Bio-Design and Manufacturing (2019) 2:76–95
https://doi.org/10.1007/s42242-019-00039-6

RESEARCH ARTICLE

Generate basic conceptual solutions for 3DPVS via utilizing TRIZ

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Received: 8 March 2019 / Accepted: 3 April 2019 / Published online: 25 April 2019

Abstract

For cell culture scaffold innovation, 3DPVS, namely 3D printed vibratory scaffold, was indicated as a future novel product, and it currently stands at conceptual development stage. One essential part for 3DPVS design is innovation, and TRIZ (algorithm of inventive problem solving) was studied as promising method for generating novel conceptual solutions. This study targets designing and solving 3DPVS problems using TRIZ in the new biodimension. We aim to utilize TRIZ to conduct a multi-layer problem-solving process, which is to address design concerns of 3DPVS, especially at super-system to system level. In this connection, TRIZ is used to address basic constraints and contradictions inside regarding trinity of 3D printing, 3D scaffold and bio-based vibratory functionality. In the study, five basic conceptual solutions for potential 3DPVS, namely magnetic, electric, mechanical, light and thermal based, have been generated. A brief evaluation has also been conducted, where magnetic-based 3DPVS shows the relatively highest applicability as potential 3DPVS. Compared with traditional experimental-oriented processes for biodesign, the approach of utilizing TRIZ can be inspiring and reinvigorating, which prepares a ground for future 3DPVS design to address detailed sub-system concerns. This study might, to some extent, fill a gap in scaffold design and TRIZ literature and hopefully provide a comprehensive perspective of a timely topic.

Keywords 3DPVS · 3D scaffold · 3D printing · Scaffold innovation · Biodesign · TRIZ · Concept generation

Introduction

Basic knowledge of scaffold engineering is useful to understand the paper scope. Cell culture scaffold is defined as a class of artificially created biomimetic products used for in vitro cell cultivation via partly mimicking properties in real tissue. Biodesigning of novel scaffold, from one perspective, can contain two directions, first as 'static into dynamic' with scientific proves that dynamic scaffolds advantage over traditional static ones. Scaffolds were focused on dimensional advancing from '2D into 2.5D and 3D.' Artificial 3D scaffolds have been invented, with better performance compared with traditional 2D cell culture methods. Another direction indicated the attempts to develop cell culturing with dynamic properties, aiming to approximate part of 'exact' dynamic environments in real tissue. Following this tendency, the concept of 3DPVS, namely 3D printed vibratory scaffold, was proposed as novel future concept to further explore the higher potentiality in scaffold engineering. Three elements were identified for 3DPVS, that is, firstly the novel fabricating technology as 3DP which benefits traditional means of scaffold fabrication, secondly the vibrating property which was proposed as one of the most evolutional aspect in dynamic developing of scaffold due to its cosmic trait for bioevolution in general [1] and thirdly the 3D scaffold itself as the very application of the innovation focus.

Prior to detailed design which is currently impractical, concept justification of 3DPVS has been completed with a basic proposal of conceptual design using three stages, so to speak, design initiation, concept generation and concept evaluation [2]. Concept generation was identified as the key stage for 3DPVS development since it focuses on innovation. Due to this nature, traditional 'trial-and-error' experimental methods for biodesign seem inadequate, at least at this conceptual design stage. TRIZ, Russian acronym for the 'Theory of Inventive Problem Solving,' in this connection has been identified as possible innovation method for generating applicable 3DPVS concepts. Three-layer design hierarchy is utilized by TRIZ philosophy, including super-system, system and sub-system [3, 4]. Super-system to system-level

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design aims to identify the basic elements of 3DPVS, at the most fundamental and background level, such as what the new vibration mechanism would be, how this mechanism possibly work, indicating the cons and pros of this mechanism over others being put forward during the same design process. Following which starts system to sub-system-level design, dealing with the detailed identification of 3DPVS parameter in terms of its geometrics, mechanical characterization, biological controls and vibratory properties. Design generally follows a theoretical abstract into detailed concrete flow. In this study, TRIZ will be used for bringing out 3DPVS concepts at super-system level, with its typical contradiction-solving philosophy following a multiple-layer problem-solving process.

A structured problem-solving process containing four layers will be utilized in this study. First three layers aim to identify problems and contradictions, use TRIZ to analyze and address them, as well as generate 3DPVS conceptual solutions at the most fundamental level. The fourth layer is used to evaluate the generated solutions via investigating their relevance, practicality or value in, respectively, super-system, system and 3DP fabricating constrains.

First-layer analyzing and problem solving

The first step of concept innovation using TRIZ, as proposed in TRIZ methodology, is to determine, identify basic solution (also called current, traditional reference solution) for achieving potential 'vibrating-scaffold' purposes. Scenario of basic solution has been studied in the literature review, regarding how vibration was applied and how traditional utilization of vibratory cell culture was approached. Studies on design initiation also discussed the components of the basic solution for 3D cell culture utilizing vibration mechanism [5], summarizing which components of basic solution(s) will be transformed into a tailored format as input for TRIZ process.

Abstracting and identifying first-layer problem

The aim of the first layer is to identify design contradictions and conflicts which are most obvious.

Abstracting first-layer problems in basic solution

After analyzing the basic model (static scaffold connected with mechanical vibrator), five fundamental problems can be identified, which could be used as input for conceptual design.

1. While designers find that scaffold being dynamic or vibratory can be of more value on 3D dynamic culture process, traditional 3D scaffold remains static or passive, which needs to be improved.
2. Traditional 3D scaffold applied together with vibration mechanism has negative effect on cell culturing, which needs to be improved.
3. Traditional vibration mechanism cannot generate tailored vibration in different areas of scaffold, while it is useful to create localized stimulation from different parts of scaffold on cells.
4. Traditional mechanism of vibration, chiefly the 'coarse' mechanical vibrators, cannot generate 'finer' vibrating stimulation, such as enough accuracy, which is required for precise dynamic control in cell culturing.
5. 3DP technologies have been previously applied on culturing static scaffold, while the application of 3DP on dynamic or potential vibratory scaffold, as what and how, yet remains unexplored.

Identifying first-layer problems using route-based mechanism

After identifying problem, the contradiction inside can be identified through the analyzing method as proposed for 3DPVS design. Table 1 shows the analysis result.

- First problem is system contradiction, meaning that the current stage of 3D scaffold being static or passive contradicts some of the requirements in 3D dynamic culture process where scaffold needs to be dynamic or vibratory.
- Second problem that belongs to contradiction type 3, negative or harmful effects from currently applied scaffold plus vibration mechanism needs to be addressed.

Table 1 Route and contradiction corresponding to the identified problems

	Contradiction type[a]	Contradiction name[a]	Route[b]	Solving approach[c]
Problem 1	Cont. 2	SC	Route 2	ACM, IPA
Problem 2	Cont. 3	NNC	Route 3	ISS, SFMA
Problem 3	Cont. 1	PhC	Route 1	SPA
Problem 4	Cont. 1	PhC	Route 1	SPA
Problem 5	Cont. 4	BC	Route 1, 2	ACM, IPA, SPA

[a] *Cont.* contradiction, *SC* system contradiction, *PhC* physical contradiction, *NNC* contradiction neither physical nor system, *BC* contradiction both system and physical

[b] Multi-route-based TRIZ containing routes 1, 2 and 3, respectively, deal with physical contradiction, system contradiction and contradiction not easily identified

[c] *ACM* Altshuller contradiction matrix, *ISS* innovation standard solutions, *SPA* separation principle analysis, *IPA* innovation principle analysis

- Third one regards to physical contradiction, that is, different parts of scaffold, being vibrated or could potentially create vibration, need to function separately in tailored way.
- Fourth problem is based on physical contradiction, meaning that the frequency from vibration mechanism cannot be precise, though precise frequency is necessary.
- Fifth problem is a hybrid contradiction, containing both PhC and SC.

Solving identified first-layer problems

Identified problems could potentially be solved using proper TRIZ route.

Solving problem 1 via ACM and IPA inside route 2

For this contradiction, it means 3D scaffold needs to be static or passive to maintain original useful functions on cell culture, as well as being dynamic or vibratory. In this connection, current structures or microstructures of scaffold cannot operate dynamic functions. Two related parameters will be selected as input, namely 'structure' and 'dynamic function.' This is single-parameter-based contradiction; therefore, the traditional 1 versus 1 matrix will be used. Several solutions can be found, and the one indicating 'materiality' will be potentially selected. In this way, the solution to solve problem one possibly lies in how and what materials will be applied for the microstructure of 3D scaffold. Therefore, changing into dynamic or smart materials can be proposed as logical solution.

Solving problem 2 via ISS, SFMA inside route 3

To address negative or harmful effects from the currently applied scaffold-vibration mechanism, SFMA will be conducted together with ISS. Basic SMA model is to mitigate negative effects of one part of system, while maintaining original positive ones of another part. The original vibration on scaffold is undesirable; S1 is vibrator, F1 the mechanical force to transmit the vibration, and S2, the scaffold to be vibrated. Existing vibration tends to be rough and imprecise, which is undesirable since we want precise and subtle vibrations. Then, a subtle vibration mechanism will be proposed, which will not negatively affect cells S2 but have positivity as F2 compared with F1. In this connection, mechanical vibration, or in other name, scaffold being vibrating in mechanical ways that is usually either too rigid or intensive, can be replaced by other vibration mechanisms which tend to be subtler, finer or gentler in terms of vibrating effect. Therefore, the solution indicates using a subtler vibration mechanism, for instance using light, sound, electronic force or magnetic force to replace mechanical vibrations.

Solving problem 3 and problem 4 via SPA inside route 1

For problem 3, the essence is a physical contradiction regarding space consumption or occupation. Using the 'Separation in Space' principle in SPA, a potential solution is generated which can be structured as follows: Different part of scaffold needs to have different characterization, so it can respond to the same external vibration in separate ways.

