load-bearing implants such as lower body replacements (hip, knee). DLC coatings, ceramics, and various composite structures offer high hardness and strength, smooth surfaces to reduce friction, reduced crack propagation, and maintained flexibility. As a result, this allows for the improvement of wear resistance and integrity.

These effects come from key mechanisms in certain nanomaterials, including grain refinement and load transfer mechanism due to size, shape, surface area (interstitial substitution); high surface energy (leads to smaller grains), and other various properties (Chen et al., 2019; Pu et al., 2024; Vollath et al., 2018).

Overall, incorporating nanomaterials into implants significantly enhances resistance and durability. Certain nanomaterials provide key properties such as hardness, low friction, and crack resistance. By utilising properties of certain nanomaterials such as refined grains, these implants have potential for longer-lasting, effective prosthetics.

5.7 Nano-based Sensors and Adaptive "Smart" Prosthetics

Within the field of engineering, sensors are devices that record and respond to values given from physical properties. Advancements in nanoscience have improved sensor capabilities, enabling faster and more precise detection and response. "Smart" prosthetics can then respond to these values accordingly, thus making sensors a significant aspect for biomedical engineers.

Nano-based sensors are devices that incorporate nanomaterials. These nanomaterials are capable of creating technology that detect and measure various parameters: pressure, temperature, and motion. This is due to the properties of certain nanomaterials, which will be further discussed later in this section. Nano-based sensors are highly sensitive, and capable of providing fast feedback, making them ideal for integration into advanced "smart" prosthetic devices. These implants are capable of responding to an user's movements, often using signals from remaining muscle and nerves (Khoshmanesh et al., 2021; Peng et al., 2020).

Nanomaterials such as metallic nanoparticles like carbon nanotubes (CNTs) and silver nanowires, graphene and its derivatives, metal carbides, and other composites are practical for sensor manufacturing. Studies highlight several advantages, including sustainability, controllable size and diameter, efficiency, and easy operation (Godja & Munteanu, 2024; Peng et al., 2020). These advantages come from properties like high surface area-to-volume ratio, and electrical conductivity, which are essential for enhancing sensor performance and sensitivity. Additionally, studies state that this shows potential for integrating tactile sensation to wearable implants, as nanomaterials like gold nanoparticles change in conductivity in response to pressure (Chun et al., 2019; Iyer et al., 2025; Su et al., 2022).

Overall, nano-based sensors play a crucial role in enhancing the ability of smart prosthetics, providing real-time feedback and response. The unique properties of nanomaterials such as CNTs and graphene, including high surface area and conductivity, offer significant advantages for detecting physical parameters. Furthermore, nanoparticles are highly scalable, making them ideal for sensors. These properties contribute to the development of smart prosthetics, allowing the integration of tactile sensation and motion detection for implant users.

5.8 Neuroprosthetics and Nanotechnology

Previously mentioned sensors can also be adapted to the nervous system. More specifically, nanosensors are implemented into brain-computer interfaces (BCIs), being able to produce external electrical stimulations through nerve or brain activity. The field of nanosensors in implants is aptly known as neuroprosthetics. These devices can be substituted for motor, sensory, or cognitive restoration, targeting damaged structures that have previously been impaired by nervous system disorders and injuries, such as Parkinson's disease or stroke, respectively. (Karim et al., 2024; Mendes et al., 2020; Milekovic et al., 2023). Once again, the ability to integrate neurosensors into neural networks comes from properties such as large surface area and tunable electroconductivity.

Nanomaterial properties give the ability to stimulate electronic response within nerves (as well as the brain), activating efferent axons that send messages to targeted muscles, known as functional electronic stimulation, or FES. Furthermore, FES is a clinically approved process that provides the ability to trigger neuroplasticity (forming new neural connections) when used in cortical implants (Gupta et al., 2023).

Other devices used are also BCIs, which involve the implementation of sensors within the brain. BCIs can read brain activity signals and convert them into commands which can control external devices, such as controlling the movement of computer cursors (Gao et al., 2021). Specific nanomaterials used in neuroprosthetics include silicon probes, capable of recording neurons within the brain (Ceyssens et al., 2019; Gupta et al., 2023). As previously mentioned in other sections, nanomaterials play a crucial role in BCIs and FES, due to their properties: improving signal processing and quality, biocompatibility, scalability (miniaturization, which is important to reduce bulkiness of external components, or in the brain), density and, etc.

Ultimately, the integration of nanosensors into prosthetics including BCIs and FES, demonstrates the potential for improving functions. However, as neuroprosthetics are a novel researching topic, it is important to signify that more studies need to be done in order to gain proper insight into the viability of neuromaterials and the advancement of neuroprosthetics.

5.9 Commercial Viability of Prosthetics

In 2019, the projected costs for nanomaterials in the global market was approximated to be 8.5 billion US dollars (Pandey & Jain, 2020). This is due to the implementation of nanotechnologies into various applications, within industrial, biomedical, and other various fields. However, while the use of nanoparticles rises, the synthesis of nanoparticles is generally known to be expensive. Additionally, environmental risks and toxicity of certain nanomaterials contribute to hesitancy in the production and manufacturing of nanostructures, thus causing conflict and resistance for commercialization.

The cost to implement nanomaterials in the designs of prosthetic devices is still heavily unknown due to the sheer amount of research that still needs to be done. This was evident due to the lack of other journals covering these specific costs. However, prosthetics generally seem to be quite expensive with an example of microprocessorcontrolled knee prosthetics ranging from €15,000 to €39,000 or $23349.97 CAD to $60709.93 CAD (Donnelley et al., 2021). From this cost, it's clear that more improvements need to be made in order for prosthetics to be more affordable to the general public.

