

Activités internationales

1. Partenaires étrangers :

R. ALAM, Indian Institut of Technology, Guwahati, Inde
A. AMOSSOV, Institut de l'Energie, Moscou, Russie
V. BERDICHEVSKY, Wayne State University, USA
L. BERLYAND, Pennstate University, USA
G. CARDONE, Université de Naples, Italie
F. DIAS D'ALMEIDA, Faculté d'Ingénierie de Porto, Portugal
K. ERDMANN, Université d'Oxford, Royaume-Uni (R. Taillefer)
A. CORBO-ESPOSITO, Université de Cassino
F. GAZZOLA, Université d'Alessandria, Italie
R. GILBERT, Université de Delaware, U.S.A.
V. GINZBURG, Université de Chicago, Etats-Unis (R. Berger)
R. GIULIANO-ANTONINI, Université de Pise, Italie
K.R. GOODEARL, Université de Santa-Barbara, Etats-Unis (L. Rigal)
E.L. GREEN, Virginia Tech., Etats-Unis (R. Taillefer)
N. HEGYVARI, Université Eötvös Lorand, Budapest, Hongrie
C. HELOU, Pennstate University, USA
M. HOLLOWAY, Université d'Oxford, Royaume-Uni (R. Taillefer)
A. JOSEPH, Institut Weizmann, Rehovot, Israël (F. Fauquant-Millet)
R. KULKARNI, Indian Institut of Technology, Bombay, Inde
E. LAPSCHIN, Université d'Etat de Moscou Lomonossov, Russie
T.H. LENAGAN, Université d'Edimbourg, Royaume-Uni (L. Rigal)
B. LICHTIN, Canada
B. LIMAYE, Indian Institut of Technology, Bombay, Inde
G. LUKASZEWICZ, University of Warsaw, Pologne
K. MATSUMOTO, Université de Nagoya, Japon
A. MIELKE, Université Humbolt de Berlin et Institut Weierstrass, Allemagne.
R. MILITARU, Université de Craiova, Roumanie
L. MISIK, Université d'Ostrava, République Tchèque
M. MONTEIRO-MARQUES, Université de Lisbonne, Portugal
S. NAZAROV, Université de Saint-Petersbourg, Russie
G. PASA, Académie des Sciences, Roumanie
M.E. PEREZ, Université de Cantabria, Espagne
A. PETROV, Institut Weierstrass, Allemagne
A. PIATNITSKY, Univ. de Narvik, Norvège, et Inst. de Physique Lebedev de l'Académie des Sciences, Russie
J. PIHKO, Université d'Helsinki, Finlande
K. PILECKAS, Université de Vilnius, Lituanie
H. SHAHGOLIAN, Université de Stockholm, Suède
V. SMYSHLYAEV, Université de Bath, Angleterre
N. SNASHALL, Université de Leicester, Royaume-Uni (R. Taillefer)
Ø. SOLBERG, NTNU, Norvège (R. Taillefer)
R. STAVRE, Institut de Mathématiques Académie des Sciences de Roumanie.
O. STRAUCH, Académie Slovaque des Sciences, Slovaquie
D.A. TARZIA CONICET, FCE, Université Australe, Rosario, Argentine
V. TOMA, Université Comenius, Bratislava, Slovaquie
J. TOMANOVA, Université Comenius, Bratislava, Slovaquie
J. TOTH, Université d'Ostrava, République Tchèque
L. TREFETHEN, Université d'Oxford, Angleterre
H. TSUMURA, Université de Tokyo, Japon

2. Projets internationaux et conventions de coopération internationale :

a) Participation au projet PICS CNRS (France-Russie) sur les problèmes de modélisation en biologie et médecine (2005-2007). La contribution du LaMuse dans ce projet concerne la modélisation de circulation du sang. Ce projet remplace le projet international de l'Institut Liapunov (France-Russie) sur les problèmes de contrôles optimales et problèmes inverses.

b) Participation au projet de recherche sur conventions internationales du CNRS (2004-2005) « Analyse asymptotique et numérique des écoulements et opérateurs discrets de dimension infinie » MJHJD85312. Ce projet a remplacé le projet international EURROMMAT ICAI - 1999-70103 sur les problèmes des écoulements micro-polaires (avec l'Institut de Mathématique de l'Académie de Roumanie). Depuis 2006, ce projet est transformé en PICS CNRS France-Roumanie (2006-2008).

