BIOMEDICAL APPLICATIONS OF PHOTON CORRELATION SPECTROSCOPY IN LASER DOPPLER VELOCIMETRY

By

B. DEVARAJ

THESIS SUBMITTED TO THE
INDIAN INSTITUTE OF TECHNOLOGY, DELHI
FOR THE AWARD OF THE DEGREE OF

DOCTOR OF PHILOSOPHY

Department of Physics
INDIAN INSTITUTE OF TECHNOLOGY, DELHI

JULY, 1988

TO

MY

BELOVED

PARENTS

CERTIFICATE

This is to certify that the thesis entitled "Biomedical Applications of Photon Correlation Spectroscopy in Laser Doppler Velocimetry" being submitted by Mr. B. Devaraj to the Indian Institute of Technology, Delhi for the award of degree of Doctor of Philosophy is a record of bonafide research work carried out by him. He has worked under my guidance and supervision and has fulfilled the requirements for the submission of this thesis.

The results contained in this thesis have not been submitted in part or full to any other University or Institute for the award of any degree or diploma.

S. CHOPRA
Professor, Physics Department
Indian Institute of Technology
Hauz Khas, New Delhi-110016

ABSTRACT

A home-made microprocessor based on a digital photon correlator was used to investigate the applications of laser light scattering to biological motion. The correlator was first tested for its performance on standard systems such as the rotating ground glass, diffusion coefficient of polystyrene, diffusion coefficient and electrophoretic mobility of Bovine Serum Albumin (BSA).

Three types of biological motion, viz., the diffusive motion, the self propelled motion and the motion in an electric field, were studied to demonstrate the Biomedical Applications of Photon Correlation Spectroscopy in Laser Doppler Velocimetry and to demonstrate the versatility of the correlator.

The heat aggregation phenomenon of zinc-insulin as a function of pH was studied for its diffusive motion. It is demonstrated that with increase in temperature the insulin aggregates into larger molecules at all pH, the rate of aggregation being highest at the neutral pH as evident by the R_h (hydrodynamic radius) values which were calculated from the diffusion coefficient obtained from correlation spectroscopy measurements and by substituting these values into the Stokes-Einstein relation. It was also demonstrated

that on reversal of temperature, the "hysteresis effect" was observed.

The effect of time, dilution and certain cations such as K^+ and Ca^{++}, on the velocity distribution of human spermatozoa was investigated for the study of self-propelled motion, wherein it was demonstrated that an increase in the average velocity on dilution is more due to a reduction in the viscosity of the medium. However, not much change was observed in sperm velocity, until a period of 5 hrs after which it drops rapidly to almost half of its value at 8 hrs after ejaculation.

Using Doppler-difference optical arrangement in the Electrophoretic Light Scattering Technique, investigations were carried out to electrokinetically differentiate normal human lymphocytes from leukemic ones and normal rabbit erythrocytes from fluoresced ones. The electrophoretic mobilities of leukemic lymphocytes were found to be 15-30% lower than those of the normal lymphocytes. In the case of the rabbit erythrocytes the fluoresced ones were found to have higher values of the electrophoretic mobility than the normal ones.

ACKNOWLEDGEMENTS

At the outset I wish to express my sincere thanks to Prof. S. Chopra for introducing me to this exciting area of research. His enthusiasm and interest in its Bio-Medical Applications was a constant driving force throughout this endeavour. But for his positive attitude towards the multi-disciplinary research and patience in grooming a novice from an altogether different field, I would have long been buried under the frustrations of a biologist in an alien area of physicists.

Being located in a Physics Department and carrying out research in an area of bio-medical interest has its own problems, which were considerably eased by Mr. Manoj Raje and Dr.S.K.Jain of AIIMS, New Delhi. I am grateful to them for their readiness to help me with the sample-preparation and for their unflinching support through various stages of this work.

I wish to record my sincere appreciation to all the members of the Quantum Electronic Fraternity, especially Dr. H.B. Bohidar, Dr. V.A. Harwalkar, Dr. V.R. Subrahmanyam, Mr. Brahm Pal Singh and the efforts of my friends Kashinath Bhoumik, Sudeep, Venkat, Prabhu, Mintu, Satish and Raghu, who kept my spirits soaring high all time through discussions on both professional and personal front.

I thank the Council of Scientific and Industrial Reseach (CSIR) for providing me with the financial support and Mr. Gajanan Hegde for his painstaking efforts in the preparation of this manuscript.

B. DEVRAJ

CONTENTS