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A FIBER OPTIC PROBE FOR THE DETECTION OF CATARACTS

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Rafat R. Ansari
NASA Lewis Research Center/CWRU, Mail Stop 105-1,
21000 Brookpark Road, Cleveland, Ohio 44135

Harbans S. Dhadwal
Department of Electrical Engineering
State University of New York at Stony Brook
Stony Brook, New York 11794

ABSTRACT

A compact fiber optic probe developed for on-orbit science experiments has been applied to detect the onset of cataracts, a capability that could eliminate physicians' guesswork and result in new drugs to "dissolve" or slow down the cataract formation before surgery is necessary. The probe is based upon dynamic light scattering (DLS) principles. It has no moving parts, no apertures, and requires no optical alignment. It is flexible and easy to use. Results are presented for excised but intact human eye lenses. In a clinical setting, the device can be easily incorporated into a slit-lamp apparatus (ophthalmoscope) for complete eye diagnostics. In this set up the integrated fiber optic probe, the size of a pencil, delivers a low power cone of laser light into the eye of a patient and guides the light which is back scattered by the protein molecules of the lens through a receiving optical fiber to a photo detector. The non-invasive DLS measurements provide rapid determination of protein crystalline size and its size distribution in the eye lens.

INTRODUCTION

A normal eye lens is a jelly-bean-size transparent tissue. A cataract is formed when this lens becomes cloudy. This cloudiness or opacification hinders light transmission through the lens and the ability to focus a sharp image on the retina at the back of the eye. The common symptoms experienced with cataracts include blurred or double vision, sensitivity to light and glare, less vivid perception of color, and frequent eyeglass prescription changes. If a large portion of the lens becomes cloudy, sight can be partially or completely lost until the cataract is removed[1]. At present there is no medical treatment which will prevent cataracts or reverse them once they develop. The only treatment is the surgical removal of the clouded lens and its replacement with an intraocular lens implant. Today, an estimated 1.4 million cataract surgeries are performed each year in the United States. In normal patients, cataracts develop gradually over a period of many years. A cataract is caused by a change in the chemical composition of the lens. These changes can be attributed to aging (senile cataract), eye injuries (traumatic cataract), certain diseases and conditions of the eye and body (secondary cataract) e.g. high blood-sugar levels in diabetic patients, and hereditary or birth defects (congenital cataract). The senile (age-related) cataracts are the most common type of cataracts. They can occur as early as age 40.

An adult eye lens is primarily comprised of about 65 wt.% water and 35 wt.% proteins, the highest of any tissue in the body. The protein molecules or crystallines in the lens are subdivided into α, β, and γ crystallines. The α, β, and γ crystallines have a molecular weight of ~10^6 daltons, ~10^5 daltons, and ~2×10^4 daltons respectively. Since α crystallines are the largest molecules, they are the strong scatterers of light in a light scattering experiment. When these protein molecules are agglomerated, they give rise to lens opacities. This has been confirmed by a variety of complementary techniques ranging from biochemical[2], light scattering[3-5], QELS[6-11] and electron microscopy[12]. Current clinical apparatus, which include visual inspection through a slit lamp microscope, and analysis of a photographic plate, lack the sensitivity and accuracy to detect small cellular and biochemical changes[13]. Biochemical studies of lens extract have demonstrated that aging in the normal mammalian lens is accompanied by conversion of the α-crystalline into higher molecular weight species[14-16]. In earlier stages of cataract formation the patients' cataracts are difficult for a physician to diagnose because of the lack of non-invasive experimental techniques. In general, progressively deteriorating vision conditions and in particular frustrating night vision conditions are unfortunately the only indications of a semi-developed cataract. This poses serious emotional situations for some patients and

forces guesswork on the physician's part for making well informed decisions concerning performance of surgical procedures.

