Приложение 1





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| Ministry of Science and Technology, Taiwan  MOST | Russian Foundation for Basic Research  RFBR |

Russian-Taiwanese Joint Research Project

Common English Application Form

* Joint Research Project【From 01 / 01 / 2019 To 31 / 12 / 2021 】(dd/mm/yyyy)

1. General Information on Research Project
   1. Research Project Title
      1. Title in English: Numerical Modeling and Engineering Reconstruction of Liver Lobule Tissue and Disease Model
      2. Title in Russian: Численное Моделирование и Инженерная Реконструкция Ткани Лобулы Печени и Модель Заболевания
      3. Title in Mandarin: 肝組織與病變之數值模擬與晶片上工程建構研發
   2. Which best describes the fields of this project: (please select by filling “ v ” )

\_\_\_\_\_\_\_ Natural Sciences \_\_\_\_\_\_\_ Life Sciences \_\_ v \_\_\_\_ Engineering and Applied Sciences

\_\_\_\_\_\_\_ Science Education \_\_\_\_\_\_\_ Humanities and Social Sciences

* 1. Key words: Bio-Microsystem Chip, 3-dimensional engineered tissue, Liver Organ Lab Chip, Numerical modeling of blood flow in liver lobule, Scientific Software for Liver Lobule Tissue, Multi-disciplinary researches, Multicontinuum model

1. Information on Russian Principal Investigator (PI)
   1. Full Name (Please write in the order of Family Name, Given Name, Patronymic Name)
      1. In English: Grigorev Aleksandr Vissarionovich
      2. In Russian: Григорьев Александр Виссарионович
      3. Date of Birth: 25 / 07 (July) / 1985
   2. Institution/Department: Ammosov North-Eastern Federal University
   3. Position: Docent-researcher
   4. Contacts
      1. Telephone numbers
         1. Office: +7 (967) 624 80 78
         2. Home/ Mobile: +7 (967) 624 80 78
         3. Fax Number:
      2. Postal Address:

677000, Russian Federation, Republic of Sakha (Yakutia), Yakutsk,

Kulakovskogo dom 42, aud. 143

* + 1. E-mail Addresses (2 addresses if possible): re5itsme@gmail.com
  1. I confirm that the information given here is correct to the best of my knowledge. Taiwanese PI and I agree to notify MOST and RFBR promptly of any changes of which we become aware and which might significantly affect the grant, if made.  
       
     Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: \_29/5/2018\_\_

1. Information on Taiwanese Principal Investigator (PI)
   1. Full Name (Please write in the order of Family Name, Given Name)
      1. In English: Cheng-Hsien Liu
      2. In Mandarin: 劉承賢
      3. Date of Birth: 06/04/1964
   2. Institution/Department: National Tsing Hua University/ Power Mechanical Engineering Department
   3. Position: Professor
   4. Contacts
      1. Telephone numbers
         1. Office: +886-3-5742496
         2. Home/ Mobile: +886-0917209900
         3. Fax Number: (886-3)-572-2840
         4. Postal Address:

Engineering Building #1, Room 517

National Tsing Hua University

Hsinchu, Taiwan 30013, R.O.C.

* + 1. E-mail Addresses (2 addresses if possible): liuch@pme.nthu.edu.tw
  1. I confirm that the information given here is correct to the best of my knowledge. Russian PI and I agree to notify RFBR and MOST promptly of any changes of which we become aware and which might significantly affect the grant, if made.  
       
     Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: 29/5/2018 

1. Information on Russian Research Team
   1. Indicate “Staff Type” in the following order: PI, collaborating PI (co-PI), assistant investigator, and postdoctoral research fellow.

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| Staff  Type | Name | Institution/  Department | Position | Role in Project | Percent of Effort\* |
| PI | Grigorev Aleksandr Vissarionovich | Ammosov North-Eastern Federal University | Docent-researcher | Numerical modeling of blood flow in liver lobule, creation new mathematical models and the coordination with Prof. Liu Cheng-Hsien’s group’s expertise and results on engineering reconstruction and simulation | 25% |
| co-PI | Vasilyev Aleksandr Olegovich | Ammosov North-Eastern Federal University | senior researcher | Scientific Software engineer and Developer, Programming maintenance, Multi-lobule problem investigator | 25% |
| co-PI | Sivtsev Petr Vasilyevich | Ammosov North-Eastern Federal University | senior researcher | Elasticity module implementation, physical maintenance, splitting schemes and adaptive methods implementator | 25% |
| co-PI | Antonov Mikhail Yurevich | Ammosov North-Eastern Federal University | leading researcher | Monte-carlo method implementation, biological maintenance, high-performance computing support | 25% |

*＊Percent of effort is defined as the percentage of the hours devoted to this project to the total  
 working hours per week. For instance, 50% means this individual will devote a half of his/her   
 working hours to this research project each week.*

1. Information on Taiwanese Research Team
   1. Indicate “Staff Type” in the following order: PI, collaborating PI (co-PI), assistant investigator, and postdoctoral research fellow.