c) Participation au projet PICS CNRS avec l'Amérique Latine (Argentine, Brésil, France, Uruguay) « Homologie et déformation en Algèbre.

d) Présidence du Centre Latino-Américain de Calcul Scientifique et d'Informatique Industrielle (CLASCSII), et coordination et participation à des projets réalisés à Quito, Equateur.
Responsable local : M. AHUES
Participation locale : A. LARGILLIER

e) Participation au projet européen SICONOS sur le programme IST (B. Briogliato et Mario di Bernardi).
Participation locale : L. PAOLI.

f) Action Luso-Française avec l'Université de Porto, Portugal.
Participation locale : M. AHUES et A. LARGILLIER.

g) Les conventions bilatérales de coopération entre l'UJM et l'Institut Energétique de Moscou, l'Université de Naples II, l'Université de Cassino sont signées en 2004 et 2005 ; on prévoit la coopération scientifique, plusieurs échanges, le coencadrement des doctorants, la coordination des programmes des masters sont effectués dans le cadre de ces conventions.
Responsable : G. PANASENKO.

h) On participe aux projets de l'Institut Franco-Indien de Mathématiques (IFIM) et dans un projet de la Région Rhône-Alpes de coopération scientifique avec l'Inde ARCUS Inde (M. AHUES, A. LARGILLIER, L. GRAMMONT, G. GREKOS, F. HENNECART). Deux post-doctorants d'Inde sont venus chacun un an. S.G. Sista a développé le sujet de modélisation multi-échelle en biologie en coopération avec LTSI (UJM) et avec l'Institut Camille Jordan (G. PANASENKO), financement : bourse CNRS. R.K. Pandey travaille avec Monsieur Georges Grekos sur un sujet de théorie des nombres.

i) Programme de recherche MIRA (financé à 80% par la région Rhône-Alpes, 2005-2007) avec Monastir intitulé : Théorie des Nombres Lyon-Monastir-Saint-Etienne (G. Grekos et F. Hennecart). Ce programme a consisté à l'accueil de d'étudiants et de chercheurs de Monastir et à l'envoi de chercheurs à Monastir pour assurer des cours de troisième cycle. Le but de ces échanges fut de favoriser les collaborations entre les deux parties.

j) G. Grekos était responsable pour la France d'un programme « EcoNet » (Ministère des affaires étrangères) avec la Slovaquie et la République Tchèque (2006 et 2007; budget français 15000 euros par année).

3. Appartenances à des réseaux internationaux :

- a) Participation au GDRE sur la modélisation de turbulence « Regular and Chaotic hydrosystems »
- b) Participation au programme européen RTN en algèbre.
- c) Par l'intermédiaire du GDR 2432 (qui en est le noeud en France), les algébristes stéphanois ont fait partie du réseau européen LIEGRITS : « Flags, Quivers and Invariant Theory in Lie Representation Theory », Marie Curie Research Training Network funded by the European Community (F. Van Oystaeyen, Anvers), jusqu'à sa clôture en février 2008.
- d) Par l'intermédiaire du GDR 2432, les algébristes stéphanois font partie du GDRE (GDR européen) « French-British Network in Representation Theory » depuis sa création début 2008.
- e) L. Rigal a été membre, de 2002 à 2007, du Groupe de recherche « Noncommutative Geometry (Quantum Algebras and Coinvariant Theory) », org. T.H. Lenagan (Université d'Edimbourg) et K.A. Brown (Université de Glasgow), financé par le Leverhulme Trust.
- f) Les algébristes stéphanois font partie du Programme International de Coopération Scientifique du CNRS intitulé PICS 3410 « Homologie et déformation en algèbre » (Argentine, Brésil, Uruguay, France).
- g) Pendant les deux années civiles 2007 et 2008, L. Rigal a été le responsable français d'un Partenariat Hubert-Curien (PHC) ALLIANCE entre la France et le Royaume-Uni, dont le responsable britannique était T. Lenagan (Edimbourg). Les algébristes stéphanois faisaient partie de ce partenariat.

