

focus on Microscopy & Microtechniques

Speeding up Research into Clotting and Bleeding

Bas de Laat, Synapse BV www.thrombin.nl Phenom-World www.phenom-world.com

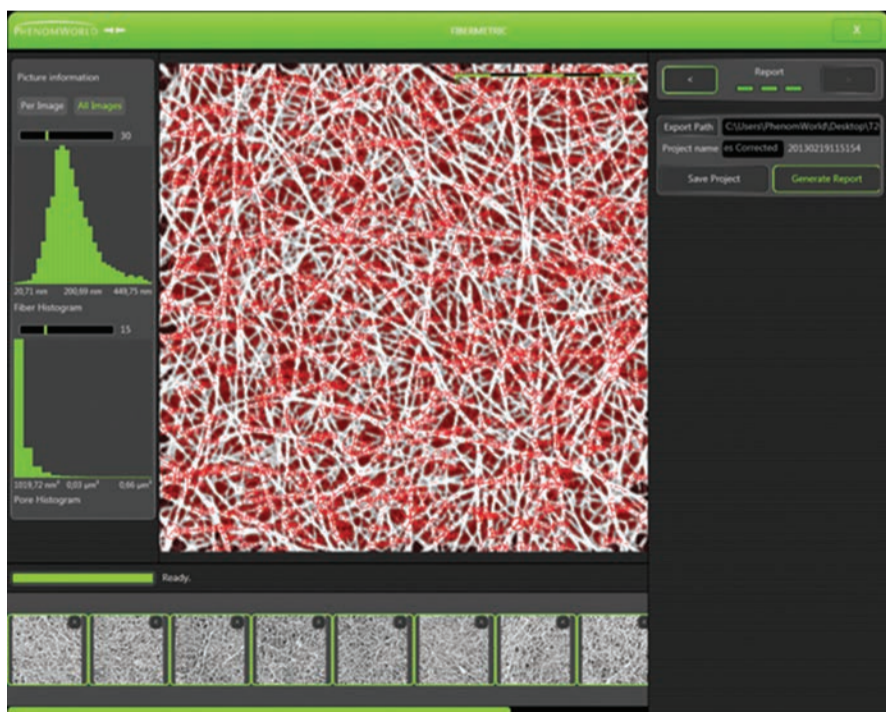
Coagulation of blood is a complicated and critical process. At the Maastricht University and spin-off company Synapse, fundamental research is taking place and practical detection methods are being developed for thrombosis and bleeding. A good snapshot of the clotting helps researchers to gain a better grasp of the phenomenon. Synapse is using the Phenom for this purpose. With the support of advanced software, this table model electron microscope accelerates the analysis of a blood sample from three days to three minutes.

If the interaction of clotting factors in the blood is not functioning properly, the clotting may be too strong (thrombosis) or too weak (spontaneous bleeding). The role of the thrombin enzyme in the conversion of the fibrinogen clotting factor into fibrin was discovered at Maastricht University. In the event of damage to a blood vessel, fibers from that protein form a network that can 'capture' platelets whereby a clot is created that seals the wound. Synapse was established in 1999 as a spin-off of this scientific breakthrough.

Measuring Thrombin Activity

Synapse researches new methods for detecting and predicting thrombosis and bleeding, said Managing Director Bas de Laat.

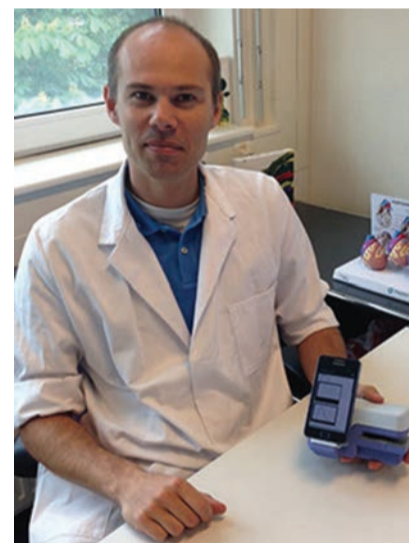
"What's unique is that we do everything from basic research to prototype. In 2009 we were acquired by the French diagnostics group STAGO, the world leader in blood coagulation tests. They have invested significantly in us and we have secured many grants, whereby we have grown to 35 employees and five labs."



