International Journal of Engineering Education Vol. 32, No. 5(A), pp. 2025–2032, 2016
Printed in Great Britain
0949-149X/91 $3.00+0.00

Developing Practical Abilities through a Teaching Reform of Tissue Engineering Course for Undergraduates*

HAIFENG LIU,[1,**] XILI DING,[1] GANG ZHOU,[1] XIAOMING LI,[1] PING LI,[1] XIANGHUI GONG,[1] XUENAN GU,[1] FANG PU,[1] HAIJUN NIU,[1] DEYU LI[1] and YUBO FAN[1,2,**]
[1] Key Laboratory for Biomechanics and Mechanobiology of Ministry of Education, International Research Center for Implantable and Interventional Medical Devices, School of Biological Science and Medical Engineering, Beihang University, Beijing 100191, People's Republic of China.
[2] National Research Center for Rehabilitation Technical Aids, Beijing 100176, People's Republic of China.
E-mail: haifengliu@buaa.edu.cn, yubofan@buaa.edu.cn

This work describes a teaching reform of Tissue Engineering course that designs a laboratory course for senior undergraduate students, where students are challenged with a real-life tissue engineering application and provided with a hands-on experience applying oriented biomaterial technology and cytotechnology by conducting an experiment. Forty senior undergraduate students coming from School of Biological Science and Medical Engineering in Beihang University attended the course. The laboratory course was designed to guide students in raising research questions, generating strong hypotheses, identifying appropriate methodologies, and collaborating with each other to solve problems. Feedback from students attended this course has indicated that, while students find the expectations challenging in the early stages of the course, finally they are able to increase awareness and deepened their understanding of this field. We hope that this kind of educational modality could spread out to other interdisciplinary fields and contribute to the fast development of modern interdisciplinary science and technology.

Keywords: interdisciplinary field; Tissue engineering; laboratory course; practical abilities; undergraduate students

1. Introduction

Tissue engineering is a fast-growing and interdisciplinary field that mainly combines materials, cells, growth factors and bioreactors, with the goal of creating new tissues and organs to remedy a range of maladies (as shown in Fig. 1) [1]. How can a mentor present various and occasionally contradictory developing ideologies so that the students have the ability to understand the complexities of this field and then to form their own opinion about future directions in tissue engineering research? It is challenging for biomedical engineering undergraduate students who do not have any research experiences in such a new and developing area to incorporate an in-depth study of tissue engineering.

Over these years, we have mainly focused on understanding the interplays of cells, scaffolds, growth factors and bioreactors, and using this knowledge to develop new therapies and innovative technologies for tissue engineering. Customarily, engineering curriculum heavily relies on the awareness that basic facts can be imparted through didactic approaches [2]. However, the didactic approach has been shown to be insufficient and students cannot take active part in the dynamic world of research [3]. A growing awareness that engineers need a broad range of practical skills, which require more to develop than the traditional didactic approach, has resulted in emphasizing critical-thinking skills [4]. Moreover, engineers are better prepared to solve problems when they have a first-hand understanding of the problem and its cause [5]. To deal with these educational issues and meet the development requirements of tissue engineering, it is necessary to develop a better teaching approach to the educational reform of tissue engineering with focusing on the research skills. Only by this means, can the students realize the significance of this interdiscipline and improve their practical abilities in this field to face future challenges.

Therefore, we develop a laboratory course to address these issues and give biomedical engineering undergraduate students the insights and research skills which are essential to understand and help solve problems in tissue engineering. The aim of this course is to guide students in raising research questions, generating strong hypotheses, identifying appropriate methodologies, and finally solving problems. Thus, this teaching reform is organized with the purpose of making students to have the ability to deeply comprehend this new and fast growing interdisciplinary field by cultivating their professional skills through cooperative learning experiences which purposely reflect the activities engaged in by practicing tissue engineers. We want to enable students to develop an early understand-

** Corresponding authors.

* Accepted 15 May 2016.

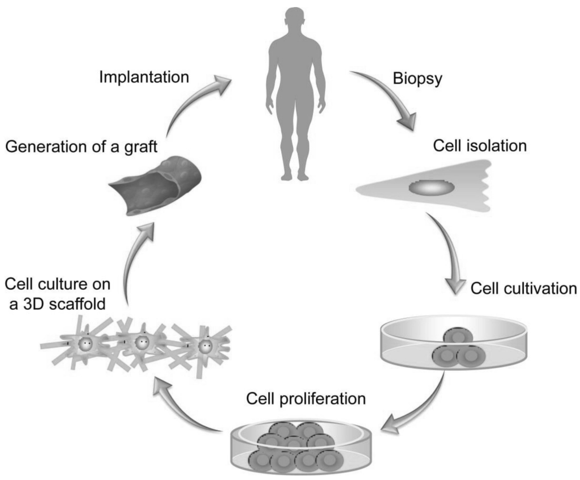

Fig. 1. The schematic diagram of tissue engineering.

ing and interest in tissue engineering and to provide them the opportunities to continue pursuing this interest.

