V. A. Noskin. *Laser correlation spectroscopy of quasielastic scattering.* The study of the correlation characteristics of the intensity of recorded radiation is called laser correlation spectroscopy.[1] Unlike traditional spectroscopy, where the intensity of the radiation spectrum is measured, in correlation spectroscopy the spectrum of the intensity, i.e., ultimately the spectrum of the signal of the photodetecting apparatus, is determined. This interchange of the squaring and spectrum-analyzing elements is accompanied by a practically unlimited increase in resolution owing to the transfer of spectral analysis into the radio-frequency band. This enables the use of correlation spectroscopy as ultrahigh resolution Rayleigh spectroscopy with extensive applications in molecular biology, polymer physics, biophysics, and medicine.

There are several specific realizations of correlation spectroscopy. One realization is the direct determination of the spectrum of fluctuations of the intensity of the scattered radiation—the so-called homodyning method. (In the case that the radiation obeys Gaussian statistics the homodyne spectrum is the result of self-beating of harmonics of the standard radiation spectrum.) Another realization is the method of heterodyning, where the spectrum of beats of the harmonics of scattered radiation with a reference monochromatic wave (usually part of the probing radiation) is measured, making it possible to determine the part of the spectrum that is symmetric relative to the frequency of the reference wave. Other realizations include some variants of non-Gaussian correlation spectroscopy,[2] which make it possible to determine other characteristics of the radiation which are not contained at all in the standard spectrum of the radiation.

The applications of correlation spectroscopy involve primarily the use of this technique for determining coefficients of diffusion and rates of directed displacements of scatterers. As is well known,[1] the spectrum of light scattered quasielastically by a solution of small monodispersed particles is described by a Lorentz curve:

$$I(\omega) = \frac{A\Gamma}{(\omega - \mathbf{qV})^2 + \Gamma^2}, \qquad (1)$$

where $\Gamma = Dq^2$ is the diffusion broading (D is the coefficient of diffusion, $q \equiv |\mathbf{q}| = (4\pi n/\lambda) \sin(\theta/2)$ is the wave vector, and θ is the scattering angle) and $\mathbf{qV}$ is the Dopler shfit ($\mathbf{V}$ is the velocity of the directed motion of the scatterers).

Thus by determining the half-width and shift of the spectral line it is possible to determine the velocity and coefficient of diffusion (and hence the size) of the scatterers. The typical values of the Doppler shifts and diffusion broadening for macromolecules in solution lie in the range 1–10^6 Hz and, as is obvious, the required resolution at the level 10^8–10^{14} lies outside the capabilities of classical interferometric spectroscopy.

Laser correlation spectroscopy owes its great reputation to the nonperturbative character of the measurements, the quickness of the method (5–30 min), and the accuracy (1%) with which the sizes of macromolecules are determined. In many applications, however, the polydispersity of the systems studied significantly complicates the situation. In this case

$$I(\omega) = \int \frac{A(\Gamma)\,\Gamma}{\omega^2 + \Gamma^2}\, d\Gamma, \qquad (2)$$

where $A(\Gamma)$ is a function which can be easily expressed in terms of the particle-size distribution function. Unfortunately, the reconstruction of the function $A(\Gamma)$ from the spectrum $I(\omega)$, i.e., the solution of the integral equation (2), is a mathematically improperly posed problem: small pertu-

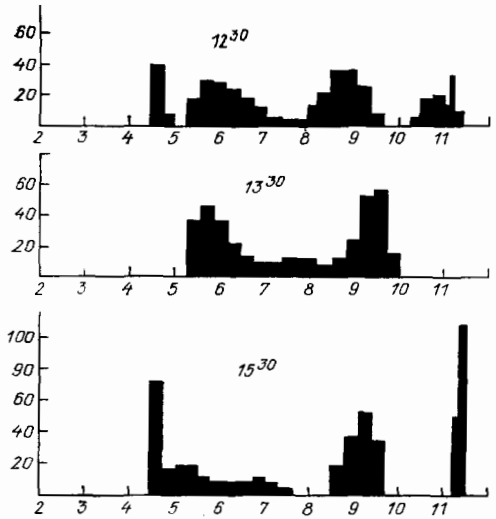

FIG. 1. The sizes of macromolecules in samples of synthetic rubber at different stages of polymerization.

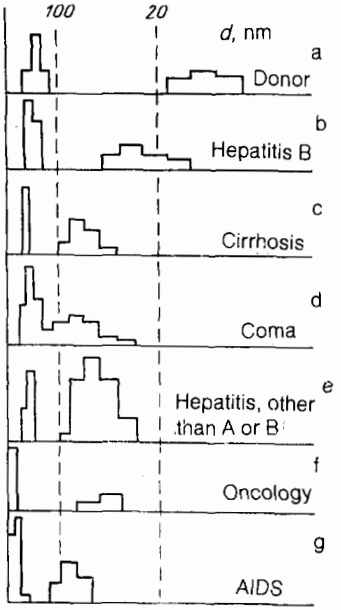

FIG. 2. Typical size distributions of the scattering power of particles in the blood serum of healthy people (b) and people sick with different diseases (b–g).

bations of $I(\omega)$ produce large changes in the solution $A(\Gamma)$. Until recently this difficulty was circumvented by seeking not $A(\Gamma)$ itself, but rather its stable characteristics—the parameters of trial functions best approximating $A(\Gamma)$ or the moments of the distribution $A(\Gamma)$ (the so-called method of cumulants[3]). These approaches, however, do not yield information about the specific form of $A(\Gamma)$, which is often extremely important.

The situation changed radically when it was realized that the method of regularization[4] could be used to find a smooth quasisolution of Eq. (2). The adoption of such methods for mathematical analysis of the results substantially expanded primarily the applied possibilities of correlation spectroscopy. Here only two quite dramatic examples will be given.

Figure 1 shows the molecular-mass distributions in commercial samples of synthetic rubber at different stages of polymerization, measured with the help of laser correlation spectroscopy. The significance of the fast determination of a basic parameter, such as the size of a macromolecule, for controlling the polymerization process and for quality control requires no comment.

Figure 2 shows the particle-size distribution for the blood serum of sick and healthy people. In healthy people there are no particles with sizes from 20 to 100 nm. Viral diseases or being a carrier and some other pathologies lead to the appearance of particles in this size range in blood serum. This method is extremely promising for massive scanning in order to identify high-risk groups.

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