

## REVIEW ARTICLE

## Influence of porous structures on the degradation behavior of additively manufactured magnesium and magnesium alloy orthopedic implants

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**Citation:** Zeng H, Huang H, Li Q, Song C, Wang L, Fan Y. Influence of porous structures on the degradation behavior of additively manufactured magnesium and magnesium alloy orthopedic implants. *Mater Sci Add Manuf.* 2026;5(1):025290063. doi: 10.36922/MSAM025290063

**Received:** July 15, 2025

**Revised:** August 11, 2025

**Accepted:** August 12, 2025

**Published online:** October 7, 2025

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### Abstract

The escalating incidence of bone defects has prompted a substantial demand for orthopedic implants, and additively manufactured biodegradable porous magnesium and magnesium alloy orthopedic implants have demonstrated significant potential for clinical applications. However, the mismatch between degradation-induced changes in mechanical properties and tissue regeneration remains a major challenge hindering their applications. As porous structure is a critical factor influencing the degradation behavior of magnesium/magnesium alloy orthopedic implants, this study aims to comprehensively review the current state of research in this area. The degradation behavior of magnesium/magnesium alloy orthopedic implants has been investigated using both experimental and numerical simulation methods. Degradation experiments have enabled direct observations of the influences of structures on degradation behavior and underlying mechanisms. Numerical simulations have been employed to analyze the stress and strain distributions within the structure during degradation and surrounding tissue regeneration, facilitating the investigation of the “structure-stress-tissue regeneration” regulation on degradation. Porous structures play critical roles in regulating mechanical properties, bearing physiological loads, and establishing a localized mechanical microenvironment of magnesium/magnesium alloy orthopedic implants. Design variables, including porosity, specific surface area, pore size, shape, and interconnectivity, influence the macroscopic mechanical properties, structural deformation, stress distribution, and contact with surrounding tissues, thereby regulating degradation behavior and tissue regeneration of implants. However, models that quantitatively describe the “porous structural variables-degradation-tissue regeneration” interaction remain to be developed. This study systematically summarizes the influences of porous structures on the degradation behavior of additively manufactured magnesium/

magnesium alloy orthopedic implants and the “structure-mechanics-degradation-biology” interaction mechanisms. This review provides a systematic understanding of the state-of-the-art research and future directions to guide the development and applications of orthopedic implants.

**Keywords:** Magnesium alloy; Porous orthopedic implants; Microstructures; Degradation behavior; Tissue regeneration

## 1. Introduction

The global incidence of bone defects resulting from trauma, bone tumors, infection, and osteoporosis is escalating annually, affecting over 20 million individuals per year.<sup>1,2</sup> In China, the number of newly diagnosed cases of bone defects exceeds 3 million yearly.<sup>3</sup> This rate is projected to further increase with the growing global aging population.<sup>4</sup> Bone repair surgery offers an effective means to restore or replace damaged bone tissues and facilitate their functional recovery. Autologous bone grafting, considered the gold standard in clinical bone defect repair, remains a widely applied surgical approach.<sup>5</sup> However, the application of autologous bone grafting is limited by donor site morbidity, restricted availability of graft material, and prolonged surgical duration,<sup>6,7</sup> potentially leading to extended post-operative pain for patients.<sup>8</sup> Compared with autologous bone grafting, orthopedic implants offer a broader range of sourcing options for bone tissue repair and replacement.<sup>3</sup> Orthopedic implants can overcome the limitations of autologous grafts, such as donor site morbidity and limited availability, leading to increased interest and broader applications.

The escalating incidence of bone defects has generated a substantial demand for orthopedic implants. To effectively repair and replace the damaged bone tissues, the ideal orthopedic implants should possess several properties. First, they must exhibit mechanical compatibility. The mechanical properties of the implant should closely match those of the surrounding bone tissues at the repair site. Excessively high stiffness in the orthopedic implant can lead to stress shielding,<sup>9</sup> hindering bone remodeling and potentially resulting in bone resorption and aseptic loosening.<sup>10,11</sup> Conversely, insufficient stiffness of the orthopedic implant may fail to provide adequate mechanical support for the regenerating bone tissues,<sup>12</sup> increasing the risk of secondary injury to the affected area.<sup>13</sup> Second, they should possess fatigue resistance, which defines the ability of orthopedic implants to withstand cyclic loading over an extended period without experiencing progressive damage or failure. Given that bones are the critical load-bearing structures in the human body,<sup>14,15</sup> they bear the

complex physiological loads generated by daily activities.<sup>16</sup> Such a mechanical environment requires adequate fatigue resistance in orthopedic implants to ensure long-term functionality without fatigue failure.<sup>17</sup> Third, the implants must be biocompatible to ensure the safety and efficacy of medical devices. During prolonged interactions with the surrounding tissues, orthopedic implants must be non-toxic and elicit minimal or no adverse immune responses,<sup>18</sup> ensuring their safety and reliability *in vivo*. Finally, successful implants require osseointegration. Osseointegration is defined as the direct and intimate connections between the implant and surrounding bone tissues without an intervening fibrous connective tissue layer,<sup>19,20</sup> which enhances the mechanical strength of newly formed bone and promotes successful bone repair. Traditional solid orthopedic implants often exhibit a significant mismatch in the elastic modulus compared to that of native bone tissues.<sup>21</sup> This pronounced stress-shielding effect impedes the process of bone regeneration. Furthermore, bone tissues have limited capacity to grow into the interior of solid implants,<sup>22</sup> hindering the formation of a strong interface and resulting in poor osseointegration.<sup>23</sup> Compared with solid implants, porous orthopedic implants offer several advantages, such as reduced stress-shielding effect and enhanced osseointegration performance. The elastic modulus of porous structures can be adjusted to more closely match that of bone tissue, effectively mitigating the stress-shielding effect.<sup>24</sup> By adjusting the porous geometry, it is possible to achieve a favorable mechanical compatibility between the implant and the host bone tissues.<sup>25</sup> In addition, the porous structures provide ample space for the adhesion and proliferation of osteogenic cells<sup>26</sup> and facilitate the transport of nutrients and metabolic waste products,<sup>27,28</sup> thereby improving osseointegration efficiency.<sup>29</sup>

Additive manufacturing (AM) is the general term for technologies that successively merge materials to create physical objects as specified by three-dimensional (3D) model data.<sup>30</sup> Over the past few years, AM has been increasingly utilized in the fabrication of porous orthopedic implants.<sup>24</sup> Compared to conventional manufacturing techniques, AM offers several advantages. One such

advantage is that AM minimizes or eliminates material waste.<sup>31</sup> The layer-by-layer construction principle enables efficient raw material utilization and allows residual materials to be reused.<sup>32</sup> Furthermore, AM facilitates the customization of porous orthopedic implants to conform to irregular bone defects.<sup>33</sup> This customization process can incorporate patient-specific anatomical data for precise adjustment.<sup>34</sup> In addition, AM enables the design of microstructural features, such as pore size and porosity, to optimize osseointegration.<sup>35</sup> Commonly used porous orthopedic implants are fabricated from non-degradable metallic materials such as titanium/titanium alloys. However, these materials necessitate a second surgical procedure for removal and are associated with potential drawbacks, including chronic inflammation and abnormal angiogenesis.<sup>36</sup> Biodegradable metal-derived porous orthopedic implants offer a promising alternative, as they are completely resorbed *in vivo*, eliminating the need for secondary surgery and reducing patients' discomfort and economic burden,<sup>37</sup> thereby addressing the limitations of non-degradable porous orthopedic implants. Among various biodegradable metals, magnesium/magnesium alloy porous orthopedic implants have demonstrated significant application potential. Magnesium, as an essential macronutrient for the human body, is involved in numerous fundamental cellular biochemical reactions and promotes tissue regeneration. Furthermore, the density of magnesium is nearly identical to that of bones, significantly mitigating the stress-shielding effect. Magnesium is also one of the most readily machinable metals, enabling the fabrication of complex geometries.<sup>38</sup> However, the application of biodegradable magnesium/magnesium alloy orthopedic implants is currently hindered by several challenges. Primarily, the excessively rapid degradation rates of magnesium/magnesium alloys lead to the premature decline in mechanical properties, failing to provide reliable mechanical support for immature bone tissues.<sup>39</sup> Secondly, the degradation behavior of magnesium/magnesium alloys is difficult to control, resulting in a mismatch between degradation rates and bone repair rates.<sup>40</sup> Numerous factors influence the degradation behavior of magnesium/magnesium alloy porous orthopedic implants, including structural design,<sup>41</sup> material composition,<sup>42,43</sup> loading conditions,<sup>44,45</sup> and physiological environment.<sup>46,47</sup> Among these factors, structural design is a critical determinant. This paper focuses on the impacts of porous structures on the degradation behavior of magnesium/magnesium alloy orthopedic implants to provide a comprehensive overview of the current research status in this field. In subsequent sections of this review, the methodologies used to investigate the degradation behavior of magnesium/magnesium alloy-porous orthopedic implants are summarized, the

