Towards Virtual Coagulation

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Complexity of blood coagulation, a delicately balanced system of numerous enzymes, cofactors, and inhibitors interacting with each other and with blood and vascular cells in flowing blood, has been both an obstacle and a stimulating, challenging factor for theoretical research in hemostasis and thrombosis for decades. Recent decades witnessed an explosion of mathematical modeling and computer-simulation-based research in all areas of biochemistry and biology, including coagulation. Initially designed for the basic analysis of the cascade structure, threshold behavior, etc., mathematical models of coagulation have been later successfully used for solution of numerous applied tasks, such as experimental planning and analysis, drug design, research and therapeutic strategy planning, development of nonthrombogenic biomaterials and rational diagnostics. The *in silico* simulation methods became both a potent independent research tool and a useful supplement of experimental research.

The present issue of the *Pathophysiology of Haemostasis and Thrombosis (PH&T)* journal is titled ‘Mathematical modelling in blood coagulation’ and is focused on all aspects of theoretical research in hemostasis and thrombosis. Papers published in this issue fall into several categories covering various aspects of this field. The introductory article [4] reviews previous theoretical research in blood coagulation and the current ‘state of the art’. To our knowledge, this is the first attempt to systematically review mathematical and computer models of coagula-

tion. The work of Jesty et al. [5] analyzes, both theoretically and experimentally, threshold behavior of a system composed of autocatalytic enzyme (factor XIIa) and its irreversible inhibitor. The study by Lo et al. [6] presents a computer model of thrombin generation assay based on a stochastic simulation approach. Two works [7, 8] simulate fibrin clot formation in flow, utilizing simple models; the former study focuses [7] on the effects of flow on thrombus growth and pattern formation, while the latter one [8] models the effect of vessel wall thrombomodulin on thrombin spatial propagation process. Finally, two other works [9, 10] describe detailed models of coagulation in flow: the study of Fogelson and Tania [9] simulates intravascular coagulation and platelet deposition on sub-endothelium, while Anand et al. [10] propose a model incorporating both coagulation and fibrinolysis processes in a vessel with flowing blood.

It might look strange that a whole special issue of purely theoretical (for the most part) studies appears in *PH&T*, which should be expected to specialize in clinical pathophysiology or, at least, experimental biochemistry and molecular biology of coagulation. Although it can be mentioned that a number of pioneering theoretical works, among them the first mathematical model of intrinsic tenase [1], the first computer models of thrombin generation assay [2] and of prothrombin time test [3] were published in *Haemostasis* (which later became *PH&T*), there are more reasons behind that. Unfortunately, mathemat-

ical modeling and computer simulation in hemostasis and thrombosis were often developed separately from the mainstream of experimental science, all the more of clinical work. The neglect is mutual: novel experimental data and conceptions slowly enter mathematical models, and results of modeling studies, which could have potential clinical significance, are rarely published in journals specialized in thrombosis and hemostasis and often tend to have such a form that makes them uninteresting to ex-

perimental and clinical investigators. The objective of this special issue was to bring together theoretical studies of coagulation with potential interest and importance for not only specialists in theoretical biology and biochemistry, but also for all readers who have to deal experimentally or clinically with hemostasis and thrombosis. If this issue is able even slightly to stimulate the interaction between theory and practice in coagulation science, we shall consider our task fulfilled.

References

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