Capillaries will measure diffusion and help in more efficient medical treatment

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A method for fast and low cost determination of diffusion coefficients of various analytes, including drugs, is being developed in the Institute of Physical Chemistry of the Polish Academy of Sciences in Warsaw. Anna Lewandrowska, a doctoral student at the IPC PAS, prepares the analyte for injection into the capillary. Aldona Majcher, also a doctoral student at the IPC PAS, keeps a coiled capillary Credit: IPC PAS, Grzegorz Krzyżewski

How strongly do two dissolved analytes react with each other? Such information is of paramount importance not only in chemistry and molecular biology, but also in medicine or pharmacy, where it is used, i.a., to determine optimal drug doses. A method developed in the Institute of Physical Chemistry of the Polish Academy of Sciences in Warsaw will allow for determining diffusion coefficients of analytes in fluids and equilibrium constants of reactions – quickly, at low cost, and most importantly: universally.

In many medical therapies, a prerequisite for efficient treatment is to maintain appropriate drug concentration in patient's blood. Soon, the selection of optimal doses can be assisted by simple measurement devices that make use of a method for measuring equilibrium constants of analytes in fluids developed in the Institute of Physical Chemistry of the Polish Academy of Sciences (IPC PAS) in Warsaw. Only a few millilitres of blood would allow, while you wait, for precise matching of a drug dose with specific patient's body features.

The research on diffusion has been for years carried out at the IPC PAS. The research is based on the phenomena occurring during flow of a liquid, similar to those observed in rivers. In a river bed water flows faster in the bed's central part than at the banks, and when vortices appear in the current, water masses are mixed more effectively. A similar physics helped researchers from the IPC PAS in development of a simple method for determining diffusion coefficients.

The crucial component of the apparatus used in the IPC PAS is a very long (30 m) and very thin polymer tube – a capillary. Inside the capillary there flows a carrier liquid: water at room temperature and pH value corresponding to that of human blood. The capillary is tightly coiled, and the flowing water moves at high velocity. The combination of the two factors makes the flow in the capillary not fully homogeneous, and results in generation of little vortices.

When a small amount of an analyte is injected into a stream of a carrier liquid flowing in the capillary, it spreads out quickly into a long streak. The researchers from the IPC PAS looked at the analyte concentration in the carrier liquid at the outlet from the capillary. In line with the expectations, the highest concentration was in the centre of the capillary, while the lowest one was found at the walls. The plot of the distribution of the analyte concentration along the capillary diameter was bell-shaped, and so it had the shape of the famous Gauss curve.

"In spite of a high flow rate and the presence of vortices, we were able to relate the variations in the distribution of the analyte concentration in the cross-section at the end of the capillary – i.e., simply speaking, the width of the Gauss bell – with the flow rate, the viscosity of the carrier liquid, the capillary curvature, and the diffusion coefficient of the analyte. The first three factors are known, which means that in practice it's enough to measure the width of the 'bell' in order to determine the diffusion coefficient", explains Anna Lewandrowska, a doctoral student at the IPC PAS.

"Interestingly, the results of our measurements were inconsistent with current theoretical models, constructed on the basis of approximated solutions of the famous Navier-Stokes equations", comments Prof. Robert Holyst (IPC PAS). "These equations, let us remind, describe the movement of fluids, and at present their solutions are known for the simplest flows only. So, we had to determine experimentally our own formula describing our measurement system and the phenomena occurring therein".

In earlier versions of the apparatus the measurements were carried out at low flow rates, only 0.05 millilitre per minute. The analysis of a single analyte required 40 minutes, yielding for some macromolecules results with errors reaching up to 30%. Now the flow speed is twenty times higher. The time needed to determine the diffusion coefficient was

reduced down to three minutes, and the accuracy of measurements increased more than five times.

The shortening of analysis time is important from the medical practitioner's point of view. The determination of a drug dose optimal for a specific patient requires not one, but three measurements. "First, we have to introduce drug molecules into the capillary and to determine the rate of their diffusion. Then we measure the diffusion of protein, with which the drug is to bind, for instance, albumin. In the third measurement we inject both the drug and the protein, with which the drug interacts, into the capillary filled with the same protein. Only the comparison of the results allows to find how efficiently the drug will bind to the protein in patient's blood", explains Aldona Majcher, a doctoral student at the IPC PAS.

The patent-pending method for determining of the diffusion coefficient in fluids is fast, versatile, and simple. It does not require any expensive and complicated measurement equipment, and so it has a chance to get popularised and end up in many hospitals and health centres, as well as chemical and biological laboratories. The experiments in the IPC PAS have shown that the method has proven in measurements with salts, amino acids, peptides, proteins und drugs.

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