For problem 4, its essence is about the frequency accuracy, which needs to be more precise. Based on the principle 'Separation upon Conditions,' a possible solution is generated: Scaffold can work at different vibration environments, such as changing from mechanical vibrator into bioreactor-based mechanism.

Solving problem 5 via ACM, IPA, SPA inside route 1 and 2

In terms of SC aspects inside the question, it is between requirement of dynamic scaffold and 3DP manufacturing capability. Parameters are related to adaptability of 3DP on scaffold and usefulness of manufacturing. This is a 1 versus 1 contradiction, and we use the AP as 'Ease of Manufacture' (parameter 36) and DP as 'Adaptability or Versatility' (parameter 32). From three principles, 2, 13, 15, namely separation/extraction, action reversed/other way around, dynamization/dynamic parts, we choose the principle 2. Based on IPA analysis and corresponding 3DPVS strategies, it indicates that dynamic scaffold can be divided into different parts which can be fabricable by 3DP means, single or hybrid.

For physical part of problem 5, 3DP has not been used popularly for fabricating bio-based 3D dynamic or vibratory scaffold via formal and maturely established approach. However, for dynamic microstructure of objects in other realm, like tissue or construction, 3DP was utilized and proven to be applicable for both static objects and dynamic ones. Using principle 'Separation from system and sub-system,' original problem therefore is converted into how to utilize 3DP available materials and structures to fabricate dynamic or vibratory scaffold. Thus, one possible solution logically indicates of using 3DP fabricable materials and structures that can operate dynamic functions, onto the design of 3D vibratory scaffold.

Generating potential concept and solution

Based on inspiration and novel ideas created in the last step, a concept can be generated, which contains a hybrid of characters corresponding to problem in layer one. Five characters can be integrated and trimmed into a trinity-component concept.

Character 1 Change materials of 3D scaffold microstructure from traditionally static materials into dynamic, smart ones.

Character 2 Using subtler vibration mechanisms, such as the vibrations created from light, sound, electronic force or magnetic force to replace mechanical vibrations.

Character 3 Different part of scaffold needs to have different characterization, so it can respond to the same external vibration in separate ways.

Character 4 Scaffold needs to work at different environments where vibration is conducted, such as changing from means like mechanical vibrator into bioreactor-based mechanism. The whole part of scaffold is in contact with vibration source, not only the bottom.

Character 5 3D vibratory scaffold can be fabricated by 3DP means, through designing both materials and geometrics into formats that is achievable by 3DP.

Description of the first-layer solution: Potential 3DPVS can be a novel scaffold which endows with a trinity of characteristics. First, 3DPVS could have 3D geometrics similar as traditional cell culture scaffolds, while fully support the subtler-form vibrations generated from within or without, as well as enabling traditional macro-level vibrations which tend to be coarser. Second, scaffold's vibratory or dynamic functionality is predominantly achieved through designing material composition. Third, fabrication for 3DPVS could be largely the same as for novel 3D static scaffolds; for specialized vibratory structures or material composition, they possibly can be segmented from original scaffold structure and fabricated by 3DP separately, where single or hybrid 3DP might be applicable.

Second-layer analyzing and problem solving

Based on the trinity-component concept generated for the first-layer problems, new problems, termed as second-layer problems in distinction with previously problems, naturally come out which will be addressed via TRIZ.

Abstracting second-layer problem

The generated concept in the first-layer problem solving derives a trinity of concepts which need to be further addressed. Using TRIZ language, the first would be '3D traditional scaffold with non-mechanical vibration,' the second as 'vibratory biocompatible material' and third as '3DP fabricable vibratory material.'

3DPVS is the 3D Micro-geometric Supporting Subtle-form Vibration. This characteristic means there need the traditionally external mechanism vibrations transformed into non-mechanism ones, while the structures of the scaffold could remain the same because there is no restrain based on this.

3DPVS is the 3D Vibratory/Dynamic through Biocompatible and Smart Materials. This means that the newly applied material on 3D scaffold needs to fabricate 3D constructs, being both vibratory in motional control and biocompatible in terms of cell culture use.

3DPVS is the 3DP Fabricable, Similarly as for Traditional Scaffold Regarding Geometric and Material Structuring. This means that the scaffold's constructing material needs to be fabricable through 3DP technologies, design requirements of scaffold need to be within the feasibility scope of 3DP, and 3DP fabricated microstructure can be vibratory or dynamic in some conditions.

Regarding the 3DPVS concept with these characteristics, several contradictions are logically identified, chief ones listed as follows:

1. For traditional types of geometrics in scaffold base models, they were rarely tested on dynamic cell culture studies. However, designers could access knowledge regarding which geometric characterization plays more positive role in other engineering contexts. The bridging issue becomes a concern.
2. Some materials being biocompatible cannot be dynamic, while some dynamic ones cannot be applicable for cell scaffold purposes. If materials are mixed by both, then it may hinder the functionality of either. So how to make best of both worlds remains a vital concern.
3. Regarding the unique benefits of different 3DP systems, the potentiality of scaffold may be limited if merely one system is applied as fabricating tool. But traditional cell culture scaffold chiefly used one fabrication method. Using multiple 3DP for fabricating 3DPVS, how and what, becomes a concern.

Problem solving regarding second-layer ideas and concepts

Connected with previous section, three contradictions identified will be analyzed, structured elements shown in Table 2.

Contradiction solving for problem 1

Firstly, we will utilize the principle 'Separation on Space,' to give possible direction that different parts of scaffold can have different geometric structures, that is, a hybrid structural microstructure inside scaffold might be positive to cooperate with some tailored dynamic functionality, while this seems not the design priority at this stage due to higher contradiction revolving materials.

Table 2 Structured analysis regarding three contradictions identified in the second layer

Problem no.	Contradiction type	Contradiction name	Route	Solving approach	Notes
Problem 1	Cont. 5	PhC + BC	Routes 1,3	ACM, IPA, SFMA	Also solvable in route 4
Problem 2	Cont. 2	SC	Route 2	ACM, IPA	ISS assisted
Problem 3	Cont. 2	SC	Route 2	ACM, IPA	3DP expertise required

Using the established NSFM model, as 3D geometrics remain passive force (P) only, the active force of non-mechanical vibration would act as active force (A). Then, material composition of scaffold will be chosen as neutralizing force (N) to cooperate the geometrics and vibration. This concept will depend on the vibration mechanism only, and 3D geometrics can be generally the ones from either of the three 3DP-based models. When it passes to the relationship of vibration and material, it comes to the following stage. Assisted with SEA analysis regarding 'structure' and 'vibration,' the following four models with different unit cell configurations designed for porous structured bone scaffold can positively be selected with vibrations as follows:

a. Cubical pore model with part- or full-structural vibration mechanisms
b. Spherical pore model with part- or full-structural vibration mechanisms
c. Shifted cubical pore model with part- or full-structural vibration mechanisms
d. Shifted spherical pore model with part- or full-structural vibration mechanisms

Further analyzing this scenario, suppose geometric structure is not stable sufficiently, then this negatively affects scaffold's dynamicity. Material dynamicity and structural stability therefore could contradict each other, which needs further addressing.

Contradiction solving for problem 2

Addressing this question possibly opens avenue bridging traditional static scaffold into novel vibratory ones. According to previous analysis, 'material' would be the basic element transmitting vibrations among geometric structures. Work here will be partly addressed via SEA, to firstly identify proper materials both dynamic and biocompatible and, secondly, dynamic but non-biocompatible materials which could be arranged in some way inside biocompatible materials, so cells only interact with biocompatible ones, while general structural vibration is still achievable by the dynamic non-biocompatible ones. Further illustration of this will be in relation to 'Material composition.' In brief, solution for question two basically fulfills five requirements:

- Requirements of specific smart material(s) for providing vibratory functions of scaffold;
- Requirement(s) of other dynamic or bioactive material(s) providing similar functions triggering macro- or micro-vibrations on scaffold.
- Material composition using new materials should fulfill traditional requirements of mechanical properties of 3D scaffold;
- Compatible 3DP requirements for dynamically designated geometrics and material composition;
- Availability of referential studies or scientific resources, that is, if little literature supports definite mechanism, then perhaps exploration from this direction at the current stage would be extremely arduous;

Contradiction solving for problem 3

Nature of problem 3 belongs to system contradiction. Using SEA to invest the general vibration mechanism, as well as studying relationship between vibration and cells, we propose that to address this contradiction, the generated vibration from new designed mechanism at the first place needs to fulfill a list of fabricating requirements, namely super-system requirements centered on 3DP. Integration of concepts after analyzing these would contribute potential evaluated solution.

Supposing solution for second-layer problems

Based on previous contradiction solving, several supposed concepts regarding vibration mechanism of 3DPVS could be generated, which may include multiple aspects. Analyzing connected scaffold system, these aspects help formulate contradictions acting as input for problem solving in the next level.

- Scaffold itself as mechanical shaker system;
- Bioreactor system with better control-precision plus liquid-active materials;
- Scaffold with materials that can react with cells to generate vibratory or dynamic functions;
- Field-based or non-traditional solutions, such as using system of electric or magnetic sources plus the electric or magnetic active materials, using piezoelectric vibra-

tion system or using electromagnetic forces motivation system;

When it comes to this phase, the basic ideas of using vibrations on definite materials have been proposed; it needs further analysis toward their interconnections. The concept here can be called ‘add-on’ to update the solutions generated in the first-layer problem realm.

Analyzing the super-system criteria in second layer

With introducing new vibrating mechanism, new problem inevitably appears which needs to be addressed. At the current stage, from design initiation, as well as literature studies [6–11], we generate a list of vital vibration constraints from super-system level, as shown in Table 3.