Overall, due to the advancements made in nanotechnology, the adoption of these nanomaterials into medical sectors continue to keep projected costs growing. The use of specific nanostructures and particles, such as titanium metals and carbon nanotubes are used in other various applications outside of biomedical engineering. The commercial viability of implementing nanomaterials into prosthetics is currently not well known and will need more time and research to determine accurate market growth (Karim et al., 2024).

6 FUTURE RESEARCH

Prosthetics have come a long way from their first prototype. They have become increasingly useful in rehabilitation for patients who have lost their limbs due to unforeseen circumstances. However, the research in prosthetics is only constantly growing. With further research, such as in 3D nanomaterial prosthetics, a new age of prosthetics is soon to arrive, allowing patients to fully regain their quality of life.

6.1 Future Research for Nanomaterials

Since nanomaterials is a fairly new area of research, it is not surprising that new discoveries and improvements are being constantly made. As stated earlier in this review, nanomaterials need more research on how to be better implemented as prosthetics. One example is the use of nanomaterials in therapeutic contexts to increase osteogenesis and improve osseointegration for implants (Abaszadeh, 2023). This approach applies to many other types of implants that can be improved.

Some of the future designs that researchers are currently tackling with nanomaterials are tiny transistors, quantum computing, and nanophotonics which will pave the way for nanomaterials to be more prevalent in biomedical engineering (Abaszadeh, 2023). Manipulating atoms at the nanoscale is also expected to allow scientists and engineers to improve the mechanical, thermal, and electrical properties of future designs, allowing for more efficient procedures.

6.2 Artificial Intelligence in Nanomaterials and Prosthetics

In the modern age, artificial intelligence (AI) has become a big component in many applications. AI has even made its way into healthcare, where it promotes the use of technology and human-machine interaction to aid in the rehabilitation and/or recovery of patients (Chopra & Emran, 2024). Prosthetics are no exception when it comes to AI implementation.

AI has been shown to be incredibly useful in the field of material science as it has reduced the need for trial-and-error along with providing the most suitable and effective synthesis routes (Zhu et al., 2023). Thus, AI can be an important tool in the synthesis of various nanomaterials used in prosthetics. In short, researchers have utilized machine learning algorithms to optimize the synthesis process of nanomaterials for biomedical applications.

Implementing computer based systems in prosthetics was first done in the 1990s when a prosthetic knee was implemented with a microprocessor (Chopra & Emran, 2024). This was considered one of the first "intelligent" prosthetic devices and was even sold commercially. This type of development only increased in the coming years.

AI enhanced rehabilitation in a way that many of the prosthetic devices expected in the future may be mind-controlled, similar to how a normal functioning limb operates (Chopra & Emran, 2024). With this type of technology, prosthetic limbs will become close to completely replacing lost limbs, offering comfortability and full functionality, as if the limb had never been lost.

6.3 Reducing Toxicity and Negative Effects

While the incorporation and contribution of nanomaterials to healthcare has been beneficial, it is important to remember that there are still potential risks involved. Recall, one of the biggest limitations of using nanomaterials in prosthetics is their potential toxicity, along with other potential negative effects such as carcinogenicity and DNA damage (Madannejad et al., 2019; Sengul & Asmatulu, 2020; John et al., 2023; Sairam et al., 2023). One future perspective is instead of focusing on implementing nanomaterials as much as possible into prosthetic devices, they can instead be used to enhance desired effects of the prosthetics without direct implementation (Liang, 2024). This can reduce the amount of nanomaterials that will end up floating inside the human body, which will reduce the chances of toxicity effects and carcinogenicity.

7 CONCLUSIONS

1. Nanomaterials have been shown to be a rapidly increasing area of research due to their potential in many different healthcare applications.
2. Since nanomaterials are as small as 1 to 100 nanometers in various dimensions, they have piqued the interest of many scientists and engineers due to their ability to be modified into many different shapes and sizes at the nanoscale.

3. There are risks associated with implementing nanomaterials in biomedical applications. In general, many nanomaterials have shown to produce toxicity effects, such as cytotoxicity, genotoxicity and carcinogenicity, when implanted in the human body.
4. Nanomaterials have been shown to provide benefits in prosthetics, osseointegration, and soft tissue integration. They have also been shown to improve wear resistance and durability, which will increase the longevity of all implants. Finally, they improve computer-human interaction, including connections with the nervous system, which can lead to better rehabilitation outcomes for patients. However, the full scope of nanomaterials' effects on the human body is still not understood well, and more research is needed for a better understanding.
5. Nanomaterials and prosthetics are an expanding market with strong commercial potential, high costs remain a barrier for middle-class accessibility. Since the market for nanomaterials and prosthetics is relatively new, more time is needed to better understand its full commercial viability.
6. Some of the most prominent future developments are using nanomaterials to create better computer components such as tiny transistors, quantum computing, and nanophotonics. Since computer-human interactions have been shown to be helpful in healthcare, the implementation of AI in nanomaterials and prosthetics have also been considered as a future goal.
7. Based on the past research presented in this article, we believe that nanomaterials will become an integral part of medicine and biomedical engineering. Based on the current limitations and the potential that nanomaterials have, more research should be conducted in these areas:
    a. Reducing the negative effects while increasing the benefits.
    b. Using nanomaterials to combat terminal illnesses.
    c. Improve physical properties to optimize their applications with prosthetics.
    d. Using artificial intelligence to benefit nanomaterials.
    e. Determining more material candidates for 3D nanomaterial prosthetics.

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