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| Staff  Type | Name | Institution/  Department | Position | Role in Project | Percent of Effort\* |
| PI | Cheng-Hsien Liu | National Tsing Hua University/ Power Mechanical Engineering Department | Professor | The development of engineering reconstruction of liver lobule tissue on LabChip, the supervision of graduate students and the coordination with Prof. Aleksandr Grigorev’s group’s expertise and results on numerical modeling  and simulation | 20% |

*＊Percent of effort is defined as the percentage of the hours devoted to this project to the total  
 working hours per week. For instance, 50% means this individual will devote a half of his/her   
 working hours to this research project each week.*

1. Mutual Visit
   1. Visit by Russian Researchers

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| --- | --- | --- | --- |
| Visitor’s Name | Grigorev Aleksandr Vissarionovich | Position | Docent-researcher |
| Duration of Visit | From 15 / 11 / 2019 To 21 / 11 / 2019 (dd/mm/yyyy) | | |
| Places to visit | National Tsing Hua University, Hsinchu, Taiwan and NAR Lab, National Center for High-performance Computing, Taiwan | | |
| Visitor’s Name | Vasilyev Aleksandr Olegovich | Position | senior researcher |
| Duration of Visit | From 15 / 11 / 2019 To 21 / 11 / 2019 (dd/mm/yyyy) | | |
| Places to visit | National Tsing Hua University, Hsinchu, Taiwan and NAR Lab, National Center for High-performance Computing, Taiwan | | |
| Visitor’s Name | Sivtsev Petr Vasilyevich | Position | senior researcher |
| Duration of Visit | From 15 / 11 / 2019 To 21 / 11 / 2019 (dd/mm/yyyy) | | |
| Places to visit | National Tsing Hua University, Hsinchu, Taiwan and NAR Lab, National Center for High-performance Computing, Taiwan | | |
| 2020 &2012  Duration of Visit and Place | To be planned | | |

* 1. Visit by Taiwanese Researchers (To be planned)

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| --- | --- | --- | --- |
| Visitor’s Name | Cheng-Hsien Liu | Position | Professor |
| Duration of Visit | From 20 / 06 / 2019 To 26 / 06 / 2019 (dd/mm/yyyy) | | |
| Places to visit | Ammosov North-Eastern Federal University | | |
| Visitor’s Name | To be planned | Position | PhD Candidate and Master student |
| Duration of Visit | From 20 / 06 / 2019 To 26 / 06 / 2019 (dd/mm/yyyy) | | |
| Places to visit | Ammosov North-Eastern Federal University | | |
| 2020 &2012  Duration of Visit and Place | To be planned | | |

1. Contents of Research Project: Do not exceed three A4 pages. Please briefly describe scientific aspect of the project, concrete results or commercialization potential, project implementation, and budget planning.

(Remark: *Please do not compose the COMPLETE project content in this Common English Application Form, but in the application forms of RFBR and MOST, respectively.)*

Many topical issues of scientific research have long been in the field of multidisciplinary research. Multidisciplinary research is extremely important for the development of many areas of human production and life. At the same time, we note that many studies are conducted within the framework of one discipline. This is facilitated by the need for a qualitative improvement in scientific results. Nevertheless, let us not forget that the vast majority of applied problems require knowledge and skills from several areas of science. For the development of medical science and its promotion to the world level requires the interaction of specialists from different areas of scientific significance. It so happened that in the Russian educational system people receive a higher education as a rule, a higher education, the second as a rule is a kind of refresher courses or a choice from a number of standard professions, a lawyer, an economist, etc. Thus, the peculiarities of the domestic educational system lead to the training of high-level specialists, but most of them are very difficult to overcome the barrier of multidisciplinary research due to a lack of an educational base on a related discipline. The simplest way out of this situation is research involving or consulting specialists from another field.

In a variety of human diseases, the liver disease such as liver cancer and its symptoms are often vague, which is liable to be confused with the symptoms of other diseases. Moreover, it is more difficult to diagnose patients whose liver has been damaged without any symptoms. The development of in vitro model systems, which generalize lobule microenvironment, has become an emergent field in liver diseases research. This research will provide information for liver diseases treatment and aid in drug discovery and monitor the dynamic process of 3D lobule construction.

In this Russian-Taiwanese Joint Research Project proposal, Professor Aleksandr Grigorev’s group will focus mainly on mathematical modeling of the processes of the internal organs of a person and the creation of specialized software for medical tasks. Research of blood flow in liver lobule will include

- Investigating mechanism and cancer cells spreading;

- Approbation of results of mathematical modeling in engineering tissue technique;

- Developing software for setting geometry of Chip.