In detailed 3DPVS design, a huge number of minor vibration-based contradictions would exist. Analyzing fundamental bio-based contradiction, namely possible vibration versus scaffold’s biological controls, is thus of prioritized significance. Here it briefly discusses listed criterion in relation to vibration mechanisms that will be possibly generated.

High predictivity of the vibration mechanism. Many vibration mechanisms tend to be unpredictive regarding effects on cells or biomedical application, that is, they may have some biobenefits, while these benefits either remain only partially known, details unknown or artificially uncontrollable. Lack of predictivity on side effects is also a concern. Proven beneficial vibration thus will be used, instead of vibration under current process of investigating, researching or proving. The opposite would increase the cost and failure rate of designing new vibration mechanism, which is the center of gravity in this research. In this connection, proposed vibration needs to be relatively predictable as being practically useful means on current cell cultivation. For some novel vibration means, its high potentiality but low predictability constitutes a design contradiction.

Better simulation of conditions in a living organism. Newly applied mechanism needs to function through the microfluidics inside scaffold which continuously provide nutrients to where cells need. This means that cells and organs under such mechanism can grow in a healthy, natural or tailored way as culturing of conditions in vivo. Some vibration forms might have proven benefits on ‘dead’ structures, like on engineered constructs or objects, while they become crippled when dealing with ‘living’ organism. The applicability of useful vibration not positively affecting on ‘living’ cells could make up a contradiction. It is interesting that bioenvironment tends to use subtler vibration compared with other engineering realms. So, a finer, subtler vibrating forms rather than traditional ‘coarse’ mechanical methods might be relatively better choice for this question.

Positive issues are caused by the effect of vibration on growth media and expansion of cells. As cells grow in 2D or 3D culture, they consume growth media and exude waste. This can result in toxic waste products, dead cells, nutrition depletion and damage of the environment cells cultured in. Vibration mechanism firstly needs to ensure it will not

Table 3 List of 3DPVS super-system vibration constraints

No.	Vibration criteria and constrains	Chief contradiction	Design importance[a]	Contradiction-level rating[b]
1.	High predictivity of the vibration mechanism	Predictivity–usefulness	1.8	2.0
2.	Better simulation of conditions in a living organism	Simulation–living being	1.6	1.7
3.	Positive issues caused by the effect of vibration on growth media and expansion of cells	Vibration simulation–cell culture applicability	2.0	2.3
4.	Stimulating effect on hydrogel ECM	Vibration simulation–cell culture applicability	1.9	2.1
5.	Effect on certain tissues which may contain undesirable elements	Vibration simulation–cell harms	3.0	3.2
6.	Integration level of vibration and flow	Vibration–liquid flow	2.9	3.1
7.	More realistic way to grow and treat tumor cells	Vibration–biohealing effect	3.2	3.3
8.	Throughput effect for multiple scaffolds	Applicability–usefulness	3.7	3.5
9.	Positive connection with other scaffold systems	Applicability–practicality	1.8	2.4
10.	Non-hindering effect on geometric control	Vibration–geometrics	2.5	2.7
11.	Material availability and cost	Usefulness–material cost	3.4	3.6
12.	Further frequency comparison	Frequency–bio-based relevance	4.0	3.9
13.	General benefits on bone cell culture	Vibration–usefulness	1.9	2.7

[a,b]Was rated on a four-point Likert scale ranging from ‘none,’ ‘slight,’ ‘medium’ to ‘strong’ through the literature studies as well as consulting relevant experts in bioengineering, design and manufacturing

[a]Importance indicates to the weight of element that designers need to consider during the process

[b]Contradiction level indicates to the possible conflict intensity that might take place when focusing on the identified criteria

negatively disturb this process. As a result, other following benefits of the definite cell culture become controllable. Since 'growth media' is the very environment cells live, and cell expansion is the basic demand for any kind of cell culturing, limitations on these would create vital conflicts for the entire design process. If positive issues are not attainable, vibrating mechanisms need to ensure their effects at least being 'neutral,' namely, not as any harmful roles for such cellular process.

Stimulating Effect on hydrogel ECM. A 3D scaffold provides hydrogel, an extracellular matrix (ECM), in which cells can survive, grow and proliferate. These ECMs normally have tiny pores allowing the passage of nutrients, gasses to give cells the environment for thriving. Well-developed ECMs also provide essential cues to cells, rendering them crucial for the establishment of physiologically relevant 3D tissue cultures. In this connection, potential conflicts between vibration mechanism and ECM functionality need to be addressed, a better cooperation of which on cell culture inevitably becomes a need when selecting suitable mechanism. For mechanisms which cannot generate proven or certain effect on ECM, its application will be difficult due to the instability and other unknown issues. A benefit on ECM but hindrance on other cell aspects will also create conflict during design process.

Effect on certain tissues which contain undesirable elements. In rare cases, 3D cultures created from specific tissue types (e.g., basement membrane extracts) can contain unwanted components such as growth factors or viruses. For definite vibrations, they might hinder this process, but help or activate these undesirable elements and disturb the aim originally planned for definite culturing. For some mechanisms, such as bioreactor based, they usually help or hinder both useful and harmful elements simultaneously during cell culturing, which contributes to a contradiction if investing further its application on 3DPVS.

Integration level of vibration and flow. Fluid flow, for example tissue blood flow, interstitial fluid flow and culture medium flow, is crucially important for proper functioning of most tissues. Cells respond to flow through differentiation and metabolic adaptation. Vibration therefore needs to positively affect the flow instead of hindering it or causing disturbance on the natural flow for instance in traditional static scaffold culturing. Sound- or electricity-based mechanisms sometimes cause such disturbance. Vibration also needs to help oxygen, or other essential nutrients flow, to the right place at right time. This is especially important for larger-scale cultures where it can be a challenge to distribute nutrients to definite places in scaffold. Integration of vibration and flow hereby will be vital in future's vibratory scaffold since its inner structures would possibly contain several sub-structural areas which require different flow and vibrating stimulations. Considering this, magnetism-based mechanism might be relatively a good option.

A realistic way to grow and treat damaged cells. 3D cell culture systems are good simulators of diseased tissue, for example cancer tumor cells. They can exhibit healing growth and treatment patterns. Meanwhile, mechanical field was typically experimented as lacking efficiency in treating damaged cells; hence, mechanical stimulation might have worse cooperation relationship compared with other vibration forms. As replacement, magnetic field could be an option due to the newly emerged bioactive magnetic materials. Other forms of current vibrating forces have been chiefly under research stage, and formal consensus has not been arrived yet. In this connection, practicality becomes a concern.

Throughput effect for multiple scaffolds. Traditional vibration techniques, such as attaching to vibrator or shaker, are cumbersome and time-consuming, and they generally stimulate scaffold on one-to-one means, that is, for each 3D scaffold a vibration device might be needed. This limits the large cell culturing; for example, many scaffolds are experimented simultaneously for drug delivery purposes. Thus, providing the throughput needed for large-scale experimentation will be considered for selecting good vibration mechanisms. Field-based mechanism has advantage over traditional mechanical others. In other words, for expensive cell culturing process, such as study on cell samples which are precious, one-to-one based approach is still of high value; therefore, methods allowing a flexible shift between both vibration modes need contemplation.

Having positive connection with other scaffold systems. As studied, two main types of tissue engineering exist, namely scaffold-based and scaffold-free. Scaffold-free systems typically use techniques such as magnetic levitation, bioprinting or whole organ printing. Since scaffold is not used for providing simulations, such approaches tend to show a higher appreciation on non-mechanical and invisible stimulating mechanisms. This could benefit developing novel simulating methods for 3DPVS. On the other hand, scaffold-based can be divided due to its chief purpose for culture oriented or tissue implantation. Positive mechanisms could mean the invented vibrating strategies potentially benefit both, though current research mainly focuses on cell culture scaffold.

Non-hindering effect on geometric control. As a consensus, vibration can shake or even crush construction. New vibration mechanism should ensure the functionality of scaffold's geometrics, meaning that the applying of it will not hinder the structures or promise the functions of geometrics that could be there at 3D static culturing. For 'coarse' vibration mechanisms like mechanical shakers, they have higher possibility to damage microstructures of scaffold or structured cells during cultivation process, as well as hindering general geometric controls.

Material availability and cost issue. For this criterion, the selected components of 3DPVS, especially for fabricating materials, are generally required to be inexpensive and easily accessible. This would give benefit for most researches who show interest toward following 3DPVS development. Compared with traditional materials, novel nanomaterials tend to have more advantage due to its bio-based functionality, while they might be more expensive for research cost. Selecting materials with multiple sub-categories would provide with more availability during design, as another consideration for designers.

Further frequency comparison. As one vital aspect of vibration, frequency-based functionality inside 3DPVS needs to be prioritized after the general selection of vibration mechanism. Previously mature investigation on effect of frequency on cell culture, especially bone cells, is largely necessary. Some novel vibration forms, such as newly emerged quantum vibrating method, are of promise but lack general control in regard to its frequencies. Fine vibration but lacking capability to generate localized stimulation, is also creating conflicts in its application. Among different vibrations, those who can generate flexible and wide-range vibrations fulfilling the needs of frequency accuracy, as well as the localized functions, while not contradicting other demands, will be prioritized. It is also important for frequency as easily controllable. Magnetism-based and other field-based methods in this connection could show high promise compared with traditional mechanical means.

General bone cell culture benefit. This will be based on how efficient and effective definite mechanisms work on cells in terms of proliferation, differentiation and tailored cellular growth. Detailed data analysis on cell studies is required to avoid possible contradictions. It is interesting that finer vibration forms generally show a more profitable effect and predicted to witness an increasing application on bioengineering. During conceptual process, designed mechanism might be beneficial whereas causing negativity in practical cell culturing, and this would be one contradiction designers need to consider at the 3DPVS development stage.