2. The main disciplines involved in tissue engineering

2.1 Biomaterials

Tissue engineering needs a biomaterial as a framework for cells to build a vital and functional tissue. The basic role of a biomaterial in tissue regeneration is to offer support and scaffolding for cell growth. Nature's template for biomaterial is the extracellular matrix (ECM); the material secreted by resident cells that supports tissue and organs. The ECM provides not only physical support and spatial organization, but also a bioactive microenvironment that supports and promotes cellular functions. Owing to the complexity of composition and ultrastructure of native ECM, synthesis of an ECM mimic with any degree of fidelity is not yet feasible [6]. For this reason, typical approaches of biomaterial design focus on a few of the mechanisms by which ECM influences cells and attempts to effectively present these cues for a given tissue. Synthetic biomaterials [e.g., poly(ethylene glycol), poly(lactic-co-glycolic acid), poly(ethylene terephthalate), polyglycolic acid] are attractive because they can be manufactured reproducibly with the ability to control strength, structure, and degradation rate [7]. Naturally occurring materials include the naturally occurring polymers (e.g., silk and chitosan), purified ECM proteins (e.g., collagen and elastin), and ECM derived by decellularization of various tissues (e.g., small intestinal submucosa, dermis, and urinary bladder matrix) [8–13]. The naturally occurring materials have certain advantages such as favorable immune recognition by the recipient and the presence of embedded structural and functional molecules.

Biomaterials are used in the form of carriers, hydrogels or scaffolds for tissue engineering applications. Carrier materials can adherent cells to produce ECM which embeds the tissue components in as a native tissue without any potentially marring framework substance. Hydrogels are water swellable and highly negatively loaded polymers with a well-defined pore size which enables diffusion of gas and nutrition to support and sustain the embedded cells. These material forms serve as a delivery carrier for the cells to regenerate the damaged tissue in the body. All of these materials and constructs serve as cell environment which has to establish optimum conditions for the adhesion and proliferation of the desired tissue cells [14].

2.2 Cells

Achieving success with tissue engineering depends on meeting some critical experimental requirements. One is to have the essential components, including the cells and the carrier or support matrix. Obtaining the number and type of cells needed for tissue engineering is crucial for repairing damaged tissues, especially in cases where either the tissue are not able to regenerate or the native reparative mechanisms are inadequate [15].

There are many sources of cells for tissue engineering, each with its own advantages and disadvantages. One of the best methods to get cells is harvesting autologous cells directly from the patient [16]. However, relatively few cells are available for harvesting and thus autologous cells may not be suitable for transplantation. One hopeful option is to use stem and/or progenitor cells in tissue engineering. Stem cells, which are found in some tissues of the body not only renew themselves but also can differentiate into many phenotypes. According to the differentiation potential, stem cells can be divided into two categories, pluripotent stem cells and multipotent stem cells. Pluripotent stem cells have the inherent ability to differentiate into any desired cell type under proper conditions. In addition, pluripotent stem cells have almost unlimited proliferation capacity and they can be manipulated in multiple passages. These unique properties make pluripotent stem cells a promising cell source in tissue engineering. To date, pluripotent stem cells used into this area have employed embryonic stem cells (ESCs) [17–25] and induce pluripotent stem cells (iPSCs). Similar to the pluripotent stem cells, multipotent stem cells also have the capacity of self-renewing and differentiating into specialized cell types. While, multipotent stem cells are harvested from adult tissues, such as bone marrow, blood, blood vessel, adipose, muscle, liver, heart, skin and so on. They play an important role in maintaining and repairing the tissue in situ.

2.3 Growth factors

Therapeutic induction of tissue repair or function restoration in tissue engineering and regenerative medicine needs recapitulation of the spatial and temporal microenvironments presented by natural ECM, in many cases by providing of exogenous instructive bioactive signals [26]. Pivotal among these signals are growth factors such as bone morphogenetic proteins (BMPs, particularly BMP-2 and BMP-7), epidermal growth factor (EGF), vascular endothelial growth factor (VEGF), and fibroblast growth factor (FGF, essentially bFGF), which offer fatal stimulation of cell recruitment, adhesion, proliferation, morphogenesis, and differentiation. Growth factor proteins are produced by cells and directly interact with or are sequestered by the surrounding ECM for presentation to the receptors on cell surface. On a larger scale, these growth factor-stimulated cellular responses are included in organism development, angiogenesis, and wound healing.