In this paper we report the application of a fiber optic probe for the early detection of cataracts in excised, but intact human eye lenses, and its incorporation in a clinical set up. Earlier investigations have been reported in our recent publications[17,18]. We believe these new technological advances will be useful in the investigation of cataracts during their early stages of formation. This could result in eliminating a physician's guess-work, reducing a patient's emotional trauma level, and this may allow pharmaceutical companies or dietitians to formulate new drugs or food supplies to "dissolve" the cataract, hence reducing the risks of costly and unwanted surgical procedures. Looking ahead to the year 2000, it is anticipated that the evolution of new drugs will slow the development of lens opacities that are leading cause of blindness worldwide[19].

Dynamic Light Scattering (DLS)

DLS is an established laboratory technique which provides non-invasive measurements of particle size and size distributions, molecular weight, and particle-particle interactions for particles suspended in dilute solutions. The range of application ranges from 3 nm to 3 μm. Several books are available on this subject[20] (see reference 20 and the references contained therein). The data analysis techniques in DLS are reported in a review article[21]. Several other names are frequently used for DLS. These are Quasi-Elastic Light Scattering (QELS), Photon Correlation Spectroscopy (PCS), and Intensity Fluctuation Spectroscopy (IFS). In these experiments the laser light is focussed into a small spot inside the sample. The scattering volume, defined by the intersection of the incident and detection geometries, normally contains submicron particles suspended in a fluid medium. The intensity of the scattered light fluctuates due to the thermal movement (Brownian motion) of the particles. The intensity fluctuations in the scattered light are detected by a photodetector. This detected signal is processed via a digital correlator to yield a autocorrelation function. For dilute dispersions of spherical particles the slope of the autocorrelation function provides a quick and accurate determination of the particle's translation diffusion coefficient, which can be related to its size via a Stokes-Einstein equation, provided the viscosity of the suspending fluid, its temperature, and its refractive index are known. For concentrated suspensions and for dispersions containing more than one scattering species in the suspending medium, however, the data analysis and interpretation of the autocorrelation function becomes more difficult. We have discussed some of these data analysis techniques in our prior publications[17,18,22,23]. The in vivo uses of conventional DLS technique as applied to the anterior segment of the eye have been reviewed elsewhere[11].

Until recently conventional DLS instruments have relied on bulky laser sources, bulk optics, and high voltage detection devices e.g. photomultiplier tubes (PMT). The incorporation of new advances in solid state technology, and the development of compact DLS spectrometers (fiber optic probes), have paved the way for a next generation laser light scattering instrument (LLSI). More recently, a compact, rugged, and modular LLSI has been conceived for microgravity experiments on board the space shuttle orbiter and possibly space station Freedom to study a range of phenomena[24]. These phenomena include, among others, nucleation in crystal growth, aggregation, polymer induced flocculation, gelation, critical phenomena, and spinodal decomposition.

The most promising clinical technique that has become available is based on quasielastic light scattering (QELS). Early work establishing the utility of QELS for detection of molecular changes in the lens were demonstrated by Tanaka and Benedek[25]. A recent clinical QELS study[26] of diabetic and non-diabetic patients has attempted to correlate the QELS results with visual inspection. Early researchers were concerned with solving the mystery concerning the transparency of a normal adult lens, given the high concentration of proteins in an aqueous solution[27-30]. A reliable, quantitative technique, causing the least trauma to the patient, has been a long sought goal for the study of cataractogenesis and other ocular disorders. Although the technique of QELS or DLS was first applied to study cataractogenesis by Tanaka and Benedek many years ago[25], its commercial scope has remained limited because of elaborate instrumentation, bulk optics and associated optical alignment problems, statistical errors in data analysis,

multiple scattering problems associated with mild and severe cataracts, and the polydisperse nature of the cataract itself.

