# THE BULLETIN

Mount Desert Island Biological Laboratory Centennial Edition

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Volume 38 1999

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Printed on Recycled Paper

Published by the MDI Biological Laboratory May 1999 \$10.00

# THE BULLETIN

VOLUME 38, 1999

Mount Desert Island Biological Laboratory Salisbury Cove, Maine 04672

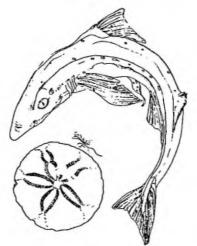


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### THE MOUNT DESERT ISLAND BIOLOGICAL LABORATORY

#### RESEARCH AND EDUCATION IN THE BIOLOGY OF MARINE ANIMALS

#### INTRODUCTION

The Mount Desert Island Biological Laboratory (*MDIBL*) is an independent non-profit biological station located on the north shore of Mount Desert Island, overlooking the gulf of Maine about 120 miles northeast of the Portland near the mouth of the Bay of Fundy. The island, well known for Acadia National Park, provides a variety of habitats including shallow and deep saltwater, a broad intertidal zone, saltwater and freshwater marshes, freshwater lakes and streams, forests and meadows.

The Laboratory is the largest cold water research facility in the Eastern United States, and its unique site provides an outstanding environment for studying the physiology of marine and freshwater flora and fauna. During 1998, the scientific personnel included 58 principal investigators and 98 associates, representing 39 institutions in 21 states and 4 European countries.

#### HISTORY AND ORGANIZATION

*MDIBL* was founded in 1898 at South Harpswell, Maine by J.S. Kingsley of Tufts University. Its present site at Salisbury Cove was donated by the Wild Gardens of Acadia, and relocation was

eted in 1921. The Wild Gardens of Acadia, a land-holding group headed by George B. Dorr and hn D. Rockefeller, Jr., who was instrumental in the founding of Acadia National Park.

In 1914, the Laboratory was incorporated under the laws of the State of Maine as a non-profit scientific and educational institution. Founded as a teaching laboratory, *MDIBL* is now a center for marine research and education that attracts investigators and students from across the U.S. and around the world. Since the pioneering work of H.W. Smith, E.K. Marshall and Roy P. Forster on various aspects of renal and osmoregulatory physiology of local fauna, the Laboratory has become known worldwide as a center for investigations in electrolyte and transport physiology, developmental biology, electrophysiology and marine molecular biology.

The Mount Desert Island Biological Laboratory is owned and operated by the Board of Trustees and Members of the Corporation; at present, there are 430 members. Officers of the Corporation -Chair, Vice-Chair, Director, Secretary, Treasurer, Clerk - and an Executive Committee are elected from among the Trustees. The Chair and Executive Committee oversee and promote long range goals of the Laboratory. The Director, with the aid of a full-time Administrative Director, staff and a Scientific Advisory Committee is responsible for implementing the scientific, educational and public service activities of the Laboratory.

#### NIEHS TOXICOLOGY CENTER

In 1985, with the support of the National Institute of Environmental Health Sciences (NIEHS), *MDIBL* established a center dedicated to the study of the toxic effects of heavy metals and other environmental pollutants that pose an increasing health risk to humans and a threat to the marine environment. The focus of The Center for Membrane Toxicity Studies (CMTS) is the use of marine animals like the shark, the founder and the skate to define sites of action of metals such as mercury and cadmium that enter the environment due to improper disposal of industrial waste and as a component of some pesticides. The effects of these pollutants are wide-spread in the human body, with affected organs including the brain, the kidney, the liver, the gastrointestinal tract and the reproductive system. The goal of the CMTS is to identify the molecular targets of toxic substances and to provide the scientific basis for the development of treatments for heavy-metal intoxication. Inquiries concerning the center are welcome.