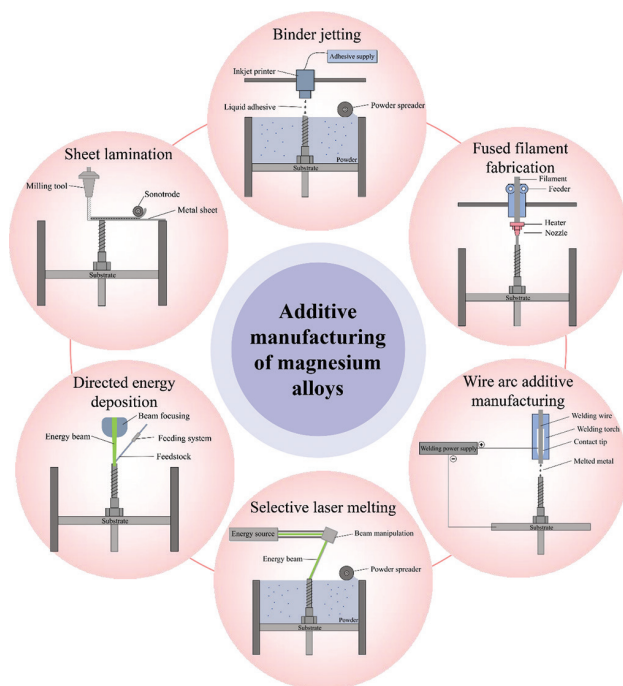
relationships between porous structures and degradation behavior of implants are systematically analyzed, and the "structure-mechanics-biology" interaction mechanisms and limitations of the existing research are discussed. This study aims to provide a systematic understanding and summary of the current research state and future research directions in this field, ultimately guiding the structural optimization and application of biodegradable magnesium/magnesium alloy orthopedic implants.

## 2. AM and degradation assessments of porous magnesium/magnesium alloy orthopedic implants

### 2.1. AM of porous magnesium/magnesium alloy orthopedic implants

AM methods can be categorized based on the initial state of the material, such as liquid, filament/paste, powder, and solid sheet.<sup>32</sup> Alternatively, they can be classified according to their manufacturing principle. Magnesium and magnesium alloys maintain a strong connection with various industries. Their high specific strength makes them highly suitable as structural materials in aerospace, automotive, and electronics industries. Concurrently, magnesium and magnesium alloys have garnered significant attention within the medical field due to their inherent biodegradability and their lower elastic modulus, which closely mimics that of natural bone.<sup>30</sup> At present, the primary AM methods (Figure 1) employed for magnesium/magnesium alloy primarily include<sup>48</sup> powder bed fusion (PBF), directed energy deposition (DED), indirect AM (I-AM), wire arc AM (WAAM), friction stir AM (FSAM), fused filament fabrication (FFF), solvent-cast 3D printing (SC-3DP), binder jetting (BJ), paste extrusion deposition (PED), and sheet lamination (SL).<sup>49,50</sup> FSAM and WAAM have limited applicability for medical uses due to the potentially coarse scaffold structures produced.<sup>51,52</sup> Other novel AM techniques are also suitable for fabricating porous bone implants from magnesium/magnesium alloys, such as DED with an externally applied ultrasonic field<sup>53</sup> and DED with arc oscillation.<sup>54</sup>

PBF and DED are currently among the most frequently utilized AM methods. A representative technique of PBF is selective laser melting (SLM), which has been successfully applied in the fabrication of implant materials such as 316L stainless steel and Ti6Al4V, and is progressively being extended to the manufacturing of magnesium/magnesium alloy implants.<sup>55</sup> SLM offers several advantages, including excellent mechanical properties, high precision, efficient material utilization, and near-net-shape capability,<sup>56</sup> along with well-defined grain morphology and good structural integrity.<sup>57</sup> However, SLM also presents notable drawbacks,



**Figure 1.** The process of additive manufacturing of porous magnesium/magnesium alloy structures

such as long manufacturing times and high residual stress.<sup>58</sup> Furthermore, due to the large surface area of magnesium powder, its high flammability poses operational safety concerns when using laser melting.<sup>59</sup> Selective electron beam melting (SEBM), another PBF technique, utilizes an electron beam as the energy source instead of a laser. SEBM offers shorter manufacturing times and lower residual stresses compared to SLM, while maintaining comparable precision and structural fidelity. However, SEBM is limited to conductive materials due to its reliance on electrical conductivity.<sup>58</sup> In contrast to PBF, DED does not require powder materials to be spread on a bed, and the materials can be added to a substrate and existing components.<sup>60</sup> Laser-engineered net shaping, a common form of DED, offers superior cooling effects and better remanufacturing capabilities compared to PBF.<sup>61</sup> Due to its high cooling rate, laser engineered net shaping can produce parts with excellent mechanical properties. However, this technique also has drawbacks, such as low manufacturing efficiency and high surface roughness.<sup>62</sup>

Other AM methods are employed less frequently. I-AM requires modeling in software, followed by the generation of a polymer template using AM techniques. This template is then infiltrated with a sodium chloride (NaCl) slurry, and the polymer is removed through a heating process. Subsequent sintering forms a negative NaCl template, into which molten magnesium is cast. The desired magnesium implant is obtained after dissolving the NaCl.<sup>51</sup> I-AM offers

high precision, but the resulting negative NaCl template is susceptible to corrosion, and replicating complex geometries can be challenging.<sup>63</sup> Another technique, FFF, involves heating a filament composed of magnesium alloy and a polymer binder to a molten state, followed by extrusion through a nozzle and layer-by-layer deposition along a predetermined path, solidifying on cooling. FFF is popular due to its low cost and ability to provide personalized prototyping of complex shapes without requiring expensive molds.<sup>64</sup> SC-3DP, an emerging AM technique, extrudes an ink containing metal or other powder particles, along with a binder system composed of polymers and volatile solvents, through a nozzle. The 3D-printed structure then undergoes debinding and sintering. SC-3DP offers high precision, enables 3D printing at room temperature, and fabricates complex structures with hierarchical porosity and desired alloy compositions. However, the high reactivity of magnesium powder limits the selection of the binder component.<sup>59</sup> BJ involves spreading a layer of powder on a build plate, followed by the deposition of a binder that hardens and bonds the particles. This process is repeated layer by layer until the desired geometry is achieved.<sup>61</sup> BJ technology exhibits good material adaptability and precision, enabling the creation of complex shapes and internal structures that are difficult to achieve with traditional processes.<sup>51</sup> PED is a process in which a paste is extruded from a syringe onto a substrate, with the substrate moving relative to the syringe to form the desired 3D contour. This method is primarily used for implants containing organic components that cannot withstand high temperatures, but it suffers from lower precision.<sup>65</sup> Ultrasonic AM (UAM) and laminated object manufacturing (LOM) are two common methods of SL. UAM is an ultrasonic welding technique that merges metal sheets, while LOM can heat or pressurize metal sheets using a heated cylindrical roller. UAM and LOM can construct layers with good accuracy and resolution, but achieving geometric accuracy in the Z-direction is difficult, thus limiting overall structural fidelity.<sup>58</sup> Different AM methods offer distinct advantages and disadvantages, and the selection of a specific method should be based on the particular manufacturing requirements.