Growth factors also play a vital role to transfer information between different cells and their microenvironment, the ECM, and throughout the processes of tissue regeneration [27]. It is well known that growth factors are typically multimodal, showing a different mechanism of action depending on the concentration and/or exposure time and on the phenotype of the target cells. They control a lot of biological processes, thus growth factors are widely used to regenerate many tissue types, such as neural, musculoskeletal, hepatic, and vascular systems [28]. New tissue growth, both in vivo during development and in vitro in tissue engineering applications, is increasingly understood as a complex process that requires exact spatial and temporal interaction between cells, three-dimensional (3D) ECM, mechanical forces, and various growth factors.

2.4 Bioreactors

Despite the early promise of tissue engineering, the major challenge faced by the researchers is to transfer the cells and tissue-based constructs into clinically effective and safe large-scale products [29]. Bioreactors are normally defined as devices in which biological and/or biochemical processes develop under closely monitored and tightly controlled environmental and operating conditions. Bioreactors have played a key role in tissue engineering as they can culture mammalian cells under a controlled environment. The high degree of reproducibility, control and automation introduced by bioreactors for specific experimental bioprocesses is very important for their transfer to large-scale applications [30]. Some operational conditions including temperature, pH value, oxygen tension, and perfusion of the cells as well as mechanical stimuli can be modified and controlled. Some operational conditions including temperature, pH value, oxygen tension, and perfusion of the cells as well as mechanical stimuli can be modified and controlled. Bioreactors can be employed to develop new tissues in vitro as they can provide the physical and biochemical regulatory signals needed for cells. For instance, bioreactors can provide mechanical stimulation in vitro to aid cells to produce ECM within shorter a time-span under the optimal mechanical stiffness for the construct. It has also been shown that mechanical stimulation can encourage stem cells down different lineages and enable different cell types to be obtained [31]. Moreover, the mechanical stimuli can modulate cell function has motivated the development of functional simulations systems to recellularised tissues in vitro by exposing them to physical stimuli [30].

3. Assessment and discussions

As mentioned above, tissue engineering is an interdisciplinary field aiming to restore or improve impaired tissue function. A combination of biomaterials, cells, engineering methods, and physiological and biochemical factors is used to produce the desired tissue organs. In order to make the students deepen the understanding of this interdisciplinary subject and improve their practical ability in this field, we designed a laboratory course asking groups of students working together to suggest solutions to a practical problem in tissue engineering. The purpose of this teaching reform is to support the use of learned knowledge to real situations and the development of a learning approach which is student-centered and grounded in collaboration. More importantly, this approach to teaching is based on constructivist theory, emphasizing that learning is about action.

The laboratory course is performed in the public experiment platform of School of Biological Science and Medical Engineering in Beihang University. The experiment platform comprises biomaterial laboratory, cell culture room, bioreactor laboratory, molecular biology laboratory, histology laboratory, mechanical laboratory, scanning electron microscope and the related testing equipment. Forty senior undergraduate students coming from School of Biological Science and Medical Engineering attended this course. Before the year of 2015, all of the course content and the knowledge spots were taught by the teachers through didactic approaches (before teaching reform). The reformed Tissue Engineering course consists of three components:

an initial introduction to the basic concepts and general experimental setup and procedure in tissue engineering by the teachers, a research-based assignment where students collaborate with his/her group members to perform the experiments, the completion of a laboratory report and a viva presentation by the students that applies techniques presented and practiced in a series of laboratory experiences to a specific and practical application. With the emphasis on linking laboratory experience with current research directions, this course is developed to offer students a project cooperated with other classmates. At the same time, engaging with the academic literature and developing basic research skills enable students to locate and apply current research skills to their own researches and investigations.

The laboratory course is demonstrative in nature and the students are asked to use their research and analytical skills to perform a hands-on experience. The basic tools and techniques related to the processing and fabrication of biomaterial scaffolds, characterization of the scaffolds, basic cell seeding and culture techniques, and characterization of cell-scaffold constructs are studied in laboratory experiments (as shown in Table 1). The laboratory course is designed as a vehicle for learning about different scaffolding biomaterials, their processability, physicochemical property, biocompatibility, and the tools which can be used to characterize these cell-scaffold constructs for potential tissue engineering applications. Students select the topic that interests them, and their first task is to learn and duplicate the techniques required to prepare the experiment. Before performing these laboratory experiments, students are given some background reading materials. Moreover, some graduate students, who usually have more in-depth knowledge of material science and biological systems, assist the undergraduates to improve their laboratory skills.