4. Organisation d'événements :

- a) International Workshop FBP 2009 : FREE BOUNDARY PROBLEMS AND APPLICATIONS TO FLUID MECHANICS, FRICTION AND IMPACT PHENOMENA, novembre 2009, Faculté des Sciences et Techniques, Université Jean Monnet, Saint-Etienne, (Organisateurs : M. BOUKROUCHE et L. PAOLI).
- b) 26èmes Journées Arithmétiques de Saint-Etienne (6-10 juillet 2009) <http://ja2009.univ-st-etienne.fr> [organisateurs : D. Essouabri, F. Foucault, F. Hennecart, F. Pellarin, O. Robert et l'aide de A. Faisant et F. Gramain]. Congrès rassemblant près de 200 participants, un des plus grands congrès mondiaux en Théorie des Nombres, subventionné par le Ministère (3000), la région Rhône-Alpes (3000), la Mairie de Saint-Etienne (réception, cadeaux et subvention en attente), le CNRS - GDR Théorie des nombres (9000), le Conseil Général de la Loire et Saint-Etienne-Métropole (4000) et le laboratoire (4000).

5. Séjours à l'étranger :

- Grigory Panasenko : Norvège (High Technical School of Narvik) 2006 (deux semaines), 2007 (deux semaines)
- Grigory Panasenko : Espagne (Université de Cantabria, Santander) 2005 (1 semaine).
- Grigory Panasenko : Italie (Universités de Cassino, de Naples) 2006 (deux semaines), 2007 (deux semaines), 2008 (trois semaines)
- Grigory Panasenko : Russie, l'Institut de l'Energie de Moscou, 2005 (deux semaines), 2007 (deux semaines), 2009 (1 mois)
- Grigory Panasenko : République Tchèque, Doppler Institute 2007 (une semaine)
- Grigory Panasenko : Lituanie, Institut de Mathématiques et Inf. de Vilnius, 2008 (1 semaine)
- Depuis 2006, séjours de L. Rigal à l'Université d'Edimbourg, de Canterbury, de Buenos-Aires.

- Séjour de F. Fauquant-Millet à l'Institut Weizmann (Israël) du 20 au 30 janvier 2008, au "Winter Master Class on Enveloping Algebras and Related Topics".
- Séjour de R. Berger de 1 mois en Argentine (Mar del Plata, Buenos-Aires, Cordoba) en 2006.
- Séjour post-doctoral de B.Kriegk à l'université d'Hasselt, en Belgique, auprès du professeur M. Van den Bergh, depuis janvier 2009.
- Séjours de recherche de F. Hennecart : Budapest, Institut Rényi et Université Eötvös, oct. 2006 (2 semaines) , oct. 2008 (2 semaines), oct. 2009 (2 semaines).

PROJECT MULTIMOD

“Multiscale Models in Physics, Biology and Technologies: Asymptotic and Numerical Methods”

State grant of the Russian Federal Agency for Research and Innovations
No 02.740.11.5091 (2009-2010)

Invited Director of the Project: Grigory PANASENKO, Professor of the University Jean Monnet (Saint-Etienne), LAMUSE

Vice- Director of the Project: Andrey AMOSOV, Professor, Head of the chair, Moscow Power Institute (Technical University)

LIST OF PARTICIPANTS :

1. Andrey AMOSOV, Professor, Head of the chair, Moscow Power Institute (Technical University)
2. Alexander ZLOTNIK, Professor, Moscow Power Institute (Technical University)
3. Alexander PERESKOKOV, Associate Professor, Moscow Power Institute (Technical University)
4. Marina CHEREPOVA, Associate Professor, Moscow Power Institute (Technical University)
5. Alexey VESTFALSKY, Associate Professor, Moscow Power Institute (Technical University)
6. Ilya BOROVIKOV, Ph.D. student, Moscow Power Institute (Technical University)
7. Ivan GOSHEV, Ph.D. student, Moscow Power Institute (Technical University)
8. Anna KREMKOVA, Ph.D. student, Moscow Power Institute (Technical University)
9. Vladimir GAVRILKIN, graduate student, Moscow Power Institute (Technical University)
10. Vladimir GULIN, graduate student, Moscow Power Institute (Technical University)
11. Ilya ZLOTNIK, graduate student, Moscow Power Institute (Technical University)
12. Mikhail KRYGIN, graduate student, Moscow Power Institute (Technical University)
13. Anna LAPUKHINA, graduate student, Moscow Power Institute (Technical University)
14. Anna LIPSKAYA, graduate student, Moscow Power Institute (Technical University)
15. Mikhail SHUMAROV, graduate student, Moscow Power Institute (Technical University) and ENISE (Saint-Etienne)
16. Grigory PANASENKO, Professor of the University Jean Monnet (Saint-Etienne), LAMUSE