Different processing methods lead to distinct microstructural evolutions, and these evolutions enhance the mechanical properties of implants through mechanisms such as homogenization, solid solution strengthening, and second-phase strengthening.<sup>66</sup> Compared to conventionally processed counterparts, magnesium/magnesium alloy orthopedic implants fabricated through AM techniques exhibit superior mechanical properties (Table 1).<sup>67</sup> This is attributed to the moderate cooling rates experienced during the AM process, resulting in a finer

Table 1. The mechanical properties of various magnesium alloys

Magnesium alloy	Production method	Mechanical properties			References
		Yield strength (MPa)	Ultimate tensile strength (MPa)	Elongation (%)	
WE43	Laser powder bed fusion	296	308	12	69
WE43	Extrusion	284	306	22	
WE43	Casting	145	189	4	
AZ80M	Wire arc additive manufacturing	119	237	12	70
AZ80M	Extrusion	207	324	17	
AZ80M	Casting	76	158	7	
GZ151K	Selective laser melting	345	368	3	71
GZ151K	As cast	184	277	5	
AZ61	Selective laser melting	219	272	3	72
AZ61	As cast	99	149	5	

and more homogeneous microstructure.<sup>68</sup> Such a fine and homogeneous microstructure, in turn, contributes to improved strength and hardness of magnesium/magnesium alloy bone implants.<sup>67</sup>

Process parameters in AM techniques are critical factors influencing the microstructure of orthopedic implants,<sup>67</sup> and the specific parameters of interest vary across different AM technologies. For instance, PBF focuses on powder size, energy density, laser power, scanning speed, and layer thickness. At lower energy densities, less elemental evaporation occurs, leading to a higher density in the final implant. WAAM is concerned with actuator precision, welding parameters, pattern, and arc thermal stability. Grain size decreases with increasing pulse frequency, resulting in a finer microstructure in the final implant. FSAM considers tool speed, travel speed, plunge depth, tool geometry, and feed rate, with different microstructures observed due to temperature gradients and spatial strain distributions. BJ prioritizes printing direction, printing speed, scanning technique, heating power ratio, and powder distribution. Optimized binders can effectively penetrate fine pores to form strong and uniform neck connections, ensuring the mechanical strength of the implant.<sup>51</sup> Therefore, it is crucial to select the specific AM technique and its process parameters based on the particular requirements of the implant.

## 2.2. Research methodologies for degradation behavior of porous magnesium/magnesium alloy orthopedic implants

The degradation behavior of magnesium/magnesium alloy orthopedic implants has been investigated using both experimental and numerical simulation methods. These methodologies offer distinct advantages and limitations in characterizing and describing the degradation process.

### 2.2.1. Degradation experiments

Degradation experiments are the most direct and commonly employed method to study the degradation behavior of magnesium/magnesium alloy orthopedic implants. Degradation experiments are typically categorized as *in vitro* or *in vivo* experiments (Figure 2). *In vitro* degradation experiments necessitate the establishment of a simulated physiological environment. To mimic the physiological environment of the human body, the temperature of the *in vitro* degradation experiment is consistently maintained at approximately 37°C.<sup>73</sup> Commonly used solutions for simulating body fluid environments include phosphate-buffered saline,<sup>74</sup> physiological saline solution,<sup>75</sup> Hank's balanced salt solution,<sup>76</sup> and Dulbecco's Modified Eagle Medium.<sup>77</sup> While each of these solutions can be used to simulate the body fluid environment, their fidelity to actual physiological conditions varies. The phosphate-buffered saline and physiological saline solutions lack the essential buffering components of the human body,<sup>78</sup> which may lead to pH fluctuations and deviations from the actual situation. Hank's solution lacks the common proteins of the human body,<sup>79</sup> influencing the degradation rate of magnesium/magnesium alloy orthopedic implants and affecting the accuracy of experimental results.<sup>80,81</sup> The Dulbecco's Modified Eagle Medium provides a better simulation of the actual body fluid environment, but is susceptible to bacterial contamination, which may increase the content of collected carbon dioxide and hydrogen gas, leading to inaccurate measurements of the magnesium/magnesium alloy orthopedic implant degradation rate.<sup>82</sup> After the establishment of a simulated body fluid environment, magnesium/magnesium alloy orthopedic implants are immersed within the solution. The immersion conditions can be classified into three

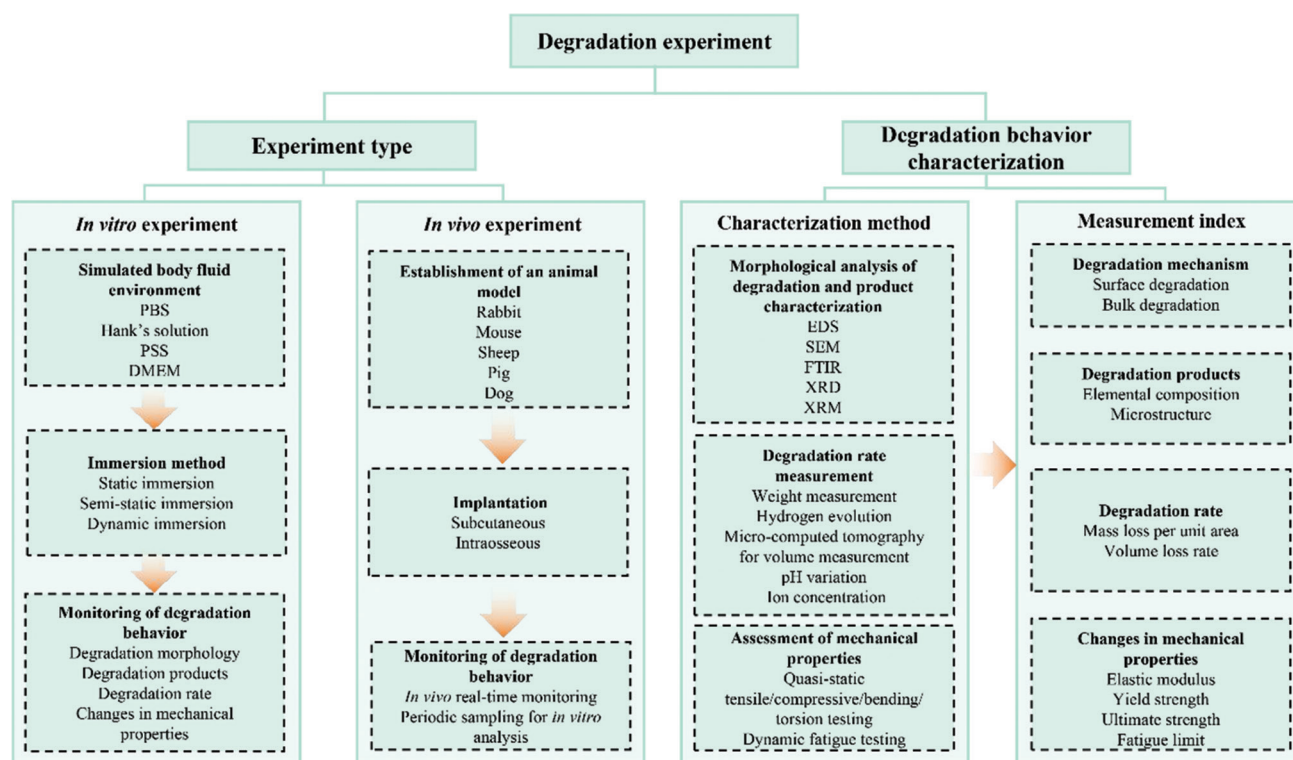


Figure 2. Workflow of the degradation experiments

Abbreviations: DMEM: Dulbecco's Modified Eagle Medium; EDS: Energy dispersive spectroscopy; FTIR: Fourier-transform infrared spectroscopy; PBS: Phosphate-buffered saline; PSS: Physiological saline solution; SEM: Scanning electron microscopy; XRD: X-ray diffraction; XRM: X-ray microscopy

types: static,<sup>74</sup> semi-static,<sup>83</sup> and dynamic.<sup>84</sup> Semi-static conditions are achieved through periodic replacement of the solution,<sup>83</sup> while dynamic conditions are realized by controlling the flow of the solution at a specific flow rate through the peristaltic pump.<sup>84</sup> Most studies employed the static or semi-static immersion conditions. Under the static conditions, corrosion products accumulate on the implant surface, forming a protective layer that reduces the degradation rate compared with the dynamic conditions.<sup>74</sup> Furthermore, the static and semi-static conditions fail to simulate the body fluid flow features of the *in vivo* environment.<sup>85</sup> Dynamic conditions simulate the body fluid flow, thereby offering a more accurate simulation of the *in vivo* environment compared with the static and semi-static conditions. The flow rate of the simulated body fluid adopted in the *in vitro* experiments is generally set to 2 mL/(100 mL·min), which is close to the body fluid flow rate observed in the musculoskeletal system.<sup>86</sup> The *in vitro* degradation experiments enable a direct observation of the structural changes and the measurement of degradation rates in magnesium/magnesium alloy orthopedic implants during degradation.<sup>87</sup> However, the duration of *in vitro* experiments is often limited to 28 days or less,<sup>88,89</sup> making it difficult to observe the long-term degradation behavior of magnesium/magnesium alloy orthopedic implants and

to simulate the influences of surrounding bone tissue growth. In contrast, the *in vivo* degradation experiments, which involve implanting magnesium/magnesium alloy orthopedic implants into animals for extended periods, can address this limitation<sup>87</sup> and provide a more accurate assessment of the practical degradation behavior of magnesium/magnesium alloy orthopedic implants in the physiological environment.<sup>90</sup>