EXPERIMENTAL PROCEDURE

Fiber optic probe

Our fiber optic probe employs two monomode optical fibers. The fibers have a core radius of about 4 μm. One fiber is used to transmit a Gaussian laser beam to the scattering volume. The second fiber positioned at a backscatter angle of 155° acts as a scattered light receiver. In concentrated dispersions, we have found that the backscatter regime allows recovery of particle sizes well beyond the cutoff point for the conventional state of the art laser light scattering systems, without requiring any additional corrections for multiple light scattering[28]. This feature is useful in the study of cataractogenesis because cataractous conditions may give rise to multiple scattering effects. Depending upon the severity of the cataract, multiple light scattering effects will introduce high frequency components in the light scattering spectrum. This may cause a loss of resolution and a subsequent broadening of the particle size distribution . The fiber optic probe used in this study alleviates these problems. The detailed design considerations of the fiber optic probe and its range of application to investigate concentrated dispersions have been published elsewhere[28]. Compared to conventional commercial state-of-the-art DLS spectrometers, our probe is 1-2 orders of magnitude smaller in physical size, and is inexpensive to fabricate.

Experimental set up

The DLS system employed in this work is schematically represented in Figure 1. Our integrated probe is comprised of two optical fibers, which are positioned in close proximity to each other and mounted into a single stainless steel ferrule. A monomode optical fiber pigtailed to a semiconductor laser, guides a Guassian laser beam to a point inside the eye lens. The optical fiber is ruggedized by threading it through a teflon tubing and an outer plastic monocoil tubing. A bare portion of this monomode optical fiber is epoxied into a precision machined hole. A second optical fiber, is positioned into another machined hole in close proximity to the transmitting optical fiber, and is used for coherent detection of the light scattered from the eye lens in the backward direction. The receiving optical fiber is threaded through the same teflon sleeve and monocoil tubing up to the point where the transmitting and receiving fibers are separated. The receiving fiber terminates in a connector which is mated directly with a miniature photomultiplier tube.

Clinical Set up

Figure 2 shows a schematic of the clinical apparatus which can be used for measuring the intensity autocorrelation from patients. The integrated probe shown in Figure 1 is mounted on a slit-lamp apparatus: an instrument of choice for the ophthalmologists. The position of the probe can be adjusted using the standard joystick; control lever for horizontal and vertical movement, available on the slit-lamp apparatus. This arrangement provides precise positioning and location of the scattering volume in any substantially transparent region of the anterior segment of the eye. The probe tip is positioned so that a point inside the patients' eye lens is illuminated with an expanding Gaussian laser beam, having a diameter of 4 μm. The second optical fiber collects the scattered light at a fixed scattering angle and is connected to a miniature photomultiplier tube, followed by a compact data acquisition system. The photon pulse train after suitable amplification and discrimination is correlated using a digital correlator in a lap-top computer.

The application of the fiber optic probe for the measurement of cataractogenesis is procedurally similar to techniques familiar to ophthalmologists, most notably applanation tonometry and ultrasonography. The procedure can be easily done at a slit lamp under the installation of topical (drop) anesthesia. The eye movement is negated by having the patient direct vision in the contralateral eye on the fixation light. Findings from other clinical systems[31-34], introducing laser beams into patients' eyes, have concluded that a 20 minute exposure is the upper limit before patient fatigue becomes a limiting factor. Our measurements should take less than 2 minutes per autocorrelation function i.e. one test per patient. The maximal retinal

irradiance is a function of wavelength, incident power, numerical aperture of the cone of laser light and exposure time. In our fiber optic system we expect retinal irradiance to be less than 0.05 mW/mm^2, which is three orders of magnitude below the damage threshold of 2 W/cm^2 for a 10 second exposure[35-38].

RESULTS

Figure 3 summarizes the results of this investigation on excised, but, intact human eye lenses. The five pairs of cadaver human eye lenses employed in this study belonged to 18, 43, 55, 65, and 73 year old patients. The crystalline size increase as a function of patients' age is consistent with the development of senile cataract in the middle age to golden age patients. Upon visual examination, by a professional ophthalmologist (Dr. M.A. Dellavecchia of the Bryn Mawr Eye Clinic in Philadelphia), the lenses of younger patients were found to be transparent while the older lenses seemed to have a yellowish tint in them, consistent with senile cataractous changes. Clinically, these older lenses can be classified as having a mild to moderate cataract. None of the lenses were completely opaque.