Table 1 Research topics and preparations

Research Topic	Choices	Learning Points	Evaluation
Biomaterial scaffolds fabrication	Biomaterials (silk fibroin, collagen, chitosan, PLA, PLGA); Fabrication techniques (Electrospinning, freeze drying, solvent casting, salt leaching)	Solution preparation, documentation and laboratory journal skills, fabrication and processing technique, scaffolds characterization, data processing and analysis	Does the student understand biomaterials and biomaterial properties? Can the student apply what he or she has learned in class to the experiment? Can the student choose the suitable biomaterial and fabrication technology? Can the students deal with experimental data? Does the student follow standard laboratory practices, i.e., keeping records, cleaning equipment, and following disposal regulations?
Cell culture	Endothelial cells, smooth muscle cells, fibroblasts, bone marrow stem cells, osteoblasts	Solution preparation, documentation and laboratory journal skills, preparing culture medium, cell seeding, cell culture, passaging cells, assessing cell activities, data processing and analysis	Does the student understand different cells and cell properties? Can the student apply what he or she has learned in class to the experiment? Can the student choose and culture the desired cells? Does the student follow standard laboratory practices, i.e., keeping records, cleaning equipment, and following disposal regulations?
Seeding cells on scaffolds	Seeding cells on the scaffold surface, injection cells into the scaffolds	Solution preparation, documentation and laboratory journal skills, seeding techniques, cell adhesion assays, cell morphologies observation, assessing cell activities and functions, data processing and analysis	Can the student apply what he or she has learned in class to the experiment? Can the student seed cells on scaffolds? Can the student co-culture cells with scaffolds? Can the students deal with experimental data? Does the student follow standard laboratory practices, i.e., keeping records, cleaning equipment, and following disposal regulations?
Developing cell-scaffold constructs	Cultured with growth factors, cultured in a bioreactor, cultured with growth factors in a bioreactor	Solution preparation, documentation and laboratory journal skills, setting up the bioreactor, operating the bioreactor, assessing cell activities and functions, data processing and analysis	Can the student apply what he or she has learned in class to the experiment? Can the student select the appropriate growth factors? Can the student maintain the growth factors effective? Can the student culture cell-scaffold constructs in a bioreactor? Can the student adapt software to control the bioreactor? Can the students deal with experimental data? Does the student follow standard laboratory practices, i.e., keeping records, cleaning equipment, and following disposal regulations?

In the laboratory course, the students should select the biomaterials, scaffold fabrication method and cells to prepare a cell-scaffold construct and suggest possible alternatives. They also must identify the method of characterization, justifying their selection. The experiments are confined to one of the following areas: bone, vascular, or skin tissue engineering. In addition, based on the experiment results, a laboratory report and a viva presentation should be completed by the students. The reports must present an introduction defining the need for clinical application, a detailed explanation of the reason for selected materials, cells and methods, and an analysis for the results explaining why the proposed methods are appropriate for the intended application. Moreover, as a piece of academic writing, students write the reports and must provide a bibliography summarizing the works cited.

After the laboratory course, the students were surveyed about various aspects of the course. Students from classes of 2014 (before the teaching reform) and 2015 (after the teaching reform) participated in this survey. This evaluation is essential to help demonstrate the effectiveness and viability of this teaching method.

Question 1: Did you gain insights from your desired professors?
Question 2: How about your interest in this course?
Question 3: Do you understand the importance of the course to your further study and work?
Question 4: Did you learn a lot during this course?
Question 5: Would you recommend this course to others?

The questionnaires pursue feedback on some specific aspects of the course. Figs. 2, 3, 4, 5 and 6 show the responses of students to the five questions about the course. The questionnaires of the students in 2015 year were compared with those of the students in 2014 year (before the teaching reform). It is found from Fig. 3 that the students' interest in this course is significantly increased after the teaching reform. In addition, after the teaching reform, the students have a clear understanding of the importance of the course and learn a lot about frontier knowledge and research skills in tissue engineering field, which definitely benefits their future study and research (Fig. 2, 4 and 5). Furthermore, it is shown from Fig. 6 that the students are much more willing to recommend this course to others after the teaching reform. After communicating with the students, we got some information that some students considered it as a challenging work in the early stage of the course, particularly the reading and preparation for the laboratory course. Initially students were worried about the expectations of the course, but this changed as a related sense of accomplishment manifested them. In addition, while acknowledging that tissue engineering is a fast-developing interdisciplinary area, most of the students increased awareness of this field and deepened their under-