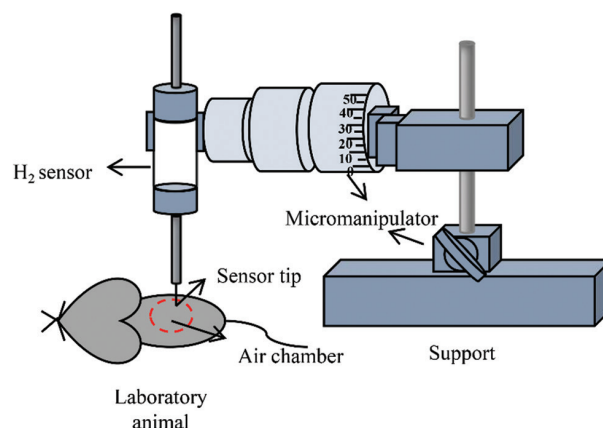
Based on the *in vitro* or *in vivo* degradation experiments, the degradation behavior of magnesium/magnesium alloy orthopedic implants can be further characterized and analyzed after various immersion/implantation periods. This process typically includes the characterization of degradation morphologies, the measurement of degradation rates, and the evaluation of mechanical properties. Characterization methods for the degradation morphologies of magnesium/magnesium alloy orthopedic implants include scanning electron microscopy equipped with energy-dispersive X-ray spectroscopy, X-ray diffraction, Fourier-transform infrared spectroscopy, and X-ray microscopy.<sup>84,85</sup> Scanning electron microscopy equipped with energy-dispersive X-ray spectroscopy enables the observation of macroscopic and microscopic surficial features of magnesium/magnesium alloy orthopedic implants,<sup>76</sup> allowing the degradation mode and

uniformity analysis.<sup>89</sup> Furthermore, the X-ray diffraction and Fourier-transform infrared spectroscopy techniques can be used to identify and analyze the chemical structure of degradation products,<sup>89</sup> facilitating the investigation of the micro-mechanisms of degradation product deposition. The X-ray microscopy analysis enables further exploration of the 3D distribution of degradation products,<sup>85</sup> providing more comprehensive experimental data for the degradation behavior analysis of magnesium/magnesium alloy orthopedic implants. The degradation rate of magnesium/magnesium alloy orthopedic implants, as a function of degradation time, can be quantitatively described by directly measuring the mass loss after different degradation periods.<sup>91,92</sup> However, the chromic acid used in this process can produce carcinogenic substances and requires cautious handling.<sup>93</sup> For structures with large surficial area and small pore sizes, the mass loss measurement results may be unreliable.<sup>89</sup> During the degradation of magnesium/magnesium alloys, the release of hydrogen gas and magnesium ions increases the pH value and osmotic pressure of the simulated body fluid.<sup>85</sup> In addition, the pore size of porous magnesium/magnesium alloy orthopedic implants increases with the degree of degradation; thus, the change in pore size distribution can directly reflect the degree of degradation.<sup>83</sup> Therefore, the degradation rate of magnesium/magnesium alloy orthopedic implants can also be indirectly and qualitatively characterized by measuring the variation of pH values,<sup>91</sup> the release of magnesium/calcium/phosphorus ions,<sup>65</sup> the osmotic pressures of the simulated body fluid, and the distribution of the pore size.<sup>83</sup> By measuring the hydrogen evolution rate and converting it to mass loss based on the magnesium corrosion equation,<sup>83</sup> the real-time degradation rate of magnesium/magnesium alloy orthopedic implants can be obtained, without being affected by the deposition of degradation products. Compared to the direct mass loss measurement, this method provides a more accurate measurement of the degradation rate.<sup>94</sup> In addition to mass loss, volume loss is also an important indicator to quantitatively describe the degradation rate of magnesium/magnesium alloy orthopedic implants. In general, the 3D models of the implant before and after degradation can be obtained through micro-computed tomography scanning, where the volume change can be calculated.<sup>95,96</sup> The mechanical properties, including elastic modulus, yield strength, and ultimate tensile strength, of magnesium/magnesium alloy orthopedic implants after different degradation periods can be assessed through mechanical tests.<sup>89</sup> Based on the mechanical testing data, the relationships between the mechanical properties and degradation behavior can be quantitatively analyzed. In the *in vivo* degradation experiments, the degradation rate of magnesium/magnesium alloy orthopedic implants located

relatively superficially under the skin can be monitored by contacting the tip of a highly hydrogen-sensitive biosensor to the skin above the air cavity at the implantation site. A miniature positioner (Figure 3) can be used to move the biosensor tip if needed.<sup>97</sup> Moreover, the degradation rate of magnesium/magnesium alloy orthopedic implants can be monitored by placing a visual hydrogen sensor on the skin at the center of the visible air cavity.<sup>98</sup> Compared to the *in vivo* degradation rate monitoring techniques, the visual hydrogen sensor method is simpler, more convenient to operate, and requires less stringent experimental conditions. It can accurately and quantitatively measure the hydrogen concentration in the air cavity in real-time, especially for the rapidly corroding implants. However, the time required for the color of the visual hydrogen sensor to change is relatively long.<sup>98</sup> Moreover, the visual hydrogen sensor method cannot measure the overall corrosion rate over the entire implantation period.<sup>98</sup> The degradation morphology characterization, degradation rate measurement, and mechanical testing results obtained through degradation experiments provide basic experimental data, based on which the factors influencing the degradation behavior of magnesium/magnesium alloy orthopedic implants and the corresponding mechanisms can be analyzed and investigated further.

### 2.2.2. Numerical simulation of degradation

Based on the degradation morphology characterization, degradation rate, and mechanical properties changes obtained through degradation experiments, numerical simulation methods can be applied to further investigate the mechanical regulation mechanisms governing the degradation behavior of magnesium/magnesium alloy orthopedic implants (Figure 4). Numerical simulation models commonly used to simulate the degradation



**Figure 3.** Schematic diagram of the visual hydrogen ( $H_2$ ) sensor setup. Figure 3 was created with Microsoft PowerPoint 2021 (Microsoft Corporation) by Haoxuan Zeng (2025)

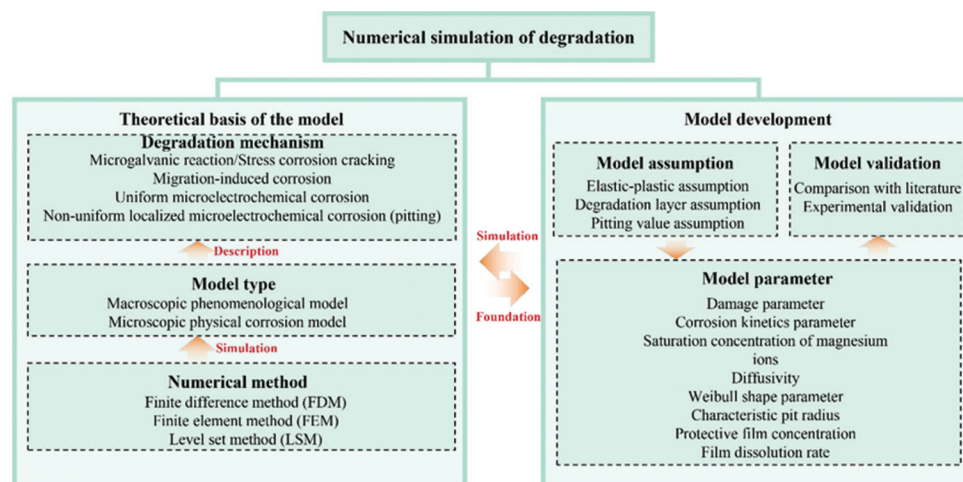


Figure 4. Workflow of the degradation numerical simulations

of magnesium/magnesium alloy orthopedic implants can be categorized into macroscopic phenomenological models and microscopic corrosion physics models.<sup>99</sup> The macroscopic phenomenological models focus on describing the overall material loss during the degradation process,<sup>99</sup> while microscopic corrosion physics models offer a more detailed simulation of the degradation process. The microscopic corrosion physics models are capable of capturing the potential chemical interactions, thereby enabling the simulations of processes such as coating effects, protective layer formation, and pH changes<sup>100</sup> and effectively complementing macroscopic phenomenological models.<sup>101</sup> The degradation mechanisms of magnesium/magnesium alloy orthopedic implants under physiological conditions are complex, including micro-electroplating reactions, uniform micro-electrochemical corrosion, non-uniform pitting micro-electrochemical corrosion, stress corrosion cracking, and migration-driven corrosion.<sup>102</sup> Some studies focused on the development of degradation models to thoroughly and meticulously describe a specific mechanism,<sup>101,103</sup> while others developed degradation models that comprehensively considered multiple mechanisms to simulate actual degradation behavior more accurately.<sup>104,105</sup> The commonly used numerical calculation methods include the finite difference method,<sup>106</sup> the finite element method,<sup>107</sup> and the level set method.<sup>37</sup> The finite difference method is among the earliest methods adopted in numerical simulation and can be used to simulate the one-dimensional degradation behavior of materials. More recent studies employed a combination of the finite difference method and the finite volume method, which were able to simulate the degradation behavior in higher dimensions.<sup>108</sup> Furthermore, the level set method enables the acquisition of locally refined meshes without the need to re-mesh the entire domain, thereby reducing the computational costs.<sup>106</sup>