Professor Cheng-Hsien Liu group will focus mainly on engineering reconstruction of Liver Lobule Tissue on Lab chip, which will be designed and microfabricated based on MEMS and IC fabrication techniques. We will collaborate the studies using nanotechnologies based on engineering reconstruction in order to improve the quality of work of medical personnel. Professor Cheng-Hsien Liu’s group would apply the results obtained in the results of mathematical modeling from Professor Aleksandr Grigorev’s group to tune the Liver LabChip design and studies. Professor Aleksandr Grigorev’s group would also modify the numerical model and mechanisms based on the experimental results from Liver Lab Chip. We together would like to develop the state-of-the-art 3-dimensional Liver-tissue Lab Chips for liver disease studies and personal medicine applications. It would serve as a high-throughput drug screening platform, and be along with the low dose of the drug testing platform. In addition, the screening drugs are mainly for effectively Liver disease preventions, treatments and suppressions with any symptom.

We have common interests in the research of liver diseases. In particular, the common theme is the spread of cancer cells in the liver, the dynamics of liver behavior and the possibility of treatment, including surgery. During surgery an operation is performed to resect a large part of the liver which directly affects blood flow processes. Through the implementation of this joint project, we will train interdisciplinary experts with engineering background for Taiwan's bio-medical industry and Russian’s science researchers capable of working on interdisciplinary research. In Taiwan, we target on training BioMEMS experts to get in/boost biomedical, semiconductor, MEMS and other related industry. Training students in the design, production and cross-field cooperation enables students to have future competitiveness. In this three-year project, we expect to develop a series of state-of-the-art 3-dimensional Liver-tissue Lab Chips which integrate smart-microsystem techniques, organ on chip techniques, 3-dimension engineered tissues techniques, Lab on chip techniques to provide in-vitro engineered tissues/organs for the study platforms of liver diseases, cancers, and Cancer metastasis. In addition to be recognized as the top/ state-of-the-art research and development technology internationally, we wish to contribute a little to the reduction of the number of liver patients and decrease of medical treatment for liver patients. Meanwhile, we wish to aim at the investment for the innovation required for the coming-decade biomedical industry in Taiwan. Besides the patents and potential spin-in would be outcome of this project. Both teams have the same object of investigations. Mainly not only same object but also same interest in research field. Lobule is a structural unit of the liver has a hexagonal geometry. Assume that the boundary conditions of the lobule in the liver are periodic (correct) which corresponds to the healthy functioning of the liver. In periodic boundary conditions it is assumed that the mode of operation of the liver in each lobule is the same. This is an ideal assumption of course in practice the situation is completely different. Liver diseases such as cirrhosis, hepatitis, hepatosis, cancer as well as various liver injuries, resection and shunting operations it is necessary to consider non-periodic boundary conditions. To solve this problem plan of the work include the creation of a scientific software for the generation of the geometry of the liver consisting of lobules. Also note that for the majority of medical problems characterize by multiphysics direction . To adequately describe the processes occurring in the liver it is necessary to model the multiphysics processes such as the flow of blood, its filtration, elastic deformations, dynamic changes in the geometry of the lobules and so on. When considering the real geometry of the liver, when the number of lobules significantly increases, the question arises of using high-performance computing systems. Similar studies are planned for modeling the physiological processes taking place in the kidneys. Nephron is a structural unit of the kidneys, it is more complex in terms of geometry. Therefore, research in this direction will be a logical continuation of research for the liver. The research is planned to be carried out on the following computational basis: various finite element variants implementations using open (free) computational libraries as well as methods that take into account the specific and structure of data problems such as multicontinuum models, multiscale methods, splitting methods. For example already existing developments for the liver, double porosity (multi-continuum) models are used based on the characteristics of the problem. The double porosity model is used to describe the flow of a fluid in fractured porous media its peculiarity is the introduction of a connection between flows in a fractured and porous medium. Thus for the case of a lobule analogous to the cracks are sinusoids (sinusoidal capillaries), and the porous space is a sinusoidal space near the given sinusoids. The multiscale method is also well suited for describing these tasks, in fact we have 2 levels - the level of structural units (lobule, nephron) and the level of organs (liver, kidneys). Thus, the application of a multiscale method is self-evident in this context. The solution of cumbersome multi-physical problems is complex both on the part of the model and on the part of the computational implementation, which requires the use of advanced computational methods, the most logical of them in this situation are the splitting methods that allow the problem to be "split" into a series of simpler ones and simplify the logic of the problem. We also interested in studying cancer propagation problem. We plan to construct new mathematical models that describe cancer cells spreading on different level.