Third-layer analyzing and problem solving

Several problems logically appear at this stage after analyzing problems in second layer. TRIZ IPA process will be used as chief tool for generating solutions.

Abstracting third-layer problem

For attributes of 3DPVS on system level, they will be separated into sub-system components as the smallest functional unit of each attribute. Addressing attribute-based contradiction at system level is vital before passing into components sub-system level. Contradiction between attribute and component, for example 'dynamicity' as one attribute parameter, and 'structural stability' inside geometric properties control, resulted from fabricated materials, is a sub-parameter at component level. These two 'parameters' at two system levels can conflict each other. In this connection, several problems can be identified after second-layer problem solving.

1. Dynamicity of materials can contradict the requirements of scaffold in terms of mechanical strength. Structural stability, in this connection, becomes a vital concern when focusing on material dynamicity.
2. As the problem passing from second layer, material dynamicity can contradict its biocompatibility or other biomedical properties, for instance, in tissue scaffold materials need to be biodegradable, while in cell culture scaffold there is no such need.
3. For further addressing dynamic aspects of materials, with relation to their 3DP fabricability, more dynamicity-based parameters need to be identified and selected. 3DP fabricability could conflict with definite dynamicity, and this should be detected at the first place.
4. For potential smart materials, suppose it could endow scaffold with dynamic functions, its biological effect in terms of positive, required cell stimulation, may not be adequate. Lack of bio-based research on smart materials might also conflict with design proposal.
5. After solving issues of the G-, M-, B-parameters conflicting with possible V-properties, inner contradiction, namely new contradictions possibly exist in G, M, B, V, respectively, needs to be further identified and addressed.

Prior to address above-mentioned issues, it is important to understand the basic contradiction level between GMBV characterization of 3DPVS. As summarized in Table 4, it shows the contradiction level when pair of characterization encounters. From TRIZ, we see that one 3DPVS property may ascend at the cost of descent of another, which creates fundamental GMBV conflict. The result was rated

Table 4 Contradiction matrix of 3DPVS GMBV characterization at encountering

Contradiction ranking matrix of 3DPVS GMBV characterization				
↓ ↑	G-	M-	B-	V-
Geometrics (G-)	1.1	1.4	1.9	2.0
Mechanicalness (M-)	1.8	2.7	3.1	4.0
Biological properties (B-)	1.9	2.1	3.2	3.8
Vibratory properties (V-)	1.7	2.8	3.4	3.2

on a four-point Likert scale ranging from 'none,' 'slight,' 'medium' to 'strong,' following the same procedure as previously described.

From this table, we could basically conclude three chief contradictions at super-system level, that is, 'Material Dynamicity' with 'Structural Stability,' 'Material Dynamicity' with 'Material Biocompatibility,' as well as 'Material Dynamicity' with 'Material Fabricability.' Mechanical properties meet with vibratory properties, and material becomes the center of gravity. Vibratory properties encounter with biological ones, and biocompatibility needs to be carefully addressed. Conflict within vibratory properties itself lies in the constrains of the current vibration mechanisms; a better vibration is therefore promising to tackle with this. In the following section, these three contradictions will be focused.

Identifying innovation principles for third-layer contradiction

In this section, ACM, with one to three parameters for ascending and descending column, will be flexibly applied with IPA process. In this connection, for the first problem, namely the contradiction between material dynamicity and structural stability, detailed steps with analyzing process are illustrated as below.

Identifying principles for contradiction between 'material dynamicity' and 'structural stability'

This part will illustrate how to solve one contradiction, or conflict, namely between design parameters of dynamicity in material composition and stability in structural design. Five steps, as discussed in TRIZ methodology, will help to achieve proper innovation principles.

Step 1 Designer needs to find right Material for 3DPVS (EX1)[1] but lack the means.
Step 2 Material Dynamicity (PE1)[2] is the most appropriate parameter to evaluate that goal is reached.
Step 3 The most obvious way to make Material Dynamicity evolve in the wanted way is that
Vibratility (PA)[3] is Vibratory (VA)[4].
Step 4 If Vibratility was Static or Inactive (VAB)[5], structural stability (PE2)[6] would be the most positively impacted.
'Vibratility' must be 'Vibratorily Active' to satisfy Dynamicity of material and Static or Inactive to satisfy structural stability. Table 5 simply shows the four resultant effect when contradictory elements meet. Note that in this scenario:

[1]Explain with an infinitive verb + a complement. This is the goal of design process.
[2]Explain with which parameter you will estimate that goal (to find right Material for 3DPVS) is reached.

Table 5 A simple illustration for the combined effect of contradictory element

Contradiction	Vibratility	
	Vibrationally active	Static or inactive
Material dynamicity	Positive	Negative
Structural stability	Negative	Positive

[3]Explain which parameter being a lever to make Material Dynamicity evolve in the wanted way.
[4]Define with an adjective the state of Vibratility.
[5]Define with an adjective the opposite state of Vibratorily Active for vibratility.
[6]Explain which parameter would be most positively impacted if vibratility was Static or Inactive.

Step 5 Utilizing TRIZ ACM (Alstruller's Contradiction Matrix)

Firstly, we select the generic parameters in the matrix that fit with the parameters of the proposed contradiction. The inventive principles can be obtained from ACM which help solve this contradiction. For this case, 15 principles are obtained. After calculating the rate of these principles, top several will be prioritized for analysis, and final number of principles is usually limited below three. Based on literature studies and other evaluation means, one final design principle, separate as one of 40 innovation principles or a hybrid of multiple, will be chosen for solving the focused contradiction. To be specific, in each IPA more than ten principles would be available, and designs need to choose suitable most ones to ensure efficiency and accuracy of innovation process. Table 6 shows an ACM with calculated rates of applicability of obtained principles.

From the principles analyzed in Table 6, a possible solution would be to change existing physical and chemical parameters of 3D static scaffold, such as from static materials into smart dynamic materials. Periodic action, as second prioritized, would mean a timely controlled functionality not creating too much intensity on scaffold's structures. Inserting atmosphere could also help protect stability of structures, via creating some supporting forces among geometrics, etc.

Identifying principles for contradiction between 'material dynamicity' and 'material biocompatibility'

After the previous step, the question comes, even if the selected materials can be dynamically vibratory and ensure the stability of structures built upon these materials, they might be biotoxic or incompatible with cell culture applications, so the second parameter aside from structural stability comes into play, that is, biocompatibility of materials. For biocompatibility parameter, the analysis and calculated rates are shown in Table 7.

The principles obtained here are to ensure the material composition can either guarantee the dynamic functions, as well as fulfilling end-use cell culture context. Note that based on the new scenario, three parameters selected in for 'Material Dynamicity' are partly different with the previous 'structural stability' one.

Identifying principles for contradiction between 'material dynamicity' and 'material fabricability'

Third contradiction comes between material dynamicity and material fabricability. As discussed, the ideal fabrication methods for 3DPVS would be 3DP. However, materials might be both biocompatible and vibratory whereas unable to fulfill 3DP fabrication requirements. At current conceptual stage of 3DPVS, there could be materials which show potentiality in terms of generating possible vibrations, but 3DP has not been maturely investigated on their fabrications. Here, three principles for fabricability are selected and the contradiction matrix is shown in Table 8.

For local quality, it could mean using different 3DP methods to fabricate different parts of scaffold, to make best the advantage of each 3DP system, namely, droplet-based, laser-based and nozzle-based systems. Changing some mechanical parts with optical or acoustic means might also be applicable.

Table 6 TRIZ IPA focusing on finding principles for the contradiction of structural stability and material dynamicity

IPA analysis	
Structural stability → Material dynamicity ↓	8. Volume of stationary object 13. Stability of object's composition 14. Strength
9. Use of energy by moving object 16: Durability of action of stationary object 27: Reliability	35. Change of physical and chemical parameters (18%) [selected] 19. Periodic action (13%) [selected] 5. Combining; 2. taking away; 39. inert atmosphere; 11. beforehand cushioning (each 7%) 28. Mechanical principle replacement. 24. Intermediary 13. Other way round 3. Local quality 34. Rejecting and regeneration of parts (each 5%)

Table 7 TRIZ IPA focusing on finding principles for the contradiction of material dynamicity and biocompatibility

Material biocompatibility → Material dynamicity ↓	17. Temperature 26. Quantity of substance 31. Object-generated harmful factors
9. Use of energy by moving object 15: Durability of action of moving object 35: Adaptability and versatility	35. Change of physical and chemical parameters (17%) [selected] 3. Local quality (16%) [selected] 19. Periodic action (10%) [selected] 2. Taking away (9%) 39. Inert atmosphere (6%) 34. Rejecting and regeneration of parts. 27. Cheap short life instead of costly long life. 21. Skip. 16. Partial or excessive action (Each at 5%): 24. Intermediary. 23. Feedback (each 4%) 6. Universality. 15. Dynamicity. 10. Prior action (each 3%)

Table 8 TRIZ IPA focusing on finding principles for the contradiction of material dynamicity and 3DP fabricability

3DP fabricability → Material dynamicity ↓	29. Manufacturing precision 26. Ease of manufacture 31. Productivity
9. Use of energy by moving object 15: Durability of action of moving object 35: Adaptability and versatility	35. Change of physical and chemical parameters (15%) [selected] 28. Mechanical system/interaction substitution (15%) [selected] 27. Cheap short life instead of costly long life (11%) [selected] 3. Local quality [selected]; 12. equipotentiality (each 6%) 26. Use of copies (copying); 13. other way round; 17. another dimension (5%)

Analyzing contradiction issues of smart material stimulus–response

Based on innovation principle, smart material could be enabling with newly designed vibration mechanism. Using TRIZ, the complex contradiction inside desired vibration might be transferred into simple mechanical problem. Part of solutions to material problem lies in analyzing the demands of material to variably 'respond' to different cell culture conditions. Two questions are logically related, the first 'what vibration response does this situation require' and the second 'what is changing so to act as a stimulus to create such response.' In this connection, we could analyze problem through TRIZ SFMA (Su-filed modeling analyzing). In the vibration mechanism replacement problem, the primary stimulus is field. Changing the field, therefore, acts as a stimulus which can trigger material response, for instance a mechanical stimulus is used to trigger a mechanical response. The SFM corresponding relationships between smart materials, vibration mechanism and scaffold can be illustrated in Fig. 1. Neutralizing force indicates to design elements that either strengthen or hinder definite functions of S1, S2 or F, so to help S1 generate normal, desired vibration on S2.