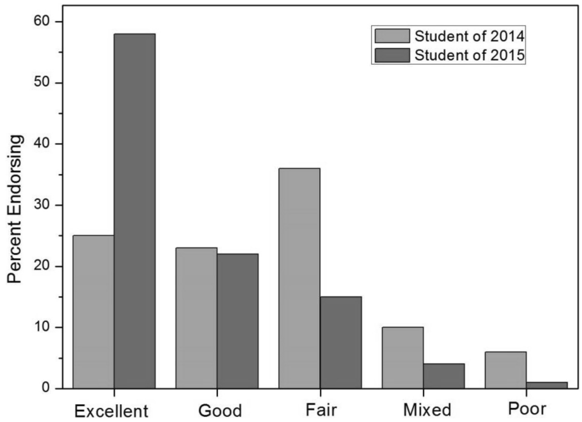

Fig. 2. Student responses to the question: Did you gain insights from your desired professors? The result showed that the students gained more insights from the professors after the teaching reform.

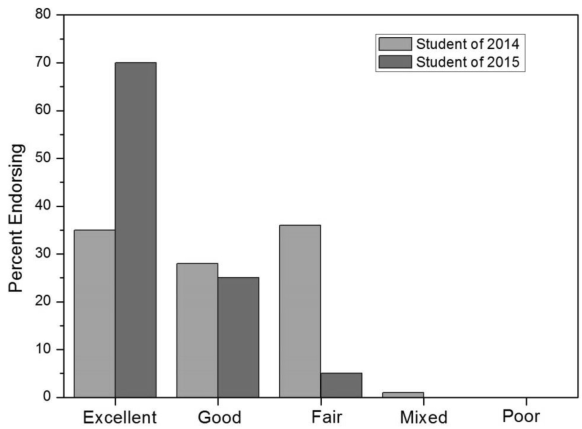

Fig. 3. Student responses to the question: How about your interest in this course?

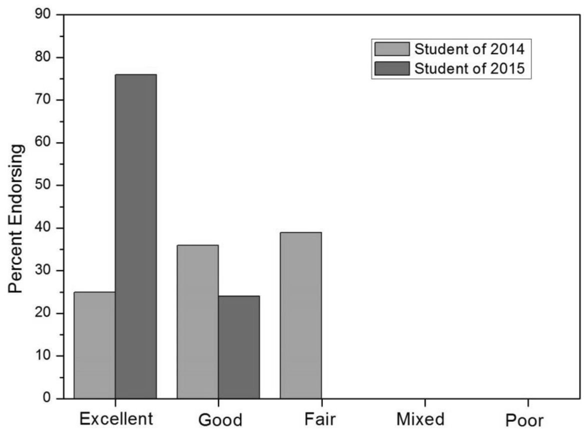

Fig. 4. Student responses to the question: Do you understand the importance of the course to your further study and work?

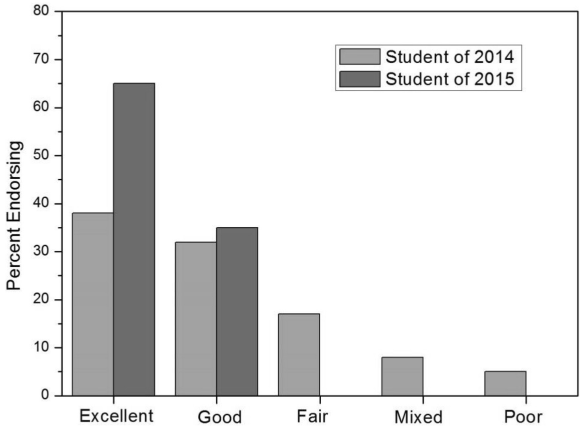

Fig. 5. Student responses to the question: Did you learn a lot during this course?

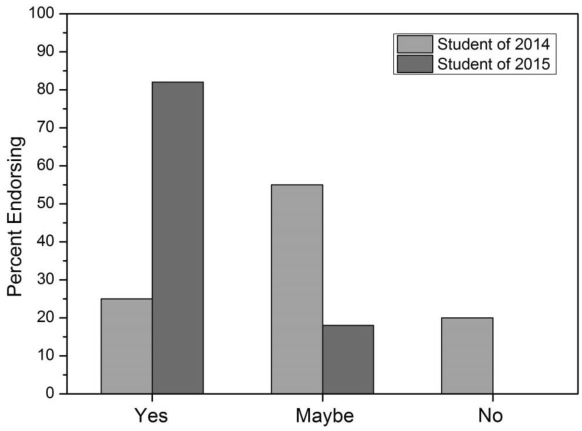

Fig. 6. Student responses to the question: Would you recommend this course to others?

standing of its influence on future clinical medicine. Exhilaratingly, some of them also expressed an enhanced interest in pursuing a research-based career.