#### **APPLICATIONS AND FELLOWSHIPS**

Research space is available for the entire summer season (June 1 - September 30) or a half-season (June 1 - July 31 or August 1 - September 30). Applications for the coming summer must be submitted by February 1st each year. Investigators are invited to use the year-round facilities at other times of the year, but such plans should include prior consultation with the *MDIBL* office concerning available facilities and specimen supply.

A number of fellowships and scholarships are available to research scientists, undergraduate faculty and students, and high school students. These funds may be used to cover the cost of laboratory rent, housing and supplies. Stipends are granted with many of the student awards. Applicants for fellowships for the coming summer research period are generally due in January.

For further information on applications and fellowships/scholarships, please contact:

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#### ACKNOWLEDGEMENTS

The Mount Desert Island Biological Laboratory is indebted to the National Science Foundation and National Institutes of Health for substantial support. Funds for building renovations and new construction continue to permit the Laboratory to expand and upgrade its research and teaching facilities. Individual research projects served by the Laboratory are funded by private and government agencies, and all of these projects have benefited from the NSF and NIH grants to the Laboratory. For supporting our educational initiative, *MDIBL* acknowledges the Cserr/Grass Foundation, Milbury Fellowship Fund, American Heart Association – ME, NH, VT Affiliate, Blum/Halsey Fellowship, Bodil Schmidt-Nielsen Fellowship Fund, Maine Community Foundation, NSF - Research Experience for Undergraduates and Hearst/Hancock County Young Scholar Program for High School students and many local businesses and individuals.



#### Roy P. Forster (1911 - 1998)

Roy Forster died on November 3, 1998 at the age of 87. With his passing, MDIBL lost one of its most admired leaders and loyal friends. His love for the Laboratory and his dedication to its welfare will long be remembered.

Roy was born on September 28, 1911 in Milwaukee, WI. He did his undergraduate work at Marquette University where he majored in chemistry and zoology. He attended graduate school at the University of Wisconsin where he received his Ph.D. in zoophysiology and physiological chemistry in 1938. A resident of Hanover, New Hampshire, Roy was Emeritus Professor of Biology at Dartmouth College and Emeritus Professor of Physiology at Dartmouth Medical School.

Roy came to MDIBL in the late 30's and worked there almost continuously (with the exception of a couple of years when the lab as closed during WWII) until his retirement from the Lab in 1983. He served as Director from 1940 to 1947 and President from 1964 to 1970. It was during his term as Director that Roy provided a crucial service for which the Lab will always be indebted. During the WWII years the physical plant of the Lab fell into a state of disrepair. It was questionable whether there was the will or the money to restore the place. Roy took it upon himself to procure financial aid from some of the wealthier summer residents on and around Mount Desert Island. He managed to raise sufficient funds (several thousand dollars) to rebuild the dock and get the Lab up and running. The Lab probably would not have survived, at least with its present mission, were it not for Roy.

Professionally, Roy excelled as a scientist, scholar, teacher and mentor. His most notable scientific contribution remains a landmark in the field of renal physiology. This involved the development of the isolated, teased fish renal tubule. With this technique a whole new way of studying the physiology of the renal tubule in a controlled, in vitro environment arose. Roy and his colleagues used the technique to show that the transport of organic acids by the renal tubule was linked to metabolic energy, most likely in the form of ATP which had recently been shown by Fritz Lipmann to be the universal energy source for working cells. Roy's teased tubule research laid the foundation upon which renal physiologists later built the isolated perfused renal preparation, a method which was, and still is used to solve some the most significant problems in renal physiology.

Roy's talents as a scientist were well recognized. He was awarded the prestigious Guggenheim Fellowship twice. The first was in 1948 at Cambridge University, England. The second, in 1955-56, gave Roy the opportunity work at Stazione Zoologica in Naples, Italy. Roy also served as Program Director for Regulatory Biology at the National Science Foundation in 1959-60. At MDIBL, Roy's talents as a leader were recognized by his election as Director and then President. Informally, Roy served for many years after he left office as the senior statesman of MDIBL who was often consulted in planning its future directions. Roy's talents as a leader and mentor were remarkable. Known affectionately as "Renal Roy", he gave unselfishly both his time and attention to all who worked with him, from undergraduates to postdocs. In return, Roy's disciples were a very devoted group, often forming lifelong friendships.