THE GOAL of the project is the development of the theory, methods and codes for multi-scale problems in physics, biology and technologies describing the processes in materials, media and devices with strongly varying properties; namely, in composite materials, nano-materials, metals, elasto-plastic and visco-elastic media, in biological tissues and in blood circulation. These problems are described by partial derivative equations (PDEs) or integro-differential equations containing small parameters. The project develops the special asymptotic and numerical methods for these problems and provides the rigorous mathematical study of these methods including the proof of theorems on existence and uniqueness of solutions, convergence and error estimates for the approximate solutions. In the frame of the project one Habilitation States Doctor dissertation and two Ph.D. theses will be defended.

PUBLICATIONS OF THE PROJECT:

1. G.Panasenko,
Boundary conditions for the high order homogenized equation: laminated rods, plates and composites,
C.R.Mecanique, 337 (2009) 8-14.
2. Z.Abdessamad, I.Kostin, G.Panasenko, V.P.Smyshlyaev,

Memory effect in homogenization of a viscoelastic Kelvin-Voigt model with time dependent coefficients,

Mathematical Models and Methods in Applied Sciences, 19, 9 (2009) 1603-1630.

3. G.Panasenko, R.Stavre,

Well posedness and asymptotic expansion of solution of Stokes equation set in a thin cylindrical elastic tube,

in "Around Research of Vladimir Maz'ya", (vol. 11-13 of International Mathematical Series), Springer, 2009.

4. A.Amosov, G. Panasenko.

Homogenization of the integro-differential Burgers equation,

Integral Methods in Science and Engineering, vol. 1. Analytic Methods, C. Constanda and M.E. Perez (eds.), Birkhauser, Boston, 2009, pp. 1-8.

5. A.Amosov, G.Panasenko.

Integro-differential Burgers equation.

Solvability and homogenization, Nonlinear Analysis. TMA (submitted).

PROJECT PICS CNRS – RUSSIE 2010-2012

Mathematical modelling of blood diseases

Team leaders: Vitaly VOLPERT (Research Director, CNRS)

**Fazly Ataullakhanov (Professor, Vice-Director of the Russian National Center for Hematology)
Saint-Etienne University is presented in the project by the LAMUSE as a partner, G.Panasenko as
the local responsible.**

1. Scientific context

The project concerns the development of new mathematical methods of multi-scale modelling in biology and medicine and their applications to modelling, diagnostics and treatment of various diseases such as hemophilia, leukemia, and atherosclerosis. Multi-scale modelling in biology and medicine is a rapidly developing area of research at the cutting edge of modern science. It requires joint efforts of inter-disciplinary groups with participation of mathematicians, computer scientists, physicists, biologists and medical researches. The two main directions of the development of multi-scale modelling in medicine concern mathematical modelling of cancer and of heart (e.g. [1]).

We develop a new approach to multi-scale modelling in biology and medicine. The main point of this approach is to use dissipative particle dynamics (DPD) in order to describe cell populations. Dynamics of cell populations will be coupled with intra-cellular regulatory networks described by ordinary differential equations (ODE) and with extra-cellular phenomena described by partial differential equations (PDE). We develop this program during last several years [3,4]. It is a general method of modelling of cellular structures. In the framework of this project we will continue its development and will apply it to model blood diseases, which represent the area of our competence [5,6].

Dissipative particle dynamics is a relatively new method in mechanics and physics which is developed in order to describe hydrodynamics of complex media [2]. We will use it to describe dynamics of cell populations in biological tissues where cell-cell interaction is determined by elastic forces, adhesion and friction. In this context, each particle corresponds to a biological cell. They move due to the forces acting on them from the surrounding cells and from the external medium. An important developed of this method consists in the fact that we introduce cell division and death, which change the number of particles, and cell differentiation, which change their properties. Cell proliferation, differentiation and apoptosis (programmed cell death) are determined by intra-cellular regulatory networks described by ordinary differential equations written for each cell, and by external regulation which can be described by diffusion equations for bio-chemical substances in the extra-cellular matrix.