Analysis of a network of fibrin fibres using the Phenom FiberMetric software application. The software measures in an automated manner the thickness of the fibrin fibres and the size of the pores in the fibrin network. These parameters are important characteristics of the structure of the fibrin network.

Synapse has its own technical lab, but also often works with companies in the vicinity, such as Maastricht Instruments. "After we have built a prototype, we transfer it to our parent company or to another company for production. We then have revenues from the licensing of our patents."

Synapse has developed a measuring apparatus for the thrombin activity in blood plasma (the liquid blood from which the blood cells have been removed).



Bas de Laat

Fibre Measurements

Synapse also continues to develop its research on coagulation. Important parameters are the number of fibers and the thickness of the fibres in a fibrin network.

"If it's a fine and strong network, there is more risk of thrombosis. If there are large gaps in the network, there is more risk of bleeding. Until recently we viewed a drop of blood under an optical microscope. It took three days to fully analyse. Now we put the sample under the SEM and we're ready in three minutes."

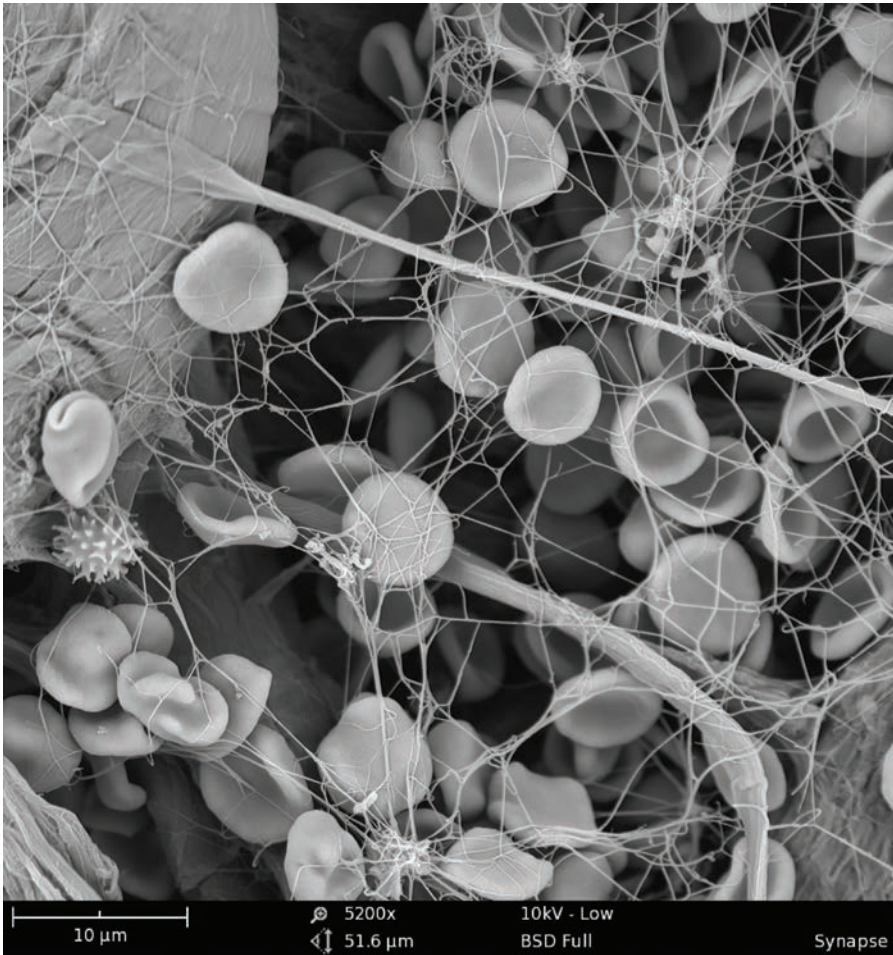
De Laat refers to the tabletop scanning electron microscope from Phenom-World Eindhoven, that started five years ago as a spin-off from FEI, the manufacturer of 'large' electron microscopes. After a long build-up, Phenom-World is now in an upward trend, with sales last year of about 300 pieces, including to research and educational institutions and research and analysis labs of businesses. The speed of the Phenom was said to be due to its mechatronic construction and smart image processing software.