Analyzing problem in this stimulus–response manner enables us to classify smart material solutions effectively. Table 9 presents the results via arranging already-known smart materials, re-worked from sources [12–15]. Several smart material resources were identified, namely electrical, magnetic, optical, thermal, mechanical based. Different responses listed on top indicate possible desired results. Stimulus column on left illustrates what is changing or can be changed in system level so to trigger desired response. Different classes of stimulus provide with a range of possible options for the same desired reaction. In vibration replacement problem, single or multiple stimulus might need to work together due to definite design requirements. In other words, the table guides into a scientific effect to find solutions and contributes to judging flexible stimulus–responses of possible 3DPVS.

On the other hand, different field stimulus could also contradict with each other. Analyzing material contradiction solving with SFM and innovation principles, chemical methods tend to show least potentiality; for mechanical and for electrical, optimal, thermal, magnetic based, they indicate relatively high practicability utilized for possible 3DPVS design. Here using SFA for analysis, magnetically vibratory materials (S1) applied with magnetic field (F) show the relatively higher flexible stimulus–response functionality among other possible methods, aiming to fulfill the desired vibratory functions from S1 to scaffold (S2).

Analyzing issues regarding 3D printing system(s)

As novel 3DP materials and methods emerge, 3DP on scaffold fabrication tends to be more effective while more sophisticated [5, 16–18]. Biomanufacturing is predicted to witness the trend of multi-3DP fabricated product, compared with previous bioproducts which were generally achieved by single 3DP [19–21]. However, there lacks systematic study regarding how to cooperate one 3DP with another regarding bio-based product manufacturing. Studying 3DP techniques could contribute to design strategies in terms of proper vibration-based functionality. In real design scenario, perhaps one solution merely prefers one 3DP as optimal method if possible, but analyzing the hybrid still shows future value.

On the other hand, contradiction follows as whether to identify proper 3DP tailored for a definite conceptual solution of 3DPVS at first place or to select 3DP first and then conceive corresponding 3DPVS concept. In this connection, output from system-level components, contradictions, will act as parametric input for analyzing 3DP materials, geometrics and methods, which helps identify definite 3DP hybrid system as proposed. Basically, two ways might exist for potential 3DP hybrid system. First, multiple direct 3DP technologies integrate into one hybrid 3DP system, and

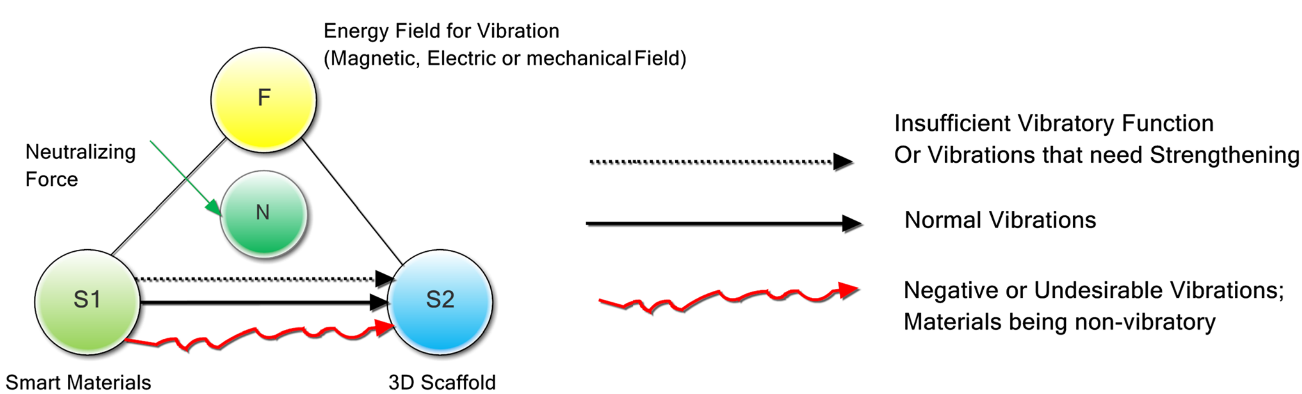

Fig. 1 SFAN model for smart materials, vibration field and 3D scaffold

Table 9 Smart materials stimulus and response potentially useful for 3DPVS

Currently investigated smart material resources					
Response stimulus[a]	Electrical	Magnetic	Optical	Thermal	Mechanical
Electrical		Magnetoelectronics, spin-electronics, spintronics	Electrochromic, electroluminescent, electro-optic, piezochromic, Kerr effect, Pockel effect	Thermo-electric (Peltier)	Piezoelectric, electrostrictive electrorheological electrokinetic
Magnetic	Magnetoelectronics, spin-electronics, spintronics, Hall effect		Magneto-optic, piezochromic	Magnetothermal	Magnetostrictive, magnetorheological
Optical	Photo-conductive	Opto-magnetic	Optical bi-stability	Photo-thermic	Opto-mechanical, photo-acoustic
Thermal	Thermo-electric, super-conductivity, radiometer effect, pyro-electric	Curie point	Thermo-chromic, thermo-luminescent		Shape memory
Mechanical	Piezoelectric, electrostrictive	Magnetostrictive	Mechanochromic, rheochromic		Rheopexic, auxetic, shear-thinning, dilatants, non-Newtonian, pseudo-plastic

[a]The horizontal represents the desired response, while the vertical indicates variable stimuli

second, direct 3DP technologies combine with indirect 3DP technologies. Before addressing these which are vital task for future design, basic 3DP criteria corresponded with TRIZ need to be considered at the first place.

From another perspective, 3DP creates contradictions inside 3DPVS innovation. A fundamental analysis of 3DP-based innovation principles is necessary. From perspective of TRIZ, we possibly obtain seven prioritized criteria or requirement concerning 3DP-based contradiction, as shown in Table 10. Conflict level was estimated on a four-point Likert scale. Analyzing the contradiction, we could search out four basic solutions, which might be universal for all 3DPVS design concerning 3DP, as extraction, dynamicity, self-service and copying. Translation of this helps direct the following design process. The contradictions and solutions identified here can be useful for universal application of 3DPVS, despite what 3DP will be used. It does not contribute directly to design solutions but act as vital support for bettering design process.

Analysis generated TRIZ principles for conceptual 3DPVS

Analyzing design process, we find that most contradiction concerning material dynamicity, biocompatibility and fabricability has prioritized relationship with the following principles, from which we could possibly address conflicts preliminarily. The sequence of principles follows the relative applicability level during design.

1. Change of physical and chemical parameters (92%)
2. Inert atmosphere (85%)
3. Mechanical principle replacement (84%)
4. Local quality (78%)
5. Periodic action (72%)

Fundamental solution extracting from these principles: Generated principles contribute to components of conceptual solution at third-layer problem solving. ‘Change parameters’ indicate to replacing traditional scaffold materials with novel ones which have different physical and chemical parameters. In this connection, the previous assumption of using smart materials might be verified to some extent. Following which, ‘inert atmosphere’ and ‘mechanical principle replacement’ could possibly indicate the new vibrating mode as non-mechanical one, with stimulating atmosphere participated, where the atmosphere could directly control and manifest the vibration functionality. ‘Local quality’ principle further proves that a localized parametric scaffold is practical and promising. In scaffold design, this might mean different localization regarding either geometrics or material composition, or both. In this way, vibration stimulation would become localized as well. In addition, material composition inside 3DP which can generate periodic action, that is, periodic vibratory action, will be a possible approach to tackle some cell culture contradictions, which is inspired by TRIZ principle ‘periodic action.’ This fulfills one possible technical objective of 3DPVS as generating tailored and localized vibrations on cells cultured inside scaffold.

Table 10 TRIZ parameters corresponding to prioritized 3DP-based criteria and possible solution

	TRIZ CTQs TRIZ classification	TRIZ parameters	Conflicts level	Optimization
1.	Dimension between x–y level	Convenience of use	4.0	Ascent
2.	Weight between x–y micrograms or grams	Weight of moving object	3.0	Descent
3.	Global or localized elasticity	Tension or pressure	2.1	Neutral
4.	Fabrication material type and quantity	Complexity of device	2.2	Descent
5.	Design and production cost	Manufacturability	3.0	Descent
6.	Number of attributes, components	Level of automation	2.1	Descent
7.	Mean time between failures (MTBF)	Reliability	1.1	Ascent

Principles generated from TRIZ innovation principles and translations

Extraction This recommendation can be transposed into practice by designing a scaffold containing a single component (extract, remove or separate part or property) but allowing the scaffold to flex, move or vibrate during cell culturing

Dynamicity This recommendation can be transposed into practice by adding parts of smart, elastic materials so that certain parts of the scaffold are not static, rigid (change position relative to each other)

Self-service This recommendation can be translated by reducing the number of moving parts of scaffold system in order to eliminate as far as possible the maintenance of the scaffold

Copying This suggestion can be translated via using a simple and inexpensive scaffold material copy. This could reduce the total number of components of 3DPVS, and the resultant scaffold could consist of a single piece with two-part materials: one traditional static, rigid and the other dynamic, vibratory

Concern follows regarding what is the periodic control and how to manifest this periodicity. It is also interesting that, for previous contradiction solving between 3DPVS's material dynamicity, biocompatibility and fabricability, the analyzed result will not be merely limited for 3DPVS but possibly has wider context for other bioengineering designs. That is, the obtained principles could contribute to a universal reference for biodesigns concerning the trinity of dynamic, biochemical and fabricating issues.