CONCLUSION

In this paper we have shown the application of a fiber optic probe to non-invasively detect the onset of cataracts in human eye lenses, and its incorporation into a slit-lamp apparatus for complete eye diagnostics of the anterior chamber of the eye. The probe has a unique design which does not require any lenses, has no moving parts, does not need alignment, and is insensitive to vibrations and RF interference. In a clinical environment this new capability, when used in conjunction with regular eye examination on an yearly basis, will let the physician detect an incipient cataract before it forms.

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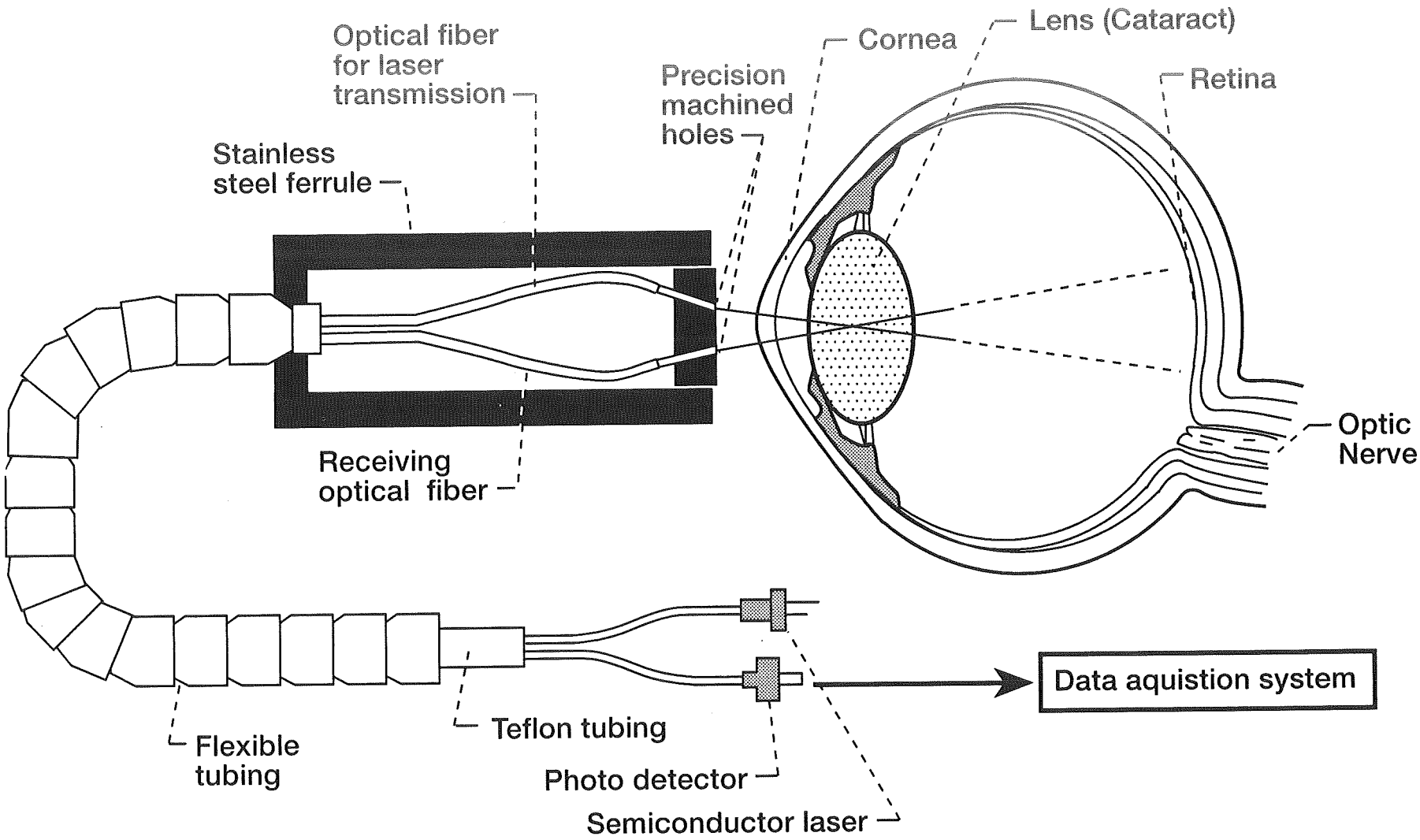