The main concept of this teaching reform is to pursue the involvement and participation of the students in all activities related to the experiments during the entire laboratory course. Students are challenged with a real-life tissue engineering application, the production of a cell-scaffold constructs for regenerative medicine. Just as what Confucius (a Chinese educator and philosopher, around 450 BC) said "Tell me, and I will forget. Show me, and I may remember. Involve me, and I will understand". During the laboratory course, the undergraduate students are provided with a task which has real world application. In addition, the students can actively experience the interconnection between material, biology, and engineering sciences. Each group of students is assigned to a topic, including the fabrication of biomaterial scaffolds, preparation of culture medium, the cell culture, the setup and calibration of the equipment, and the sampling procedure up to a critical evaluation of the data. By this way, the students are provided with a hands-on experience applying oriented biomaterial technology and cytotechnology by conducting an experiment for the first time.

It is well known that the elementary concept behind the real-world tasks in teaching applications is to enhance students understanding of the subject matter and develop the critical-thinking skills [32]. A scientific teaching approach for experimental research is to enhance students' engagement in learning by inclusion of some activities during lectures and tutorials. In the current teaching reform, the laboratory course is used to strengthen students' participating in learning. As part of the successful teaching approach, these methods have previously been reported to improve learning outcome for the students [33].

Of course, there are also some limitations for this course. A concern from an educational standpoint is to develop a complete system of metrics. In this course, the instructors have intimate knowledge of the students and the researches they performed. While the laboratory report and viva presentation provide a tangible example of work that the student has performed, ultimately grading is dependent on the instructor's impression of the student and her/his work ethic. In addition, the abilities of the students to perform their overall laboratory skills were considered, which is somewhat subjective and is an observed metric. Furthermore, the course will need more written examples of the work product, such as research papers and project proposals. Future courses will need an evaluation of the course by students that include the strengths and weaknesses of the course and suggestions on improving the course.

4. Conclusions

In conclusion, we think that the success of this teaching reform depends on a combination of the following factors:

1. The course focuses on the real problems of training engineers.
2. Students participate in tissue engineering leaning and have a hands-on experience of designing protocols and solving problems.
3. The course provides students a more in-depth project to be completed in collaboration with his/her classmates, which can also foster integration and teamwork.
4. Before the laboratory course, all the teachers actively discuss and carefully design the experiments in order to make the laboratory course carry out smoothly.

5. The course contains the most up-to-date interdisciplinary knowledge that is beneficial for students to broaden their perspectives and open their minds.

Thus, this course has gained high recognition and persistent supports from Beihang University. Since this kind of teaching reform for undergraduate students has never been tried in any school of Beihang University before, the course is a challenge and prospect-based project, which is designed to pilot the instructional environment at this university and imitate educational reform approaches in other universities.

Acknowledgements—This work was supported by the National Key Technology R&D Program (2012BAI18B06, 2014BAI11B02, 2014BAI11B03), National Natural Science Foundation of China (31470938, 11421202, 61227902, and 11120101001), International Joint Research Center of Aerospace Biotechnology and Medical Engineering from Ministry of Science and Technology of China, 111 Project (B13003), Research Fund for the Doctoral Program of Higher Education of China (20131102130004), The transformation project for major achievements of Central Universities in Beijing (ZDZH20141000601), and Fundamental Research Funds for the Central Universities.