Applicability of principles into selecting fields for vibratory functionality: Following the process of principles corresponding, a data-based evaluation has been established, which is illustrated previously in Fig. 2. Multiple fields have possibility to be applied for 3DPVS corresponding to definite smart materials. Among which, magnetic field as field for vibration (F-element inside SFMA) has a relatively higher percentage in terms of its applicability of TRIZ principles, see in Fig. 2. This means that designing magnetic-based would give higher convenience and practicality compared with others. However, if system requirements change, other field like electric or mechanical might have their own unique strengths over magnetic one regarding applicability. Also, applicability of TRIZ gives a clue but not a definite answer as which solution is optimal in real design. Further study and comparison therefore are necessary, as possibly conducted in the next section.

In this connection, regarding vibration mechanisms which correspond with material dynamicity, several mechanisms can be considered proper, as trimmed into several categories:

- Electric field or sources with 3DP electroactive materials;
- Magnetic field with magnetic-stimulated 3DP materials;
- Heat-based field with thermosensitive active 3DP materials;
- Mechanical means with predictable mechanically reacting materials;
- Acoustic-based field with acoustically activating 3DP materials;

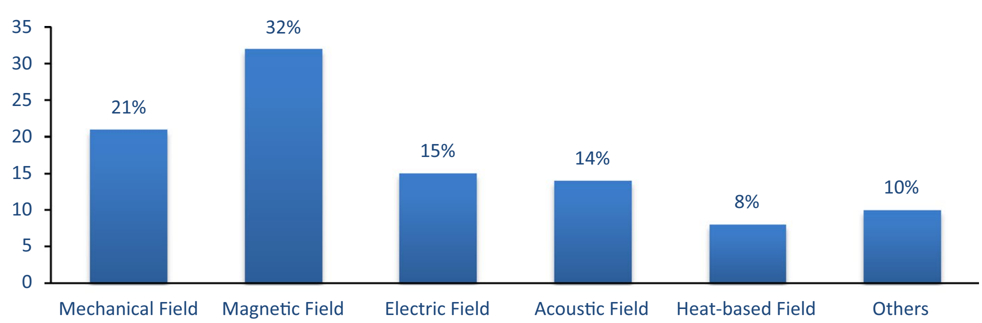

Fig. 2 The applicability of TRIZ design principles onto selecting potential fields

- Others such as light field based with the light-stimulated 3DP materials;

In accordance with these, five general solutions have been created. Future work will be passing into detailed subsystem components and generate concepts at specific level.

Proposing conceptual solutions of 3DPVS generated at super-system to system level

Five novel solutions, as studied, show the potentially to achieve 3DPVS utilizing TRIZ. A translation from super-system into system could be as follows.

Magnetic-based solution: 3DP fabricable magnetic nanomaterial, with external magnetic field. Using the change in the alternating magnetic field to control the dynamicity of scaffold, material can mix with traditional materials in cell scaffold. Magnetic-based shape memory alloys (SMAs) or shape memory polymers (SMPs) could come into play. Also, magnetic field could positively stimulate cell cultivation and enhance some cell performances. As studied, most cells could be receiving a tailored reaction under magnetic stimulations. The shift of field could also be easer comparing magnetic based with other fields. Challenge lies on selecting magnetic-oriented materials, especially nano-based novel materials that can generate micro-level vibrations. Flexibility of 3DP to fabricate magnetic smart materials, which has proven methods, is another benefit employing such as potential 3DPVS concept.

Thermal-based solution: Scaffold has the thermal-activated microstructure constituted of timely controlled shape changing of thermosensitive SMPs. With inserted thermal field, shape change of scaffold can be activated by shifting temperature. The temperature needs to remain at a level where cells will not be hindered in terms of ordinary growth factors. Since in most cases, cells need to remain at a relatively stable temperature for usual cultivation process, this shift, being possibly dramatic and frequent, might negatively affect cells. But for some specific cell cultivation, such as scientific studies on analyzing definite cellular reaction based on temperature and vibration, as well as other studies where cells could tolerate a relatively high or low temperature, such as many types of virus cells, this conceptual scaffold could be a possible option. For bone cells, the applicability is relatively lower, at the consideration of current research need.

Electric-based solution 3DPVS can be fabricated through composite of piezoelectric nanoparticles and photo-liable polymer. Scaffold can produce electrical charge when stress is applied and vice versa. Electricity stimulates the cells cultured inside. Similarly, composite of dielectric elastomers and normal biocompatible material also can be applicable, which could produce large strains upon activation by electricity. For definite cell culture where electric stimuli can help cell proliferation, this method has unique benefit. Negative issue is about the cost of device. Electricity might be needed for each scaffold to generate proposed functionality, thereby increasing the economic pressure for large-scale cell cultivation where multiple scaffolds are employed.

Acoustic-based solution Biomedical acoustic-active materials can be used cooperating with definite acoustic fields, so to generate some stimulation in cell culture. The chief limitation of this is that acoustic wave generally provides with cell culture a negative impact, namely harming or hindering cells' normal functions. Researches have been studying how to mitigate this impact instead of utilizing it for positive cell culture. So, except definite purposes for analyzing cells under the acoustic, this scaffold concept will be less likely to manifest by real designers.

Mechanical-based solution: It is also worth noting that novel mechanical field-based solution, such as using bioreactor, finer vibrator or subtly functioning vibration stage, could also be used for generating 3DPVS. In this regard, materials might not be smart materials; traditional ones would be useful if they can pass the external vibration to cells cultured inside scaffold at satisfactory level. Traditional mechanical vibration contributed the very conflict regarding vibration and scaffold, and the potentiality of whether they could successfully evolve in future biodesign remains as a concern, though numerous TRIZ innovation principles assist with this approach.

Among other solutions, a chief example which is considered as less practical or applicable is light-based method. Anti-counterfeiting structures can be applied on scaffold, using composite such as quantum dots (QDs) suspension (mixture of QDs and photopolymer resin), to mix with biocompatible rigid material. QDs absorb UV light and emit visible lights which help stimulate cells. The negative side of this method is that it could only provide some bioactive stimulation based on light, especially providing with continuous stimuli, but cannot effectively create tailored vibrations, at neither micro- nor macro- levels. How to utilize method of this category therefore becomes a challenge and requires future studies.

In this section, five chief conceptual solutions have been generated for 3DPVS. The problem generating was chiefly through TRIZ-based method, route 1–3. At the current stage, we generated these conceptual solutions without technical evaluating. When it is anchored regarding detailed and specific end-user requirements, design attributes and 3DPVS characteristics/parameters, could it be meaningful to technically evaluate the generated solutions. In brief, the concepts generated in this study are basic structures for potential 3DPVS. Since detailed design information and specification tend to vary from one cell culture scenario to another, the selection and optimization of 3DPVS will be different.

Reality case will be used to incorporate with the design of 3DPVS, so to get the optimal solutions.

Fourth-layer analyzing and solution evaluating

In this section, evaluation work, from super-system to system, will be conducted comparing the five preliminary conceptual solutions generated previously. It aims to summarize the cons and pros of each conceptual solution, as well as indicate optimal solution at the current preliminary stage.

Evaluating the basic conceptual solutions through super-system criteria

Thirteen super-system criteria for 3DPVS have been discussed previously. A quantitative comparison of five solutions related to these criteria will be conducted. It contains firstly indicating normalized weight of thirteen criteria calculated by importance and secondly that of each solution as its fulfilling level against definite criteria. Utilizing the Pugh matrix, the result is shown in Table 11. Original estimation was similarly gathered by a four-point Likert scale. Since different criteria weigh differently in this case, a normalized calculation is used instead of using the direct value from four-scale rating.

From the Pugh chart, we generate overall ideality scores of four conceptual solutions for 3DPVS in super-system scenario. Innovative concepts, respectively, weigh 0.764, 0.965, 1.204 and 0.689, with the datum solution at 0.476. Figure 3 shows a visual comparison of concepts, which shows solution 1, namely magnetic-based 3DPVS, is considered as more promising concept with highest ideality among all generated concepts. Mechanical and thermal based might be in parallel with positionality toward fulfilling super-system requirements, while electric- and thermal-based solutions tend to be slightly less ideal.

From other view point, different solutions show a variable rate fulfilling each criterion. Though the average rate for each solution does not present a dramatic difference, magnetic-based solution indicates the stable most option, which basically fulfills each criterion around a satisfactory level.

Investigating the generated solutions against system-level criteria

After analyzing super-system perspective, we investigate the generated basic conceptual solutions of 3DPVS at system-level, focusing 3DPVS product itself in terms of practical use as well as its proposed objectives (Table 12). Seven system-level criteria were identified, each of which considered as equally significant. A four-point Likert scale was used via collecting feedback from expert groups, rating 1 'none' to 4 'strongly positive.'