Figure 1: Fiber optic Probe and the Experimental Set up: Schematic of the optical system used for measuring the α crystalline size in an eye lens. The optical design is based upon the dynamic light scattering (DLS) principles.

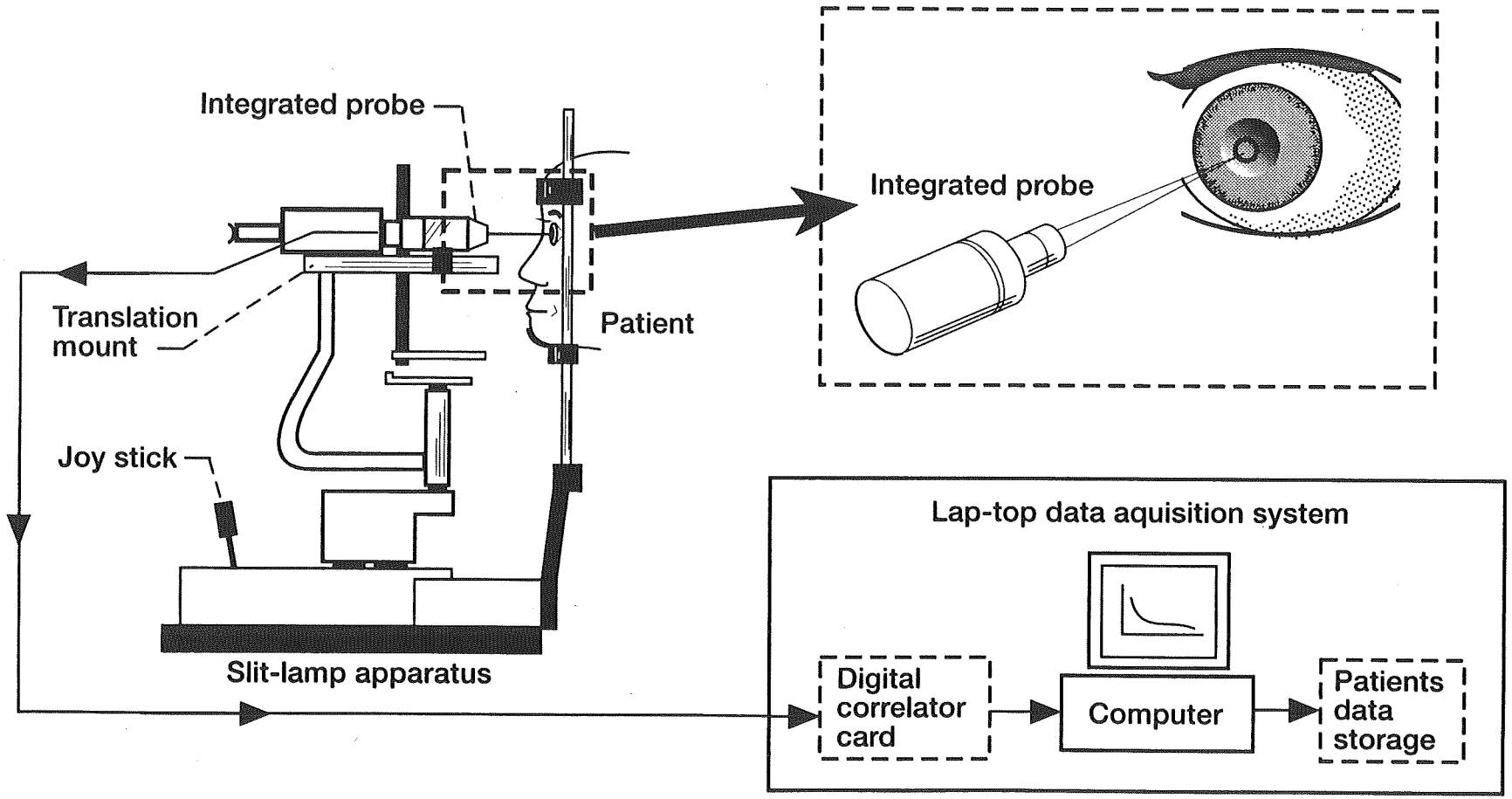

Figure 2: Clinical Set up: The integrated probe is incorporated into a slit-lamp apparatus; commonly used by ophthalmologists for regular eye examinations. The data analysis is performed on a lap-top data computer