References

1. E. Lavik and R. Langer, Tissue engineering: current state and perspectives, *Applied Microbiology and Biotechnology*, **65**(1), 2004, pp. 1–8.
2. R. M. Felder, D. R. Woods, J. E. Stice and A. Rugarcia, The future of engineering education II. Teaching methods that work, *Chemical Engineering Education*, **34**(1), 2000, pp. 26–39.
3. A. K. Ditcher, Effective teaching and learning in higher education, with particular reference to the undergraduate education of professional engineers, *International Journal of Engineering Education*, **17**(1), 2001, pp. 24–29.
4. L. J. Shuman, M. Besterfield-Sacre and J. McGourty, The ABET "professional skills"—Can they be taught? Can they be assessed? *Journal of Engineering Education*, **94**(1), 2005, pp. 41–55.
5. J. DiCecco, J. Wu, K. Kuwasawa and Y. Sun, A novel approach to physiology education for biomedical engineering students, *Advances in Physiology Education*, **31**(1), 2007, pp. 45–50.
6. J. A. Hubbell, Biomaterials in tissue engineering, *Nature Biotechnology*, **13**(6), 1995, pp. 565–576.
7. M. Ventre, F. Causa, P. A. Netti and R. Pietrabissa, Research in biomaterials and tissue engineering: achievements and perspectives, *IEEE Pulse*, **6**(4), 2015, pp. 39–43.
8. H. F. Liu, X. M. Li, X. F. Niu, G. Zhou, P. Li and Y. B. Fan, Improved hemocompatibility and endothelialization of vascular grafts by covalent immobilization of sulfated silk fibroin on poly (lactic-co-glycolic acid) scaffolds, *Biomacromolecules*, **12**(8), 2011, pp. 2914–2924.
9. X. L. Ding, X. Wei, Y. Huang, C. D. Guan, T. Q. Zou, S. Wang, H. F. Liu and Y. B. Fan, Delivery of demineralized bone matrix powder using a salt-leached silk fibroin carrier for bone regeneration, *Journal of Materials Chemistry B*, **3**(16), 2015, pp. 3177–3188.
10. X. H. Gong, H. F. Liu, X. L. Ding, M. L. Liu, X. M. Li, L. S. Zheng, X. L. Jia, G. Zhou, Y. W. Zou, J. C. Li, X. J. Huang and Y. B. Fan, Physiological pulsatile flow culture conditions to generate functional endothelium on a sulfated silk fibroin nanofibrous scaffold, *Biomaterials*, **35**(17), 2014, pp. 4782–4791.
11. H. F. Liu, X. L. Ding, Y. X. Bi, X. H. Gong, X. M. Li, G. Zhou and Y. B. Fan, In vitro evaluation of combined sulfated silk fibroin scaffolds for vascular cell growth. *Macromolecular Bioscience*, **13**(6), 2013, pp. 755–766.
12. H. F. Liu, X. M. Li, G. Zhou, H. B. Fan and Y. B. Fan, Electrospun sulfated silk fibroin nanofibrous scaffolds for vascular tissue engineering, *Biomaterials*, **32**(15), 2011, pp. 3784–3793.
13. E. Zakhem and K. N. Bitar, Development of chitosan scaffolds with enhanced mechanical properties for intestinal tissue engineering applications, *Journal of functional biomaterials*, **6**(4), 2015, pp. 999–1011.
14. E. Eisenbarth, Biomaterials for tissue engineering, *Advanced Engineering Materials*, **9**(12), 2007, pp. 1051–1060.
15. C. A. Heath, Cells for tissue engineering, *Trends in Biotechnology*, **18**(1), 2000, pp. 17–19.
16. R. Langer and J. P. Vacanti, Tissue engineering, *Science*, **260**, 1993, pp. 920–926.
17. G. Shen, H. C. Tsung, C. F. Wu, X. Y. Liu, X. Y. Wang, W. Liu, L. Cui and Y. L. Cao, Tissue engineering of blood vessels with endothelial cells differentiated from mouse embryonic stem cells, *Cell Research*, **13**(5), 2003, pp. 335–341.
18. Z. Li, J. C. Wu, A. Y. Sheikh, D. Kraft, F. Cao, X. Xie, M. Patel, S. S. Gambhir, R. C. Robbins, J. P. Cooke and J. C. Wu, Differentiation, survival, and function of embryonic stem cell derived endothelial cells for ischemic heart disease, *Circulation*, **116**(11 suppl), 2007, pp. I46–I54.
19. N. Oyamada, H. Itoh, M. Sone, K. Yamahara, K. Miyashita, K. Park, D. Taura, M. Inuzuka, T. Sonoyama, H. Tsujimoto, Y. Fukunaga, N. Tamura and K. Nakao, Transplantation of vascular cells derived from human embryonic stem cells contributes to vascular regeneration after stroke in mice, *Journal of Translational Medicine*, **6**(1), 2008, p. 54.
20. N. F. Huang, H. Niiyama, C. Peter, A. De, Y. Natkunam, F. Fleissner, Z. Li, M. D. Rollins, J. C. Wu, S. S. Gambhir and J. P. Cooke, Embryonic stem cell-derived endothelial cells engraft into the ischemic hindlimb and restore perfusion, *Arteriosclerosis, Thrombosis, and Vascular Biology*, **30**(5), 2010, pp. 984–991.
21. M. B. Nourse, D. E. Halpin, M. Scatena, D. J. Mortisen, N. L. Tulloch, K. D. Hauch, B. Torok-Storb, B. D. Ratner, L. Pabon and C. E. Murry, VEGF induces differentiation of functional endothelium from human embryonic stem cells: implications for tissue engineering, *Arteriosclerosis, Thrombosis, and Vascular Biology*, **30**(1), 2010, pp. 80–89.
22. T. P. Kraehenbuehl, L. S. Ferreira, A. M. Hayward, M. Nahrendorf, A. J. van der Vlies, E. Vasile, R. Weissleder, R. Langer and J. A. Hubbell, Human embryonic stem cell-derived microvascular grafts for cardiac tissue preservation after myocardial infarction, *Biomaterials*, **32**(4), 2011, pp. 1102–1109.
23. J. Hu, C. Xie, H. Ma, B. Yang, P. X. Ma and Y. E. Chen, Construction of vascular tissues with macro-porous nanofibrous scaffolds and smooth muscle cells enriched from differentiated embryonic stem cells, *PLoS One*, **7**(4), 2012, pp. e35580.
24. L. T. Kuhn, Y. Liu, N. L. Boyd, J. E. Dennis, X. Jiang, X. Xin, L. F. Charles, L. Wang, H. L. Aguila, D. W. Rowe, A. C. Lichtler and A. J. Goldberg, Developmental-like bone regeneration by human embryonic stem cell-derived mesenchymal cells, *Tissue Engineering Part A*, **20**(1–2), 2014, pp. 365–377.
25. X. Liu, P. Wang, W. Chen, M. D. Weir, C. Bao and H. H. Xu, Human embryonic stem cells and macroporous calcium phosphate construct for bone regeneration in cranial defects in rats, *Acta Biomaterialia*, **10**(10), 2014, pp. 4484–4493.
26. M. Biondi, F. Ungaro, F. Quaglia and P. A. Netti, Controlled drug delivery in tissue engineering, *Advanced Drug Delivery Reviews*, **60**(2), 2008, pp. 229–242.
27. P. Tayalia and D. J. Mooney, Controlled growth factor delivery for tissue engineering, *Advanced Materials*, **21**(32–33), 2009, pp. 3269–3285.
28. F. M. Chen and Y. Jin, Periodontal tissue engineering and regeneration: current approaches and expanding opportunities, *Tissue Engineering Part B: Reviews*, **16**(2), 2010, pp. 219–255.
29. S. Korossis, F. Bolland, J. Kearney, J. Fisher and E. Ingham,