Discrete models based on the DPD are related to partial differential equations of continuum mechanics. These can be Navier-Stokes equations for fluids, Darcy's law in the case of a porous medium, elasticity equations, and so on. Transition between discrete and continuous models is a difficult and important question because numerical simulations are much more efficient in the case of PDE. Moreover, mathematical analysis of partial differential equations will allow us to study their qualitative properties. We will use these modelling tools in order to study complex biological flows including cell motion in the bone marrow in normal and pathological situations and blood flows with or without blood coagulation. This is related to various hematopoietic disorders, cardio-vascular diseases, hemophilia.

Blood coagulation is described by complex nonlinear dynamical systems. It can propagate in space in the self-sustained manner as a travelling wave [7-10]. It is accompanied by clot formation which has some features of phase change and represents an example of multiscale processes. Mathematical models of blood coagulation are formulated as systems of PDEs describing the evolution of the concentrations in space and in time [8, 11, 13, 14]. These models are used for the theoretical

investigation and for interpretation of the experiments. We have developed a new experimental approach which consists in direct registration of blood clot propagation in space [9, 10, 12, 14]. These studies are carried due to joint works in the National Research Center for Hematology in Moscow and Edouard Herriot Hospital in Lyon [15]. Interpretation of the experimental data and further investigations require application of the existing methods of mathematical modelling and the development of new methods.

1. Alarcon T, Byrne HM, Maini PK. A multiple scale model for tumor growth. *SIAM. Multiscale Model Simul.* 2005, 3: 440-475.
2. Karttunen M, Vattulainen I, Lukkarinen A. *Novel Methods in Soft Matter Simulations.* Springer; 2004.
3. Bessonov N, Pujo-Menjouet L, Volpert V. Cell modelling of hematopoiesis. *Math. Model. Nat. Phenom.*, 1 (2006), No. 2, 81-103.
4. Bessonov N, Demin I, Pujo-Menjouet L, Volpert V. A multi-agent model describing self-renewal of differentiation effects on the blood cell population. *Mathematical and Computer Modelling.* To appear (2008).
5. A. Ducrot, V. Volpert. On a model of leukemia development with a spatial cell distribution. *MMNP*, 2007, No. 3, 101-120.
6. A. Plesa, G. Ciuperca, S. Genieys, V. Louvet, L. Pujo-Menjouet, C. Dumontet, V. Volpert. Diagnostics of the AML with immunophenotypical data. *MMNP*, 2006, No. 2, 124-137.
7. Ataullakhanov FI, Guriia GT. Spatial aspects of the dynamics of blood coagulation. I. Hypothesis. *Biophysics.* 1994;39(1):91-97.
8. Ataullakhanov FI, Guriia GT, Safroshkina AYU. Spatial aspects of the dynamics of blood coagulation. II. Phenomenological model. *Biophysics.* 1994;39(1):99-108.
9. Ataullakhanov FI, Volkova RI, Guriia GT, Sarbash VI. Spatial aspects of blood coagulation dynamics. III. Growth of clots in vitro. *Biophysics.* 1995;40(6):1343-51.
10. Ataullakhanov FI, Guria GT, Sarbash VI, Volkova RI. Spatiotemporal dynamics of clotting and pattern formation in human blood. *Biochim Biophys Acta.* 1998;1425(3):453-68.
11. Zarnitsina VI, Ataullakhanov FI, Lobanov AI, Morozova OL. Dynamics of spatially nonuniform patterning in the model of blood coagulation. *Chaos.* 2001;11(1):57-70.
12. Ovanesov MV, Krasotkina JV, Ul'yanova LI, Abushinova KV, Plyushch OP, Domogatskii SP, Vorob'ev AI, Ataullakhanov FI. Hemophilia A and B are associated with abnormal spatial dynamics of clot growth. *Biochim Biophys Acta.* 2002;1572(1):45-57.
13. *Mathematical Modeling and Computer Simulation in Blood Coagulation.*/Eds. F.I. Ataullakhanov and M.A. Panteleev, Karger, Basel, 2005, 94 pages.
14. Panteleev MA, Ovanesov MV, Kireev DA, Shibeko AM, Sinauridze EI, Ananyeva NM, Butylin AA, Saenko EL, Ataullakhanov FI. Spatial propagation and localization of blood coagulation are regulated by intrinsic and protein C pathways, respectively. *Biophys J.* 2006;90(5):1489-500.
15. J.C. Bordet, M. Panteleev, J.L. Plantier, Y.D. Dargaud, F. Ataullakhanov, C. Negrier. Regulation of thrombin generation and clot growth by mutant factor VIII molecule. Workshop "Modelling of blood diseases". Lyon, November 5-8, 2007, p. 2.