system, comprising of a digital correlator, a 486 processor, and data storage capability.

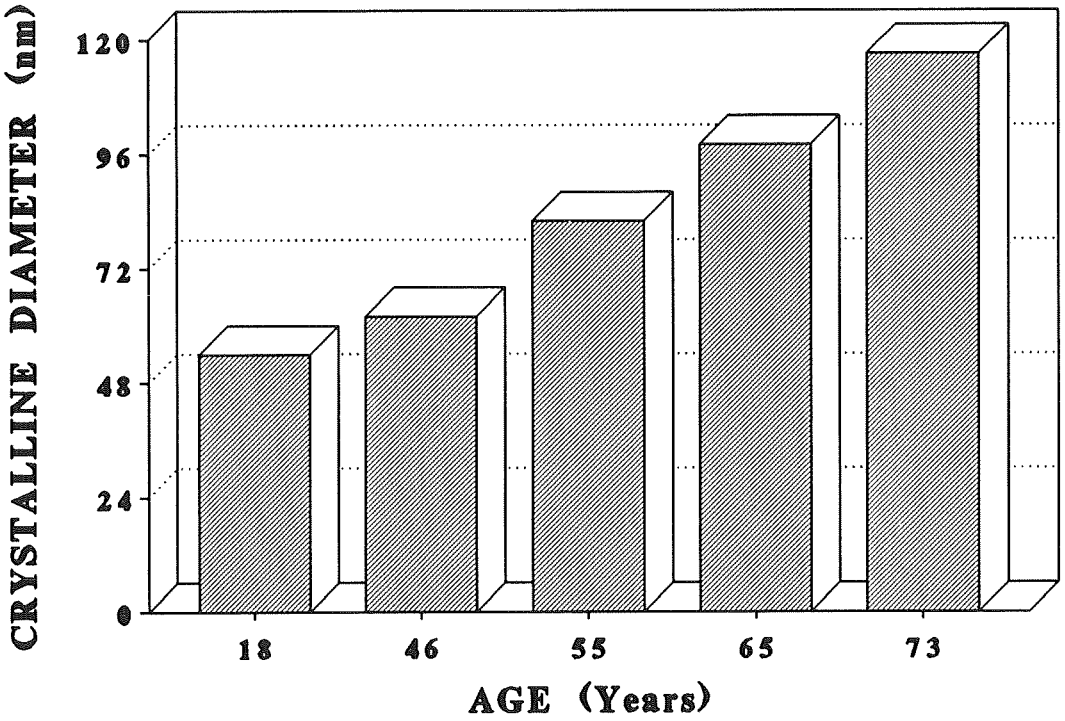

Figure 3: Aging effects (senile cataract) in human eye lenses: The average crystalline sizes are determined using the method of dynamic light scattering. Effective hydrodynamic diameter is computed from Stokes-Einstein relation by using the viscosity of water, and assuming spherical shape for the α crystalline protein molecules in the eye lens.