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The role of mechanical strains in stem cell differentiation

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The mechanical factors play important roles in stem cell fate. In particular, applied loading (strain) has a substantial effect on stem cell myogenesis as it has been shown in differentiation of mesenchymal stem cells (MSCs) and adipose-derived stem cells (ASCs) into smooth muscle cells. ASCs provide an easily accessible, abundant source for autologous cells and have a great potential to tissue engineering and cell therapies. We have recently shown that ASCs can be effectively differentiated into skeletal muscle cells (SkMCs) if cyclic strain is applied. However, the mechanism of the strain effect on ASC differentiation into SkMCs as well as the optimal regime of strain application is not clear. Here we present a modeling insight into ASC myogenesis. We describe this process as a transition through several typical stages characterized by expression of a particular combination of myogenic markers previously observed in our experiment. The cells proceed to the next stage via asymmetric division or direct differentiation. The problem is formulated as a system of ODEs whose coefficients are expressed in terms of cell division, self-renewal, death, and direct differentiation rates. In addition, we use a system of nonlinear conditions associated with cell interaction with its environment and a feedback factor due to a limit in cell density. We first adjust the model parameters by using two particular experimental conditions for zero and 10% applied strain. We compute to kinetics of ASC myogenesis in terms of the number of cells being in each stage and demonstrate the main effect of the applied strain on the process of ASC differentiation. We show that after the strain application the number of the original stem cells starts decreasing and the cells in the late stages become dominant, while, under the no-strain condition, the original stem cells keep increasing and become dominant over the cells in the late stages. Finally, we use the developed model and predict the kinetics of ASC myogenesis for conditions beyond the experiment, such as different strains and longer times. We found that there is a strain limit (about 2%) below which the process has a pattern similar to that under the static no-strain conditions. Above that level, cells follow the alternative pattern similar to that under the dynamic experimental conditions. The obtained modeling insight will help in a better understanding of stem cell myogenensis as well as in the design of new experiments to further illuminate this process.

Biography

Prof. Alexander Spector graduated from Moscow State University and later received his Ph.D. and Dr. Sci. degrees from the Russian Academy of Sciences. Since 1994, he has been working at Johns Hopkins University where he is currently Research Professor in Biomedical Engineering and Mechanical Engineering. He is also affiliated with the Institute of NanoBiotechnology, Translational Tissue Engineering Center, and Center for Hearing and Balance at Johns Hopkins University. In 2010, Prof. Spector was elected as a Fellow of the American Society of Mechanical Engineers (ASME), and in 2015, he was appointed an Associate Editor of the Journal of Medical and Biological Engineering and Computing. His major research areas are cell/stem cell mechanics and biophysics, mechanotrasduction, biological membranes, and molecular motors.