2. Objectives

2.1. Multi-scale modelling. We will develop coupled DPD-PDE-ODE models in order to describe dynamics of biological cell populations, will compare them with continuous models and will study properties of the corresponding partial differential equations:

2.1.1. Dissipative particle dynamics describes motion of a system of particles by Newton's second law. The total force includes potential, dissipative and random forces. It is related to molecular dynamics where dissipative forces are not taken into account and potential forces are considered in a different form. We will continue the development of the software "Cell dynamics". Its version "Soft sphere model" will be used to compare numerical simulations of DPD with PDE of continuum mechanics (Navier-Stokes equations, Darcy's law).

2.1.2. "Elastic cell" version of the software "Cell dynamics" will be developed in order to study complex flows. In particular, it will be applied for blood flows where elastic cells correspond to erythrocytes while small particles (soft spheres) can model either surrounding liquid (plasma) or small blood cells (platelets). The properties of such flows will be studied including velocity and concentration distribution which are particularly important for blood coagulation.

2.1.3. The next group of models of the software "Cell dynamics" will include coupling of particle dynamics with diffusion equations describing the distribution of bio-chemical substances in the extra-cellular matrix and with ordinary differential equations describing intra-cellular regulatory networks for each cell. These models will require biological justification, an important development from the point of view of computer science and their mathematical analysis. This is one of the central objectives of the project. The developed models will be used in order to study various biological and medical applications including leukemia. They can also be applied to study other biological phenomena like morphogenesis, chemotaxis and platelet plug (thrombus) formation.

2.1.4. 1D, 2D and 3D models of blood flow and vessels motion will be studied numerically taking into account flow interaction with vessel walls (fluid-structure interaction). Numerical modelling of various cardio-vascular devices and implants will be developed in order to optimize their usage.

2.2. Applications to modelling of complex flows and blood diseases

2.2.1. *Atherosclerosis*. We will apply these modelling approaches to study the initiation and development of atherosclerosis. At the first stage, this disease, which is at the origin of essential part of death causalities, is characterized by chronic inflammation in blood vessel walls. It can be modeled with reaction-diffusion equations describing concentrations of monocytes, macrophages and foam cells and of various biochemical substances (cholesterol, cytokines). The main expected result is to show how the cholesterol level and other risk factors determine the initiation of atherosclerosis. Further development of atherosclerosis results in formation of atherosclerotic plaque and remodeling of blood vessels walls. Interaction of blood flow with the plaque can cause plaque rupture or spontaneous blood coagulation which can lead to heart attack or to stroke. We will study the interaction of blood flow with vessel walls and its medical and biological consequences.

2.2.2. *Leukemia*. Similar modelling methods will be applied to study development and treatment of leukemia and other blood malignancies. We will specify the conditions under which the malignant mutation can result in the development of leukemia. These conditions are related to the rates of self-renewal and differentiation of proliferating cells and determined by the intra-cellular regulatory networks. Treatment of acute myeloid leukemia by chemotherapy will be modeled and conditions of successful treatment under various protocols will be studied.

2.2.3. *Blood coagulation and hemophilia*. Furthermore, mathematical modelling with PDE, computer simulation and systems biology approaches will be employed to study spatial dynamics of fibrin clot formation in hemophilia A, B, and C plasmas. The process of three-dimensional fibrin clot formation in the presence of blood flow will be compared in normal and hemophilia plasma; effects of blood flow, injury size, and activation intensity will be evaluated. We shall also simulate both replacement and bypassing therapy in hemophilia with currently available therapeutic agents, as well as with those

currently under development or hypothetical ones. We shall aim to identify the physical and molecular bases of the disease, and determine optimal strategies for coagulation normalization.