Analyzing from Fig. 4, all possible solutions basically show a similar rate in terms of design realizability, which indirectly supports the very assumption that five 3DPVS solutions generated via TRIZ are commonly practical and realizable. In terms of the capability of providing localized vibration, these solutions indicate another similar rating, which can be perceived from the fact that all these solutions are using field-based stimulation which easily manifest different responses inside scaffold if different parts of scaffold, namely characterization, change into unidentical. At the current stage, acoustic- and thermal-based approaches show a

Table 11 Comparison Pugh chart for generated concepts at super-system level

No. of criteria and constraints	Normalized weight	Solution 1 Magnetic based	Solution 2 Electric based	Solution 3 Mechanical based	Solution 4 Acoustic based	Solution 5 Heat based
1.	0.0641	0.0695	0.0379	0.0433	0.0422	0.0370
2.	0.0501	0.0647	0.0729	0.0867	0.0818	0.0438
3.	0.0613	0.0624	0.0845	0.1022	0.0897	0.1044
4.	0.0529	0.0767	0.0525	0.0619	0.0607	0.0842
5.	0.0836	0.0815	0.0904	0.0526	0.0950	0.0707
6.	0.0808	0.0839	0.0933	0.1022	0.0923	0.1044
7.	0.0891	0.0935	0.0700	0.0867	0.0844	0.0572
8.	0.1031	0.0935	0.0758	0.0557	0.0792	0.1044
9.	0.0501	0.0743	0.0933	0.1022	0.0897	0.0842
10.	0.0808	0.0695	0.0933	0.0712	0.0739	0.0707
11.	0.0947	0.0647	0.0583	0.0712	0.0633	0.0842
12.	0.1086	0.0815	0.0758	0.0836	0.0739	0.0572
13.	0.0808	0.0839	0.1020	0.0805	0.0739	0.0976
Overall ideality of concept		0.0782	0.0774	0.0760	0.0771	0.0776

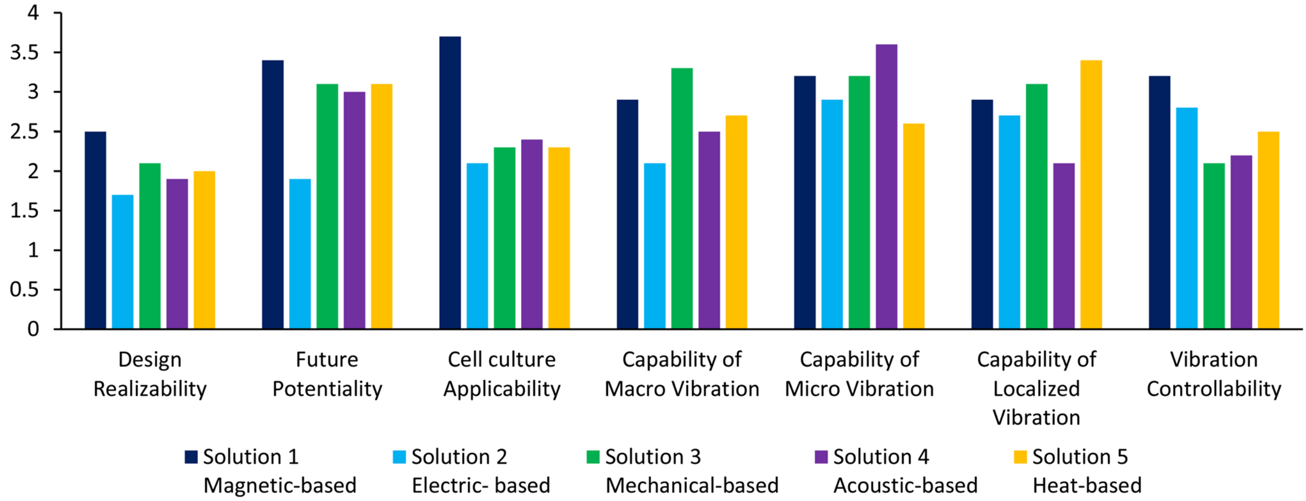

Fig. 3 Comparing the conceptual solutions against super-system cell culture criteria

Table 12 Generated conceptual solutions fulfilling 3DPVS system-level criteria

3DPVS criteria at system level and corresponding rating of various conceptual solutions					
3DPVS criteria at system level	Solution 1 Magnetic based	Solution 2 Electric based	Solution 3 Mechanical based	Solution 4 Acoustic based	Solution 5 Thermal based
1. Design realizability	2.5	1.7	2.1	1.9	2.0
2. Future potentiality	3.4	1.9	3.1	3.0	3.1
3. Cell culture applicability	3.7	2.1	2.3	2.4	2.3
4. Capability of macro vibration	2.9	2.1	3.3	2.5	2.7
5. Capability of microvibration	3.2	2.9	3.2	3.6	2.6
6. Capability of localized vibration	2.9	2.7	3.1	2.1	3.4
7. Vibration controllability	3.2	2.8	2.1	2.2	2.5
Average rate	3.11	2.31	2.74	2.53	2.66

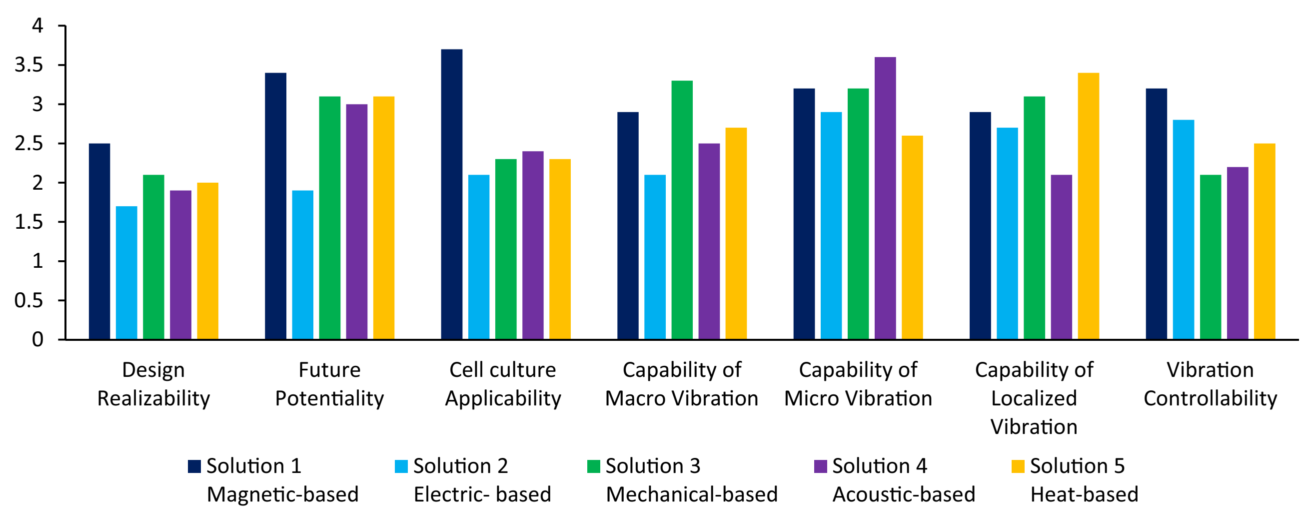

Fig. 4 Basic conceptual solutions corresponding to system-based criteria of 3DPVS

relatively lower application on cell culture, while they provide with higher future potentiality if bioscientists could find right means utilizing these methods in right place at right time. In terms of the vibration controllability, the magnetic based shows a higher rate, while traditional mechanical one shows the lowest. The low controllability of traditional mechanical means was also the very initial motivation of starting with the novel 3DPVS design which aims to conquer these limitations.

Despite the mentioned, magnetic-based solutions tend to show a least-deviation rate, namely it rates at an overall fine level compared with that of other solutions. It also has the highest applicability in cell culture, which can be justified via the rapidly emerging magnetic means onto cell engineering. In addition, all solutions show a promising future potentiality except from mechanical one, possibly due to the fact mechanical means are current mainstream strategies to generate vibration and it stays at a bottle-neck period where further evolution seems difficult. Regarding the vibration capability, magnetic means show a higher rate in average, while mechanical and acoustic means represent higher value in macro and micro, respectively. It is easy to understand that mechanical ways are convenient to shake structures, thus creating rough vibration at macro-level, while the acoustic might be feasible to create subtle vibrations via sound waves. When it comes to localized vibration, which was one proposed aim for 3DPVS compared with traditional scaffold, thermal-solution tends to be the most useful, possibly because controlling thermal issues in different parts of scaffold might be relatively easier than other solutions though others also show a fine potentiality in achieving this aim. For general vibration controllability, such as adjusting frequency or amplitude, magnetic and mechanical means could be relatively more proper compared with other three solution modes.

Analyzing the generated solutions against 3DP applicability

Another system-level concern is about future fabricability of generated concepts via 3DP, data in Table 13 with graphic analysis in Fig. 5. In this connection, a list of applicable 3DP methods is selected. Feature, benefit and property of each can be referred to previous study [5].

From this study, FDM, typical nozzle-based 3DP, shows the average highest applicability among all five generated solutions. Ink-jet, as liquid-based 3DP, shows a general high applicability and its application which inevitably contains the usage of novel liquid materials. Among layer-based 3DP, both SLS and SLA can also be considered as promising method for achieving the generated solutions, and SLA tends to be useful method for magnetic, acoustic and heat based while being less applicable for electric and traditional mechanical solutions. Indirect 3DP could also be applied as a general method for 3DPVS, while 3D plotting shows positivity toward some while having limitation against others. Also, these novel field-based solutions tend to be positively applicable via more than half of the current mainstream 3DP methods, for some solutions that cannot be applicable by definite 3DP, and they still have good alternatives regarding possible fabrication. In brief, all the generated solutions show a fine level of fabrication applicability via 3DP, which fulfills one core part of 3DPVS requirements, namely 3DP as the fabricating means for such novel vibratory scaffold.