After determining the degradation mechanism and numerical calculation method for model development, reasonable assumptions must be established for the developed numerical simulation model. The most fundamental assumption involves the simplification of material properties. The most widely accepted simplification is the elastoplasticity hypothesis, wherein the elastic deformation phase is described using linear and isotropic behavior, while the plastic deformation phase is described using the  $J_2$  flow theory with non-linear isotropic hardening.<sup>103</sup> Apart from the simplified assumptions of material properties, other assumptions adopted in the model are determined based on the specific research focus. For example, Gartzke *et al.*<sup>37</sup> focused on the influence of the degradation layer on degradation. In their simulation model, a constant magnesium concentration was assumed in the undegraded core of the structure, while the magnesium concentration in the degradation layer decreased from the interior toward the exterior.<sup>37</sup> Quinn *et al.*<sup>109</sup> primarily considered the influence of the  $\beta$ -phase component on degradation and assumed a continuous distribution of pitting values generated using a set of continuous random numbers. Parameters in the degradation model are critical elements influencing the accuracy of the model in simulating the actual degradation behavior of magnesium/magnesium alloy orthopedic implants and are closely related to the type of developed model.<sup>109</sup> The critical parameters in macroscopic phenomenological models include damage and corrosion kinetics parameters,<sup>103</sup> while in microscopic corrosion physics models, the critical parameters include magnesium ion saturation concentration and diffusivity.<sup>101</sup> Furthermore, some parameters are closely related to the specific degradation mechanisms, such as the Weibull shape parameter and characteristic pit radius in non-

uniform pitting micro-electrochemical corrosion,<sup>110</sup> the concentration of the protective film formed on the surface, and the reaction rates of film formation/dissolution in migration-driven corrosion.<sup>102</sup> Existing studies generally assigned values to the parameters in numerical simulation models of degradation by referencing previous literature. However, the validation and calibration of these parameters are necessary to ensure the effectiveness and usability of the developed numerical simulation models.<sup>111</sup> The model validation and calibration are commonly conducted through comparison with literature data<sup>112</sup> or collected degradation experimental data.<sup>113</sup> Comparison metrics often include the primary indicators of concern in degradation experiments, such as mass loss,<sup>111</sup> hydrogen evolution,<sup>114</sup> pH values,<sup>112</sup> and magnesium ion concentration.<sup>37</sup> Furthermore, some studies applied the well-validated and calibrated models to further demonstrate their advantages in the simulation of degradation. For example, Barzegari *et al.*<sup>100</sup> verified the effectiveness and usability of a degradation numerical simulation model established based on Bayesian optimization, then used hydrogen evolution as an input parameter to simulate the output pH value results.<sup>100</sup> The simulated pH values differed by 5.35% in NaCl solution and 1.03% in simulated body fluid. Subsequently, they simulated a 42-day degradation process of a degradable bone screw within 9 h and characterized the magnesium ion concentration and mass loss during the degradation process.<sup>100</sup> It was validated that the established numerical simulation model effectively predicted the degradation behavior of pure magnesium-based biomaterials and improved the computational efficiency.<sup>100</sup>

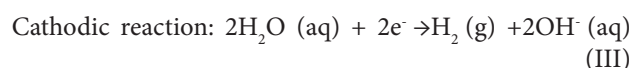
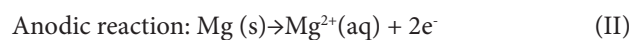
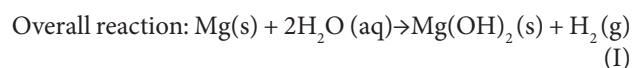
Numerical simulations enable the analysis of the influence of various factors on the degradation behavior of magnesium/magnesium alloy orthopedic implants by adjusting model parameters and boundary conditions, offering a more efficient and resource-saving approach compared with degradation experiments. Through numerical simulations, the stress and strain distributions in the structure during degradation can be computed, which are difficult to obtain through *in vitro* degradation experiments and crucial for the prediction of failure of magnesium/magnesium alloy orthopedic implants.<sup>115</sup> Moreover, the influence of the magnesium/magnesium alloy orthopedic implant structure on the growth of surrounding bone tissues can be modeled through numerical simulation. The computational fluid dynamics models can be used to simulate the distributions of the internal flow fields of magnesium/magnesium alloy orthopedic implants, which facilitate the analysis of the interacting mechanisms of “structure-stress-degradation-tissue repair.”<sup>116,117</sup> Combined with degradation experiments, numerical simulation enables

the in-depth analysis of the mechanical mechanisms by which various factors influence the degradation behavior of magnesium/magnesium alloy orthopedic implants. The results of numerical simulations can be cross-validated with those of degradation experiments, providing a basis for the design optimization of magnesium/magnesium alloy orthopedic implants. However, the numerical simulations of magnesium/magnesium alloy orthopedic implants’ degradation behavior also possess limitations. The parameters used in the numerical model may not perfectly match the practical physiological conditions, leading to deviations between the simulation results and the actual situations. In addition, it is difficult to simultaneously balance the accuracy and universality of the model. Different numerical simulation models are necessary to simulate the degradation behavior of orthopedic implants with various material compositions and structural designs.

### 3. Influences of porous structures on the degradation behavior of magnesium/magnesium alloy orthopedic implants

#### 3.1. Degradation mechanisms of magnesium/magnesium alloy implants

The degradation mechanisms of magnesium/magnesium alloys in physiological environments are complex, including uniform micro-electrochemical corrosion, non-uniform pitting micro-electrochemical corrosion, and stress corrosion cracking, as well as galvanic corrosion, crevice corrosion, fretting corrosion, and erosion corrosion mechanisms.<sup>118</sup> Despite the diverse and complex nature of these corrosion mechanisms, existing research commonly employs the electrochemical reaction of magnesium with water to describe the degradation mechanism of magnesium/magnesium alloy orthopedic implants.<sup>119</sup> The overall reaction is divided into anodic and cathodic reactions. In the anodic reaction, magnesium corrodes, releasing magnesium ions and electrons. In the cathodic reaction, water reacts with the electrons released from the anodic reaction to produce hydrogen gas and hydroxyl ions. Magnesium ions then combine with these hydroxyl ions to form magnesium hydroxide.<sup>12</sup> The final degradation products are magnesium hydroxide and hydrogen gas. The overall chemical equations are as follows (Equations I-III):<sup>119</sup>



### 3.2. Influences of alloy composition and surface treatments on the degradation behavior of magnesium/magnesium alloy orthopedic implants

The degradation rate of magnesium alloy orthopedic implants can be controlled by altering their alloy composition.<sup>42</sup> Furthermore, alloying is also an effective method for improving the mechanical properties and biocompatibility of metals.<sup>120</sup> At present, common magnesium alloy types used in biomedical applications include magnesium-calcium alloys,<sup>121</sup> magnesium-zinc alloys,<sup>122</sup> magnesium-strontium alloys,<sup>123</sup> and magnesium-neodymium alloys.<sup>124</sup> Alloying has led to varying degrees of improvement in the mechanical properties of metals, alongside products with good biocompatibility and non-toxic degradation. Specifically, magnesium-calcium alloys are widely utilized due to their biocompatibility and degradation characteristics, with calcium playing a key role in bone integration. Magnesium-zinc alloys enhance mechanical strength and promote osteogenesis through zinc's biological functions. Magnesium-strontium alloys are employed because strontium positively influences bone metabolism and healing. Magnesium-neodymium alloys aim to improve mechanical strength and control degradation, while aiding bone repair due to neodymium's effects.<sup>120</sup>