3. Interaction between the disciplines

This project is essentially inter-disciplinary. Close cooperation between different scientific disciplines is the key point of its realization. The distribution of tasks between the disciplines and the participants will be as follows:

- development of the software "Cell dynamics" – N. Bessonov
- transition between discrete and continuous models, mean field theory, rheological laws, particle interaction – N. Bessonov, V. Volpert
- analysis of partial differential equations, homogenization – A. Amosov, G. Panasenko, V. Volpert
- numerical analysis and numerical simulations of partial differential equations of continuum mechanics - Yu. Vassilevskii, N. Bessonov, S. Simakov.
- modelling of intra-cellular regulatory networks, cell self-renewal, differentiation, apoptosis, bio-chemical regulation – S. Bernard, F. Crauste, S. Genieys, L. Pujo-Menjouet
- modelling of blood coagulation in the presence of flow – E. Shnol, E. Ermakova, M. Panteleev, A. Butylin, F. Ataullakhanov
- simulating the replacement and bypassing therapy in hemophilia – A. Balandina, M. Panteleev, F. Ataullakhanov
- modelling of platelet activation and aggregation – A. Tokarev, G. Panasenko, V. Volpert, A. Butylin, F. Ataullakhanov

4. Necessity of cooperation

Joint work in the framework of this project is based on a long-term cooperation between French and Russian participants. The Russian team will develop the software "Cell dynamics", will work on hydrodynamics of blood flows, on modelling of blood coagulation and on biological and medical aspects of hemophilia. The French team will use the developed software in order to study normal and pathological hematopoiesis. Its participants will investigate intra-cellular regulatory networks and various biological and medical aspects of hemopoietic disorders (e.g., acute myeloblastic leukemia). They will also carry out mathematical analysis of the models describing leukemia and atherosclerosis development.

Biological and medical questions will be studied together with our collaborators at the University Lyon 1 and at the Edouard Herriot Hospital in Lyon. It is important to note that Russian participants of the project (group of F. Ataullakhanov) have developed original equipment which allows the improvement of the diagnostics of hemophilia. This equipment is installed at the Edouard Herriot Hospital. The training of the staff was carried out. The employment of this new diagnostic technique is based on the comparison of blood samples from the patients with the results of mathematical modelling. It allows one to establish a possible deficiency of certain proteins (e.g. factor VIII) participating in blood coagulation and to specify medical treatment.

5. Joint works of the participants

- E.A. Ermakova, E.E. Shnol, M.A. Panteleev, A.A. Butylin, V. Volpert, F. I. Ataullakhanov (2009). On Propagation of Excitation Waves in Moving Media: The FitzHugh-Nagumo Model. PLoS ONE 4(2): e4454. doi:10.1371/journal.pone.0004454
- N. Bessonov, J. Pojman, G. Viner, V. Volpert, B. Zoltowski. Instabilities of diffuse interfaces. Math. Model. Nat. Phenom., 3 (2008), No. 1, 108-125.

- N. Bessonov, I. Demin, L. Pujo-Menjouet, V. Volpert. A multi-agent model describing self-renewal or differentiation effect of blood cell population. *Mathematical and computer modelling*, 2008, doi: 10/1016/j.mcm.2008.07.023
- A.A. Tokarev, Yu.V. Krasotkina, M.V. Ovanesov, M.A. Panteleev, M.A. Azhigirova, V.A. Volpert, F.I. Ataulakhanov, A.A. Butilin. Spatial dynamics of contact-activated fibrin clot formation in vitro and in silico in haemophilia B: effects of severity and Ahemphil B treatment. *Math. Model. Nat. Phenom* , 1 (2006), No. 2, 124-137.
- N. Bessonov, L. Pujo-Menjouet, V, Volpert. Cell modelling of hematopoiesis. *Math. Model. Nat. Phenom*, 1 (2006), No. 2, 81-103.
- A. Tokarev, V. Volpert, G. Panasenko, I. Sirakov, E. Shnol, A. Butylin, F. Ataulakhanov. Erythrocytes-platelets interactions as a physical basis of haemostasis. *Workshop of Blood Deseases*, Lyon, November 2007. *Book of abstracts*, p.16.

(These publications directly concern the subject of the project. There are 12 other joint publications on other subjects.)