De Laat: "The Phenom has a nice algorithm for fibres. The FiberMetric software automatically determines the thickness of the fibres in the order of 100 nanometers (one ten thousandth of a millimeter), and the size of the pores between the fibrin threads."

Owing to the simple operation and automatic analysis, the microscope saves significant labour costs at Synapse. "Put the sample in, operate with the intuitive interface, anyone can work with it. We don't need to continue to grow in numbers of personnel and instead of looking at a sample for three days, we can now focus on smarter thinking."

Meanwhile there is a second generation of Phenom, which includes higher magnification. Bas de Laat is taken with it. "This comes in very handy when we want more detail. Currently we have to go to the university in order to put a sample under the big SEM."

More and more requests are coming from the hospital for the Phenom. "It is in constant use and we are getting the first signals that the measurements are clinically relevant." If the Phenom can be used for the direct detection of thrombosis, then it really will come into the picture in the medical world the company added.

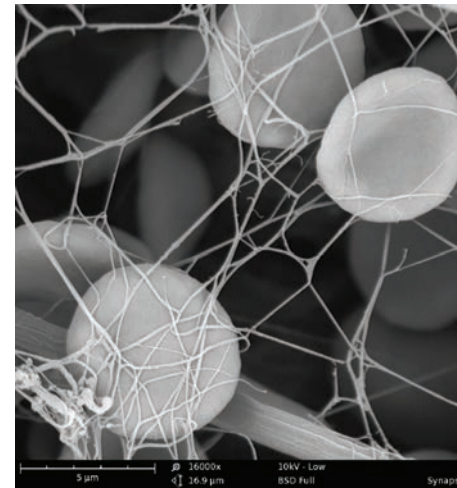


Phenom SEM image of a clot at 17500x magnification: platelets trapped in a fibrin network.

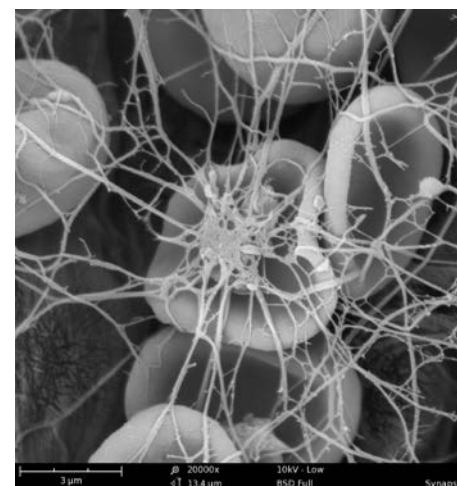
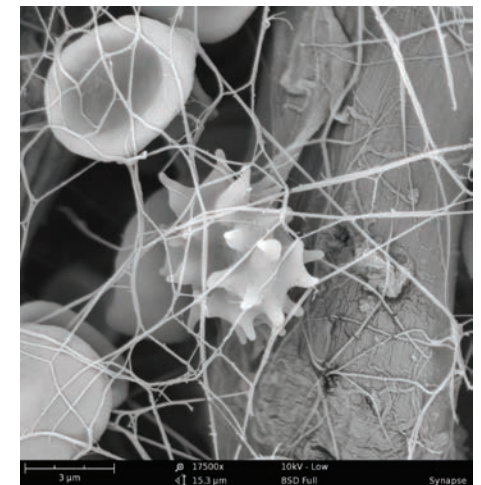
About the research conducted by Synapse

“Synapse BV provides cutting edge research in the field of haemostasis and thrombosis, especially into the role of thrombin. Thrombin is the central enzyme in coagulation because it is crucial for fibrin formation and an important activator of blood platelets. At Synapse, the scanning electron microscope (SEM) of Phenom is used to visualise the structure of the fibrin network and the structure of platelets and other blood cells. Visualisation of these structures is important because several diseases of blood coagulation are related to changes in the fibrin network and/or blood cells. For example, patients with thrombosis, such as a heart attack or stroke, form a denser network of fibrin fibres than healthy people.”

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The images show a Phenom SEM image of a blood clot at various magnifications. Blood of a healthy individual was clotted in a test tube and fixated for SEM analysis. The image shows a network of fibrin fibres, red blood cells and platelets which are trapped into this network



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