Surface treatments can also control the degradation rate by influencing surface roughness.<sup>125</sup> To enhance the corrosion resistance of magnesium/magnesium alloy bone implants, methods such as electroplating, chemical vapor deposition coatings, physical vapor deposition coatings, and organic coatings are employed.<sup>126</sup> When the same surface treatment yields different surface roughness values, the degradation rate increases with increasing surface roughness.<sup>125</sup>

However, altering alloy composition and performing surface treatments also possess respective drawbacks. Aluminum and rare earth elements are often used as alloying elements to modify alloy composition; however, their long-term biocompatibility remains uncertain and may cause adverse effects in the human body.<sup>127</sup> Moreover, magnesium alloys do not form thermodynamically stable passive layers comparable to those of stainless steel.<sup>128</sup> While implant surface treatments can reduce the degradation rate to some extent, it is challenging to achieve a good match between the degradation rate and bone repair rate.<sup>127</sup> Furthermore, there is a risk of corrosive components penetrating the metal/polymer interface and a decrease in coating adhesion.<sup>126</sup> In contrast, porous structure design offers comprehensive control over the mechanical properties, degradation behavior, and biocompatibility of magnesium/magnesium alloy biodegradable implants,

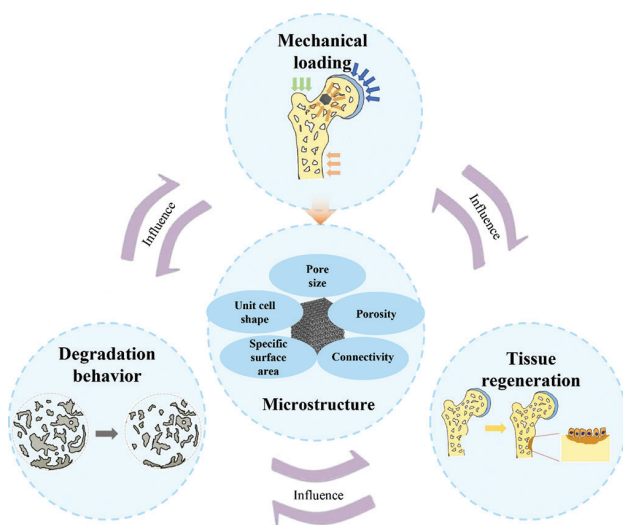
allowing for more efficient simultaneous modulation of multiple properties.

### 3.3. Influences of porous structural parameters on the degradation behavior of magnesium/magnesium alloy orthopedic implants

Porous structures play critical roles in regulating mechanical properties, bearing and transmitting physiological loads, and establishing a localized mechanical microenvironment for magnesium/magnesium alloy orthopedic implants. The porous structures of magnesium/magnesium alloy orthopedic implants significantly influence the interactions among physiological loading, degradation behavior, and bone tissue regeneration. Orthopedic implants must withstand approximately 2 million cycles of complex physiological loading generated by the movements of the musculoskeletal system annually.<sup>129</sup> Under the complex physiological loading, porous microstructural features such as the unit cell shape, pore size, and porosity affect the implant's macroscopic mechanical properties, deformation and stress distributions, and contact with surrounding tissues, significantly influencing its degradation rate and uniformity.<sup>130</sup> The degradation of the implant causes dynamic changes in the porous structure and mechanical properties, further affecting its mechanical responses under the physiological loading<sup>131</sup> and continuously altering the local mechanical microenvironment of the surrounding bone tissues.<sup>132</sup> Thus, the porous structure is a critical factor in regulating the degradation behavior of magnesium/magnesium alloy orthopedic implants to achieve the dynamic adaptation between changes in mechanical properties and the rate of bone tissue repair (Figure 5). There are various porous structural parameters, including porosity, specific surface area, pore size, shape, and pore interconnectivity.<sup>133,134</sup> This section systematically analyzes the influence of these porous structural parameters on the degradation behavior of magnesium/magnesium alloy orthopedic implants.

#### 3.3.1. Porosity and specific surface area

Porosity and specific surface area are critical factors governing the mechanical properties and degradation behavior of magnesium/magnesium alloy orthopedic implants. Increased porosity and specific surface area enhance the permeability within a unit volume of the orthopedic implant and augment the contact area with body fluids, thereby accelerating the degradation rate.<sup>135</sup> The porosity of orthopedic implants can be directly controlled by modifying the number and the pore size of interconnected pores,<sup>136</sup> while the specific surface area is directly influenced by the size and shape of the basic unit cells of the porous structure.<sup>137,138</sup> Md Saad *et al.*<sup>95</sup> modulated



**Figure 5.** Interactions among porous structures, mechanical properties, degradation behavior, and tissue regeneration. Figure 5 was created with Microsoft PowerPoint 2021 (Microsoft Corporation) by Haoxuan Zeng (2025)

the porosity of bone scaffolds by altering the number of open pores on the surface. The degradation experiments demonstrated that the degradation rate increased with an increasing number of surface pores.<sup>95</sup> Similarly, Kopp *et al.*<sup>77</sup> varied the edge length of microstructures to modify the specific surface area of bone scaffolds and found that the degradation rate increased with increasing microstructure edge length.<sup>77</sup> Furthermore, Wang *et al.*<sup>85</sup> maintained a constant porosity of orthopedic implants while varying their specific surface areas by employing disordered, ordered, and lamellar porous unit cells.<sup>85</sup> According to degradation experiments, it was found that the degradation rate of orthopedic implants increased with increasing specific surface area under the same degradation mode.<sup>85</sup> Moreover, the porosity and specific surface area directly regulate structural permeability, which influences the nutrient/metabolic waste transport and cell adhesion/proliferation, thus regulating the osteogenic potential of orthopedic implants.<sup>139</sup> The permeability of orthopedic implants increased with increasing porosity and specific surface area.<sup>137,140</sup> However, an excessively high porosity will lead to a rapid decline in the mechanical properties of orthopedic implants during degradation, while insufficient porosity results in insufficient permeability, hindering the regeneration of surrounding tissues. Therefore, an appropriate porosity design is crucial to balance the mechanical performance and permeability of orthopedic implants.<sup>137,141</sup>

### 3.3.2. Pore size

The pore size of porous orthopedic implants not only influences cell and vascular ingrowth but also affects

the surface area and strut thickness, thereby impacting degradation behavior. The influence of pore size on degradation behavior remains inconclusive in current research. Cheng *et al.*<sup>142</sup> found that, at a constant porosity, pore size variations had no significant effect on the average degradation rate of high-purity magnesium scaffolds *in vitro*.<sup>142</sup> However, scaffolds with larger pore sizes promoted early angiogenesis in newborn bone tissues, upregulated the expression of type I collagen and osteopontin, and effectively induced higher bone volume and more mature bone formation *in vivo*.<sup>142</sup> It was shown that, as long as porosity remains within an optimal range for tissue growth, appropriately increasing pore size can improve the osteogenic potential of scaffolds with minimal impact on their degradation rate. Conversely, Wang *et al.*<sup>76</sup> found that scaffolds with smaller pore sizes exhibited a larger specific surface area at a constant porosity, enabling the release of more magnesium ions during degradation, which promoted osteogenic differentiation of bone marrow mesenchymal stem cells and induced more new bone formation.<sup>76</sup> Jia *et al.*<sup>136</sup> modified the porosity of bone scaffolds by changing the interconnecting pore size and subsequently altered the specific surface area by changing the primary pore size.<sup>136</sup> They found that the permeability of the scaffolds increased as interconnectivity pore size and primary pore size increased.<sup>136</sup> Excessively small pore sizes resulted in an excessively large surface area of the orthopedic implant, potentially causing a rapid degradation in the initial implantation phase and hindering cell infiltration. In contrast, excessively large pore sizes reduced the specific surface area and mechanical strength of the scaffold, hindering magnesium ion release and failing to provide sufficient stable mechanical support for the newborn bone tissues.<sup>143</sup>

### 3.3.3. Shape and connectivity of unit cells

The shape and connectivity of unit cells influence stress distribution under physiological loading and fluid flow within the structure of porous orthopedic implants. Sharp-edged strut unit cells or sharp connections between adjacent units can act as stress and electrochemical corrosion concentration regions, leading to accelerated local degradation.<sup>144</sup> In contrast, curvature-based unit cells or smooth transitions at connections between adjacent units promote more uniform distributions of internal stress and flow fields of the structure, resulting in more homogeneous overall degradation.<sup>144</sup> Augustin *et al.*<sup>145</sup> demonstrated that the bone scaffolds based on regular circular unit cells exhibited a smoother surface after *in vivo* degradation, whereas scaffolds based on irregular unit cells displayed more pronounced, non-uniform degradation morphology accompanied by increased roughness.<sup>145</sup> Shi