6. Work program

2010 – development of bio-physical and mathematical models, development of the software based on dissipative particle dynamics and partial differential equations

2011 – mathematical analysis of the models, numerical simulations, modelling of blood diseases

2012 – further adaptation of the software, biological and clinical applications, continuation of mathematical analysis and numerical simulations

7. Other partnerships and projects

The studies in the framework of this project are related to some other ongoing project of the participants:

- ANR project "Mecamerge" devoted to mathematical modelling of complex biological phenomena, 2007-2009. N. Bessonov has spent 8 months in Lyon in the framework of this project in order to begin the development of the software "Cell dynamics"
- ANR project "Anatools" devoted to development of new methods of diagnostics and treatment of acute myeloblastic leukemia, 2007-2010. We work together with biologists and medical researches in the framework of this project in order to develop mathematical models of treatment of leukemia with ara-cytosine.
- GDRE "Regular and chaotic hydrodynamics", France-Russia, 2006-2009. We participate in this project with the aim to study complex biological flows.
- RFFI grant 05-01-22001, 2005-2008. This project included theoretical and experimental investigation of spatial clot dynamics. Theoretical investigations were carried out by the group of Prof. F. Ataulakhanov together with the French participants (V. Volpert, G. Panasenko). Experimental studies by the same group and the group of Prof. C. Negrier with the help of the equipement developed in Moscow and installed in E. Herriot Hospital in Lyon.

8. Training

Training by research plays an important role in this project. Along with permanent researchers indicated in the list of participants, a number of graduate and undergraduate students from both sides will also participate in the studies in the framework of this project and in mutual visits.

From the French side: I. Demin, N. El Khatib, P. Kurbatova (all graduate students at the University Lyon 1)

From the Russian side: A. Chernyshenko, Yu. Ivanov, T. Dobroserdova (all undergraduate students at Moscow State University), L. Parunov (graduate student, Center for theoretical problems of physico-chemical pharmacology).

Participation of undergraduate students has a particular importance from the point of view of their possible graduate studies.

List of participants:

France:

V. Volpert (DR CNRS, Inst. Camille Jordan, Lyon)

S. Bernard (CR CNRS, Inst. Camille Jordan, Lyon)

F. Crauste (CR CNRS, Inst. Camille Jordan, Lyon)

S. Genieys (MC, Inst. Camille Jordan, Lyon)

L. Pujo-Menjouet (MC, Inst. Camille Jordan, Lyon)

G. Panasenko (PR, head of laboratory, LaMUSE, St-Etienne)

Russia:

F. Ataulokhanov (PR, Director of the Center for Theoretical Problems of Physico-Chemical Pharmacology, Russian Academy of Sciences. Head of the Laboratory of Physical Biochemistry of Blood of the National Research Center for Hematology, Russian Academy of Medical Sciences, Deputy Director of the National Research Center for Hematology, Russian Academy of Medical Sciences)

M. Panteleev (Head of Laboratory of Molecular Mechanisms of Hemastasis of the Center for Theoretical Problems of Physico-Chemical Pharmacology, Russian Academy of Sciences. Principal Researcher of the Laboratory of Physical Biochemistry of Blood of the National Research Center for Hematology, Russian Academy of Medical Sciences)

A. Butylin (Research fellow of the Laboratory of Physical Biochemistry of Blood of the National Research Center for Hematology, Russian Academy of Medical Sciences. Assistant Professor of the Faculty of Physics, Department of Medical Physics, Moscow State University M.V. Lomonosov)

A. Tokarev (Research fellow of the Laboratory of Physical Biochemistry of Blood of the National Research Center for Hematology, Russian Academy of Medical Sciences)

Y. Vasilevskiy (Leading Researcher, Inst. of Numerical Mathematics, Russian Academy of Sciences)

N. Bessonov (Leading Researcher, Inst. of Problems of Mechanical Engineering, S.Peterburg)

E. Shnol (PR, Principal Researcher, Inst. of Mathematical Problems of Biology)

E. Ermakova (Researcher, Inst. of Chemical Physics, Russian Academy of Sciences)

A. Amosov (PR, Head of laboratory, Moscow Power Engineering Inst.)

S. Simakov (Associate professor, Moscow Inst. of Physics and Technology)