Bioreactors in tissue engineering, *Topics Tissue Eng.*, **2**(8), 2005, pp. 1–23.
30. I. Martin, D. Wendt and M. Heberer, The role of bioreactors in tissue engineering, *TRENDS in Biotechnology*, **22**(2), 2004, pp. 80–86.
31. J. Zhao, M. Griffin, J. Cai, S. Li, P. E. Bulter and D. M. Kalaskar, Bioreactors for tissue engineering: an update, *Biochemical Engineering Journal*, **109**, 2016, pp. 268–281.
32. B. J. Duch, S. E. Groh and D. E. Allen, *The power of problem-based learning: a practical ''how to'' for teaching undergraduate courses in any discipline*, Stylus Publishing, LLC, 2001.
33. J. Handelsman, S. Miller and C. Pfund, *Scientific teaching*, Macmillan, 2007.

Haifeng Liu is Associate Professor of School of Biological Science and Medical Engineering in Beihang University, Beijing, PRC. He holds a Ph.D. in Biomedical Engineering from Tianjin University, PRC.

Xili Ding is currently pursuing her doctorate at Beihang University. She received her MS degree in Biomedical Engineering from Beihang University.

Gang Zhou is Associate Professor of School of Biological Science and Medical Engineering in Beihang University, Beijing, PRC. He received his Ph.D. in Inorganic Chemistry from Sichuan University, PRC.

Xiaoming Li is Professor of School of Biological Science and Medical Engineering in Beihang University, Beijing, PRC. He earned his Ph.D. in Metal Materials from Central South University, PRC.

Ping Li is Associate Professor of School of Biological Science and Medical Engineering in Beihang University, Beijing, PRC. She received his Ph.D. in Biomedical Engineering from Southeast University, PRC.

Xianghui Gong is Assistant Professor of School of Biological Science and Medical Engineering in Beihang University, Beijing, PRC. She earned his Ph.D. in Biochemistry and Molecular Biology from Chinese Academy of Sciences, PRC.

Xuenan Gu is Associate Professor of School of Biological Science and Medical Engineering in Beihang University, Beijing, PRC. She received his Ph.D. in Biomechanics and Biomedical Engineering from Peking University, PRC.

Fang Pu is Professor of School of Biological Science and Medical Engineering in Beihang University, Beijing, PRC. He earned his Ph.D. in Biomechanics from Sichuan University, PRC.

Haijun Niu is Professor of School of Biological Science and Medical Engineering in Beihang University, Beijing, PRC. He received his Ph.D. in Biomedical Engineering from Xi'an Jiaotong University, PRC.

Deyu Li is Professor of School of Biological Science and Medical Engineering in Beihang University, Beijing, PRC. He earned his Ph.D. in Biomedical Engineering from Sichuan University, PRC.

Yubo Fan is Professor of School of Biological Science and Medical Engineering in Beihang University, Beijing, PRC. He received his Ph.D. in Biomechanics from Sichuan University, PRC.