*et al.*<sup>146</sup> compared the degradation behavior of magnesium alloy bone scaffolds based on strut unit cells and minimal surface unit cells, respectively, and pointed out that the shape of the unit cell affected the degradation mode of the scaffold.<sup>146</sup> During the degradation process, stagnant flow was generated as a result of the lower permeability within minimal surface scaffolds, causing the accumulation of degradation products that slowed the degradation rate and reduced the degradation uniformity of the structure.<sup>146</sup> The connectivity between unit cells in porous orthopedic implants affects the body fluid flow within the structure. Highly interconnected open-pore structures allow fluid to penetrate all surfaces within the structure, where degradation progresses gradually from the outer surface inward, forming a 3D “etching front” that promotes uniform degradation throughout the structure and avoids localized stress concentrations and sudden failure of local implant structures.<sup>147</sup> Conversely, closed cavities existing within the structure hinder fluid penetration and prevent degradation. The local closed cavities may form temporary self-passivation in adjacent regions due to the retention of degradation products. Although the self-passivation regions retard the degradation rate to a certain extent, it may lead to stress concentration and local failure of the structure, leaving isolated metal fragments that hinder the complete degradation of the implant.<sup>147</sup> The gradient design strategy of setting varying porosity or pore size in different regions of the implant has attracted increasing attention in recent years. For example, a structure with low porosity/pore size is arranged in the central region of the implant to provide stable mechanical support, while a structure with higher porosity/pore size is arranged at the bone-implant interface to promote osseointegration. Such designs theoretically enable slow degradation in the inner layer of the implant and rapid degradation in the outer layer, ensuring early mechanical stability and promoting surrounding bone tissue regeneration.<sup>148</sup> However, the precise fabrication of gradient porous structures remains challenging due to the limitations of magnesium alloy processing; therefore, the research on gradient porous magnesium alloy orthopedic implants is still in its early stage.

### 3.4. The structure-mechanics-biology interaction mechanisms in magnesium/magnesium alloy orthopedic implants degradation

The degradation of magnesium/magnesium alloy orthopedic implants in the physiological environment is a complex process influenced by multiple factors. This section reviews the “structure-mechanics-biology” interaction mechanisms in this process.

The cross-sectional area gradually decreases, and the pore size gradually increases with degradation of

magnesium/magnesium alloy orthopedic implants, macroscopically manifesting as a decline in mechanical strength and stiffness. Although the degradation products can fill the pores partially and form a deposit layer on the surface of the structure to temporarily improve or maintain its mechanical strength in the early stages, this strengthening effect is limited. As the degree of degradation intensifies, the mechanical properties of the implant will continue to deteriorate.<sup>149</sup> Under cyclic physiological loading, the stress corrosion effect, caused by the coupling of cyclic stress and the body fluid environment, aggravates the local degradation of the magnesium scaffold. Guo *et al.*<sup>150</sup> found that the cyclic compressive loading can cause evident cracks in the protective film on the surface of high-purity magnesium scaffolds, thereby accelerating the degradation and failure of the structure.<sup>150</sup> The microstructural evolution during the degradation of magnesium/magnesium alloy orthopedic implants is closely related to the reduction of their macroscopic mechanical properties, which must be fully considered during structural design to ensure that the implant can maintain the necessary mechanical support throughout the critical period of bone healing. However, the relationship between microstructural evolution and macroscopic mechanical property degradation during the degradation of magnesium/magnesium alloy orthopedic implants has not yet been systematically revealed. Models that can quantitatively describe these relationships are necessary to provide a fundamental basis for the design of magnesium/magnesium alloy orthopedic implants.

The *in vivo* degradation behavior of magnesium/magnesium alloy orthopedic implants differs significantly from that observed *in vitro*. The high concentration of proteins and inorganic ions (such as phosphate and carbonate) in body fluids, combined with the magnesium ions released during magnesium degradation, form a phosphate/carbonate deposition layer on the surface of the implant.<sup>151</sup> This biomineralized layer, resembling the natural bone mineral to some extent, slows subsequent degradation and provides a favorable substrate for bone cell adhesion and proliferation.<sup>152</sup> Consequently, magnesium/magnesium alloy orthopedic implants often exhibit an initially rapid degradation rate *in vivo*, followed by surface passivation and degradation deceleration. Moreover, the *in vivo* immune response and degradation rate vary depending on the structures of the magnesium/magnesium alloy orthopedic implants. Structures with smaller pore sizes, due to the slower corrosion and smoother surfaces, tend to induce the formation of a fibrous capsule at the bone-implant interface, which isolates the implant from the surrounding bone tissues and results in a milder inflammatory response.<sup>142</sup> In contrast, structures with larger pore sizes initially exhibit greater infiltration of

macrophages and lymphocytes, which leads to a slightly stronger inflammatory response, with a simultaneous release of osteogenic factors promoting bone remodeling.<sup>142</sup> The *in vivo* degradation of magnesium/magnesium alloy orthopedic implants is accompanied by the regeneration of surrounding bone tissues. The formation and remodeling of new bone tissues are highly dependent on the mechanical microenvironment, that is, the “mechano-biological” coupling effect. Appropriate mechanical stimulation promotes osteoblast activation and matrix deposition, while excessive micromotion can lead to fibrous union or delayed healing.<sup>152</sup> Magnesium/magnesium alloy orthopedic implants should provide sufficient stiffness and mechanical stability to the damaged bone tissues in the early stage after implantation. Meanwhile, the gradual degradation of magnesium/magnesium alloy orthopedic implants should enable a progressive transfer of stress to the newborn bone tissues to provide a graded mechanical environment during the healing process. In addition to the local mechanical environment, the released ions and local pH changes during the degradation of magnesium/magnesium alloy orthopedic implants also affect cell behavior. The magnesium ions released during the degradation of magnesium/magnesium alloy orthopedic implants can promote osteogenesis-related processes, enhance osteoblast adhesion and migration, improve angiogenesis, and exert a certain immunomodulatory effect.<sup>153</sup> When perceived by surrounding osteogenesis-related cells, moderate magnesium ion concentrations can activate osteogenic pathways, promoting the deposition of new bone matrix. This combined chemical and mechanical stimulation is beneficial for bone remodeling.<sup>154</sup> However, if the degradation is too rapid, a dramatic accumulation of magnesium and hydroxide ions will occur locally, causing an increase in pH value and accompanied by the production of a large amount of hydrogen gas.<sup>128</sup> Excessive alkalinity leads to an abnormal mineralization of the extracellular matrix or stimulation of surrounding tissues.<sup>128</sup> The large amount of hydrogen gas retained in the tissues can form bubbles, hindering close contact between the newborn bone tissues and the implant and potentially inducing inflammation or delayed healing.<sup>152</sup> Therefore, the degradation rate of magnesium/magnesium alloy orthopedic implants should match the rate of bone repair to achieve complete degradation after the completion of bone tissue repair, but not be too rapid to cause excessive stimulation to the surrounding tissues.

The influences of the mechanical environment on the “structure-mechanics-biology” interactions during the degradation of magnesium/magnesium alloy orthopedic implants vary significantly at different implantation sites. The diaphysis of long bones (such as the femur and tibia) is

typically a dominant load-bearing region with an abundant blood supply in the medullary cavity.<sup>155</sup> Studies have shown that magnesium implants degrade more rapidly in long bones than in non-load-bearing sites, such as subcutaneous tissues. Cyclic loads promote the generation of stress corrosion cracks, whereas fluid flow and higher oxygen content in the medullary cavity may accelerate electrochemical reactions.<sup>152</sup> The higher concentrations of calcium and phosphate ions in the bone tissues promote new bone formation, which will facilitate the formation of a protective mineralized layer on the magnesium surface to partially offset the negative effects of excessively rapid degradation. Non-load-bearing or low-load-bearing sites, such as craniofacial bones, experience relatively lower mechanical loads. The bone tissues in these regions primarily regenerate in the intramembranous osteogenesis mode, of which the rate is slower than that of long bones.<sup>156</sup> The catastrophic mechanical instability is less prone to occur during the degradation of magnesium/magnesium alloy orthopedic implants used for craniofacial repair. More attentions are focused on the precise reconstruction of geometry and biocompatibility of the magnesium/magnesium alloy implants used in craniofacial repair.<sup>157</sup> In addition, the biological environment at the skull is relatively closed, which may make it difficult for the released hydrogen gas to diffuse during the degradation process. Therefore, greater attention should be paid to the issue of gas release during degradation. Research on the application of magnesium/magnesium alloy orthopedic implants in craniofacial repair is relatively limited, as the effects of the region’s complex anatomical structures on degradation behavior require further study. In the internal fixation of joint fractures, the high chloride ion concentration and relatively low fluidity of synovial fluid within the joint cavity can affect the degradation behavior of the magnesium/magnesium alloy orthopedic implants. The low buffering capacity and closed cavity of synovial fluid may lead to the local accumulation of degradation products, inducing synovitis or cartilage damage.<sup>158</sup> Conversely, joint movement promotes agitation of the synovial fluid, accelerating the dissipation of corrosion products and avoiding excessive local concentrations.<sup>158</sup> Therefore, for joint fixation applications, it is essential to carefully regulate the degradation rate and product release to promote bone healing without damaging joint tissues.