From another perspective, the overall estimation indicates that the magnetic and mechanical based ranks at a relatively higher position, following which are heat-based, electric- and sound-based option in sequence. Considering the higher position of magnetic-based solution in other criteria previously analyzed, we could summarize it, or at least recommend, as optimal solution for conceptual 3DPVS at super-system to system level. Traditional mechanical means, such as attaching scaffold to external

Table 13 Feasibility of generated conceptual solutions versus 3DP fabrication methods

3DPVS conceptual solutions corresponding 3DP methods					
3DP methods	Solution 1 Magnetic based	Solution 2 Electric based	Solution 3 Mechanical based	Solution 4 Acoustic based	Solution 5 Heat based
1. 2PP	1.4	1.3	1.5	1.6	2
2. LENS	1.6	1.9	2	2.1	2.5
3. SLA	3.3	1.9	2.4	3.4	3.4
4. SLM	1.9	1.6	1.9	2.3	2.4
5. SLS	3.5	3.4	3.5	3.1	3.1
6. LOM	2.9	2.7	2.8	2.8	3
7. Ink-jet	3.9	3.8	3.7	3.3	3.1
8. FDM	4	4	4	3.5	3.8
9. 3D plotting	3.8	2.9	3.7	3.3	3.2
10. Indirect 3DP	3.4	3.2	3.7	3.2	2.6

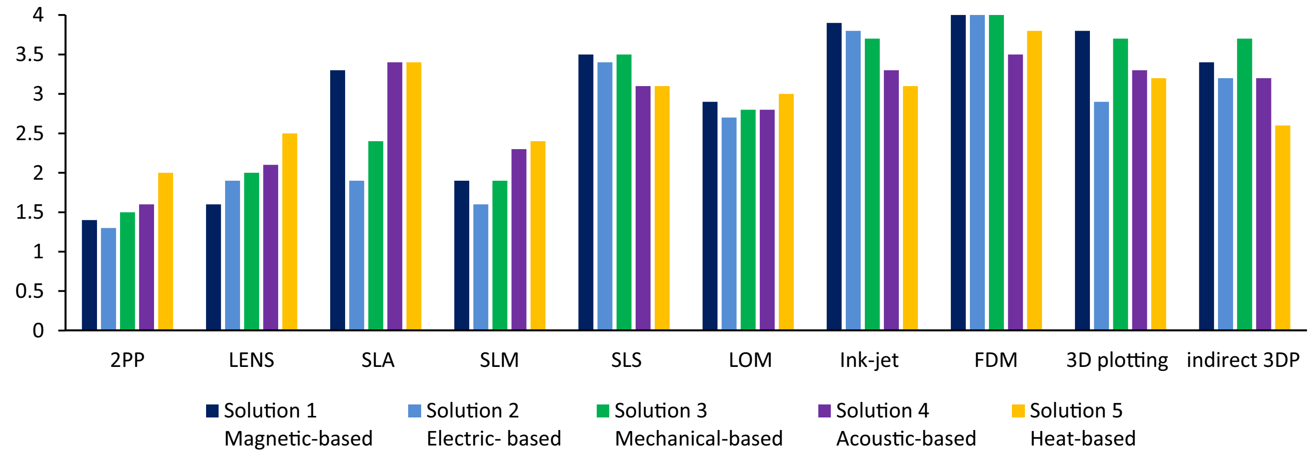

Fig. 5 Fundamental 3DPVS conceptual solutions corresponding to 3DP applicability

shaker or vibrating platform, is the starting point where novel 3DPVS was proposed to develop for mitigating limitations. This does not mean mechanical means will be out of use, but still have potential among other field-based solutions. Therefore, we might contemplate that mechanical means, such as bioreactor based or attaching with external vibrator, would still be practical for a relatively long period, along with the process novel mechanical methods being developed. Other novel but 'slightly' fewer promising approaches, namely electric, sound and thermal based, need further effort in terms of developing corresponding smart materials as well as investigating the proper functioning of fields. In brief, although the feasibility of 3DP cannot judge the practical value of conceptual solutions, it indirectly provides evidence to evaluate the flexibility of the solution. In future study, sub-system requirements, including detailed concerns of GMBV characterization, will be considered, where a more thorough view regarding which 3DP tends to play more roles in definite solution can be determined.

Furthermore, analyzing together with third-layer study concerning 3DP hybrid system, we might draw several conclusions. For magnetic based, the scaffold product can be fabricated through FDM, or poly-jet, or a hybrid system of ink-jet and FDM. For mechanical based, it can be achieved by hybrid system of FDM with one of SLS, ink-jet, 3D plotting or indirect 3DP. For thermal based, 3DPVS can be a fabricated through nozzle-based 3DP system like FDM, or SLA, or a hybrid system of both. Electric-based 3DPVS might utilize ink-jet or SLS, or a hybrid of both. Acoustic-based solution shows the intimacy toward ink-jet, 3D plotting, FDM, SLA or a relevant hybrid system between multiple of these.

Conclusion and future direction

In this study, basic TRIZ-based design methods have been utilized into generating conceptual solutions of 3DPVS, especially from super-system to system level. We tried to identify basic and typical most system contradictions, physical contradictions and several non-contradicting-based questions, which stand on the way of conceptual development stage of 3DPVS. A four-layer systematic approach was used, to establish a logical, scientific and structured concept generation process. Each layer presented a definite aim in the whole. From the first-layer analysis, we did summarize design problem from base model, indicate which TRIZ method and route would be applicable and generate five characters that potential 3DPVS solution needs to fulfill. From the second layer, the generated solution characters were further translated into a trinity of contradiction, namely the trinity aspect 'geometric stability' with ''material dynamicity,'' material dynamicity' with 'biocompatibility,' and 'vibrating capability' with '3DP fabricability.' Three design problems were identified correspondingly, with several basic solutions preparatorily selected. Thirteen super-system criteria, chiefly about bio- and cell cultivation constrains, were identified, which anchors future solution generating in right spot. That is, if super-system criteria failed to be fulfilled, all other design issues might instantly lose the value. Following this came the third-layer problem addressing, which used the TRIZ contradiction matrix to tackle the previously identified problems as well as selecting innovation principles for generating potential solutions. Field-based approaches were eventually identified as essential part of 3DPVS, and smart materials having vibrating or dynamic functionality were perceived as promising scaffold elements. A brief study regarding the relationship of smart material stimulus to response was conducted, aiming to increase the resourcefulness of further field determination. An analysis on 3DP was also presented, addressing most fundamental 3DP concerns and design principles. Resulted from this layer, five basic conceptual solutions of 3DPVS were proposed, namely magnetic, mechanical, electric, light and thermal field with corresponding 3D-printable biostimulating materials. Since solutions generated here remained highly abstract, a fourth-layer study was conducted to evaluate these solutions from various design perspectives. That is, firstly the previously established thirteen super-system criteria were utilized to indicate to what extend the solution would fulfill them. Cooperating with this, seven system criteria of 3DPVS were used to evaluate these solutions, to shift the focus of design from bioconstrains into 3DPVS innovation itself. Since 3DP is the fabricating tool for 3DPVS, this paper did another study regarding the rating of each solution against their 3DP applicability. Analyzing from the fourth layer, a preliminary conclusion was drawn that potential conceptual 3DPVS utilizing magnetic field with materials such as 3DP-fabricable magnetic nanomaterial seemed to be highly promising, with a relatively higher practicality, relevance and significance compared with other novel solutions. Mechanical solutions, though traditional modes of which fall behind and created lots of limitations, novel approaches are still promising and could be applicable for future 3DPVS design. Acoustic- and electric-based solutions are novel from theoretical view, while generally rank at a relatively lower position. Reason can be that there lack mature resources dealing with the reality design scenarios if applying such fields into cell scaffold. Due to the rapid development of material science, perhaps better ways would appear to make them practical and thus applied in future 3DPVS. In brief, this study fundamentally addressed the design contradiction of 3DPVS from super-system level to system level. Different field-based concepts were generated, as well as conducting the basic comparison, evaluation from theoretical level. Study of which is preliminary to future work which focuses on how to generate conceptual solution of 3DPVS at more detailed, concrete level and solve the sub-system contradictions.

Though concrete future solutions, for example magnetic-based 3DPVS, cannot be achieved without conducting further detailed design process, some future perspective on its solution could still be contemplated. Porous magnetic scaffold will be served as a material and structural template for bone cell like osteogenesis, while the embedded superparamagnetic material, such as FeHA microsphere into the PU (polyurethane) matrix, under an external timely changing magnetic field, will provide useful vibratory stimulation to promote cell cultivation in bone remodeling and regeneration.

On the other hand, due to the limitation of TRIZ, it is not practical to tackle all challenges in 3DPVS design at one time. Sophisticated, complex problem that remain yet addressed can be assisted by other TRIZ-supportive means. For instance, ARIZ inside TRIZ is an algorithm tool especially for dealing with issues that cannot be easily solvable by traditional means of TRIZ. Also, tools like QFD could provide with more resourcefulness in terms of generating detailed comparison of design criteria, especially the subsystem components ones that tend to be large in quantity and tedious by traditional comparison. Further, this study is an initial attempt, if not the first time, for innovating bioscaffold via TRIZ. Therefore, flaws inevitably exist, and further investigation is necessary. In other words, 3DPVS design is complex and cross-domain, and finding TRIZ-assisting tools in miscellaneous area could provide higher resourcefulness in terms of 3DPVS innovation. Last, bear in mind that for the solution evaluating as conducted in the fourth layer, the rating result could be used as indication, instead of a decisive answer.

From another future perspective, conceptual design of 3DPVS will focus from system to sub-system level, that is, detailed 3DPVS characterization will be considered onto the fundamental solutions as generated in this study. GMBD components of 3DPVS will be studied with regarding design problems addressed via TRIZ and other supportive method. It for instance includes but not limited in following focus: geometric properties, such as the porosity, the pore-size distribution and the shape of the pores; mechanical properties, like compressive strength stiffness (Young's modulus), biological properties such as surface roughness, fluid flow mediated wall shear stress, as well as vibratory properties regarding how, what vibration will be generated and manifested on scaffold. In brief, future work is challenging and further investigation on TRIZ-supportive methods is valuable.

Compliance with ethical standards

Conflict of interest The authors declare that there is no conflict of interest.

Ethical approval This study does not contain any studies with human or animal subjects performed by any of the authors.

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