#### 4. Key challenges and prospective future directions

The widely applied research methodologies in studying the degradation behavior of magnesium/magnesium alloy orthopedic implants include degradation experiments and numerical simulations, both of which possess

distinct advantages. Degradation experiments directly assess degradation morphologies, degradation rates, and mechanical properties of magnesium/magnesium alloy orthopedic implants, enabling the analysis of the regulations of porous structures on the degradation behavior and the corresponding mechanisms. In different degradation experiments, a diverse and inconsistent range of solutions is commonly employed to construct the simulated body fluid environments, with variations in both composition and concentration. This heterogeneity complicates the direct comparison of degradation rates across different studies. Moreover, most studies utilized static or semi-static immersion conditions in the degradation experiments, which could not precisely simulate the body fluid flow in the actual physiological environment of the human body. The dynamic immersion conditions with a flow rate of 2 mL/(100 mL/min) can more accurately simulate the body fluid flow in the musculoskeletal system. Significant discrepancies exist between the degradation rates of magnesium/magnesium alloy orthopedic implants observed *in vitro* and *in vivo*. Therefore, *in vivo* degradation experiments should be carried out preferentially to obtain more accurate data. In the numerical simulations of the degradation behavior of magnesium/magnesium alloy orthopedic implants, the influences of various factors can be simulated by adjusting model parameters and boundary conditions. Compared to degradation experiments, numerical simulations are more efficient and resource-saving. Moreover, stress/strain and fluid flow field distributions in the structure of the implant during the degradation process can be computed through the numerical simulations, facilitating the analysis of the “structure-mechanics-degradation” interaction mechanisms. However, current degradation numerical simulation models have limited consideration of the *in vivo* biological processes, such as the clearance of degradation products by tissues and the influences of surrounding bone remodeling on stress redistributions. Future research should focus on the development of more comprehensive multi-physics coupling models that integrate electrochemical corrosion, stress fields, and biological interactions to simulate the “structure-mechanics-degradation-biology” interactions during the dynamic degradation process of magnesium/magnesium alloy orthopedic implants more accurately.

The degradation mechanisms of magnesium and magnesium alloys in physiological environments are complex. At present, no single theory can fully explain all experimental observations. Therefore, the applications of more advanced surficial characterization, *in situ* analysis, and atomic modeling techniques are necessary to further clarify the degradation mechanisms of magnesium/

magnesium alloy orthopedic implants.<sup>144</sup> Material composition modification, surface treatments, and structural optimization are three primary approaches to address the issue of excessively rapid degradation rates in magnesium/magnesium alloy orthopedic implants. Aluminum and rare earth elements are frequently applied as alloying elements to modify material composition; however, the long-term biocompatibility of these alloying elements remains a concern due to their potential negative effects on the human body. Although the surface treatments can reduce the degradation rates to a certain extent, achieving a satisfactory match between the degradation and bone repair rate remains challenging. Structural design of implant offers advantages over the abovementioned two approaches, but further research is needed to comprehensively compare the advantages and disadvantages of these three approaches to obtain more rigorous conclusions.<sup>127</sup> To improve the performance of magnesium/magnesium alloy orthopedic implants, the optimization of porous structural design parameters is crucial. However, the current challenge lies in the balance among various performance requirements, including mechanical strength and compatibility, fatigue resistance, and tissue regeneration performance. A comprehensive consideration of the multiple factors is necessary to identify the optimal balance in porous structure design. Therefore, further research is needed to develop novel structural design methods, which can offer greater flexibility and decouple the different performance requirements, ensuring that adjusting parameters related to one property does not cause a significant impact on the others.<sup>159</sup>

Future research should be focused on the following directions. First, standardization of simulated body fluid environments and immersion conditions in degradation experiments is essential, enabling the degradation experiment results to be more instructive and allowing direct comparisons among different studies. Second, to achieve a satisfactory match between bone repair and the degradation rate of magnesium/magnesium alloy orthopedic implants, a systematic investigation of the potential synergistic effects between different influencing factors is needed. Moreover, designing structural parameters and material composition of magnesium/magnesium alloy orthopedic implants is generally conducted independently in existing studies, without sufficient consideration of their coupled influences on degradation behavior and tissue regeneration processes. Quantitative models that systematically describe the “structural design variables-material composition-degradation behavior-tissue regeneration” relationships remain to be developed. The influences of the porous structures on the mechanical properties, degradation behavior, and tissue regeneration

performance of magnesium/magnesium alloy orthopedic implants are complex, exhibiting inconsistent or even contradictory trends that require careful trade-offs in the design. Combining generative techniques based on artificial intelligence<sup>160,161</sup> (including generative adversarial networks, variational autoencoders, deep learning, and reinforcement learning) and data-driven inverse design paradigms, it is possible to achieve efficient generation of structural parameters, accurate prediction of macroscopic performances, and effective trade-offs between multiple design objectives. These advanced design technologies can overcome the limitations of traditional design methods, such as cumbersome processes, insufficient flexibility, and low efficiency, and provide a new inspiration to optimize the design of magnesium/magnesium alloy orthopedic implants. These technologies will help achieve an optimal match between implant degradation rate and tissue regeneration, facilitating the development and clinical applications of magnesium/magnesium alloy orthopedic implants.

## 5. Conclusion

Porous magnesium/magnesium alloy orthopedic implants have attracted significant attention due to their favorable biocompatibility, biodegradability, and mechanical compatibility with bone tissues. Many studies have confirmed the application potential of porous magnesium/magnesium alloy orthopedic implants. However, uncontrollable degradation behavior, the mismatch between degradation-induced mechanical property changes, and tissue regeneration rates are the main bottlenecks currently hindering the clinical translation of porous magnesium/magnesium alloy orthopedic implants. The porous structure is a critical factor influencing the degradation behavior of magnesium/magnesium alloy orthopedic implants. This study summarized the widely applied methodologies in investigating the degradation behavior of porous magnesium/magnesium alloy orthopedic implants and their respective features. The influences of the porous structures of magnesium/magnesium alloy orthopedic implants on their degradation behavior and the corresponding “structure-mechanics-biology” interaction mechanisms during the degradation process were systematically analyzed. The main findings of this study include:

- (i) AM technologies offer numerous advantages compared to traditional manufacturing methods. The specific selection of an AM technique and its corresponding process parameters is critically important, contingent on the particular requirements of the implant
- (ii) Degradation experiments and numerical simulations each possess distinct emphases and advantages

in characterizing and describing the degradation behavior of magnesium/magnesium alloy orthopedic implants. Their mutual validation provides a robust foundation for the optimized design of magnesium/magnesium alloy bone implants

- (iii) Porous structures serve as a crucial vehicle for modulating the mechanical properties of magnesium/magnesium alloy orthopedic implants, bearing and transmitting mechanical loads, and establishing the local mechanical microenvironment. They exert a significant influence on the intricate interplay between physiological loading, implant degradation behavior, and bone tissue regeneration
- (iv) The degradation of magnesium/magnesium alloy orthopedic implants within the human physiological environment is a complex process driven by multifactorial coupling. However, a quantitative description of the underlying “structure-mechanics-biology” interaction mechanisms remains presently unattainable.

This study provides a systematic understanding of the state-of-the-art research and future directions in the field of porous magnesium/magnesium alloy orthopedic implants to guide future development and applications.

## Acknowledgments

None.

## Funding

This work was supported by the National Natural Science Foundation of China (Nos. 12425209, 12402351, 12332019, 12172043), the Beijing Municipal Natural Science Foundation (No. L241067), and the Research Funding of Hangzhou International Innovation Institute of Beihang University (No. 2024KQ108).

## Conflicts of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Ethics approval and consent to participate

Not applicable.

## Consent for publication

Not applicable.

## Availability of data

Not applicable.

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