Personally, Roy was always charming, witty and warm. His original brand of humor penetrated both normal conversation and formal lectures. It was a pleasure and a privilege to listen to him.

Roy's contributions to MDIBL will be long remembered, not just for the scientific and leadership contributions that he made but also for the wonderful spirit that he instilled into Laboratory life. That spirit was never more evident than when Roy held his Presidential High Teas toward the end of each summer. The "Tea" was a delicious goose fish chowder which Roy prepared himself and served to the entire Laboratory. These were happy occasions that those of us who were lucky enough to experience will never forget, along with many other cherished memories.

--Leon Goldstein

#### Remembering Carl W. Gottschalk

On October 15, 1997, Carl Gottschalk died unexpectedly in Chapel Hill, his academic home for so many decades. With his death the international community of nephrologists lost an outstanding renal physiologist who pioneered the technique of micropuncture for the study of kidney function and made significant contributions to the understanding of the countercurrent system. He was also respected and revered for his knowledge of and interest in the history of nephrology.

The MDIBL which benefited from both, his scientific expertise and his love for renal history, lost a good friend and supporter. In 1958 Carl Gottschalk was invited by Homer W. Smith to come to the MDIBL with his research associate, Margaret Mylle. Smith wanted to exploit their experience in micro-



puncture of the proximal and distal convoluted tubule and their expertise in localizing the puncture sites by microdissection. Several years before a young woman, Willie W. Smith, a graduate student of Homer W. Smith, had made the discovery that in dogfish urine acidity is fixed at a pH of 5.7 even after intravenous administration of sodium bicarbonate (Smith, W. W.: The excretion of phosphate in the dogfish, Squalus acanthias. J. Cell & Comp. Physiol. 14: 95, 1939). Homer W. Smith was interested to determine the site of the nephron where the acidification took place. So, Carl Gottschalk and Margaret Mylle undertook the formidable task to micropuncture the kidney of the dogfish. In his typical manner Carl Gottschalk described his experiments in the following way:

"The ventral surface of the kidneys of unanesthetized dogfish (Squalus acanthias) was visualized microscopically and micropuncture of individual tubules performed. An aqueous solution of phenol red was injected with a micropipette into renal tubules to determine the site of the acidification of the urine. Multiple injection in various types of tubules were performed and in all instances, save one, the dye turned yellow indicating an acid reaction. It was not possible to subsequently macerate the kidney and isolate the injected tubule in order to definitely localize the site of puncture. Nevertheless, the majority of the punctures can be assumed to have been in the proximal tubule, for this is readily identified in vivo by its larger diameter" (published in Research Reports of the MDIBL Bulletin, pp. 70-71, 1958).

Carl Gottschalk returned to the lab the next summer. In the following years he choose to come back to the island with his family for vacation rather than for scientific research due to the - at that time – almost insurmountable difficulties to ship the delicate equipment from Chapel Hill to Salisbury Cove

In August of 1992 the MDIBL and the Boylan family honored Carl Gottschalk with the first Annual John W. Boylan Memorial Lectureship. John W. Boylan and Carl Gottschalk had been good friends from the time they met in Maine. In his lecture he presented his personal view of the contribution of micropuncture to the knowledge of kidney function.

In 1995 he was invited to organize a display "Homer W. Smith at work at the MDIBL" on the occasion of a symposium commemorating the 100th anniversary of Homer W. Smith's birth. At this display Carl Gott-schalk shared with us his excellent collection of Smith's scientific and philosophical books thereby complementing the tribute to Homer W. Smith's personality.

At the Smith symposium he met Susan K. Fellner; they were married the following year. Today, Susan Fellner is carrying on Carl Gottschalk's legacy in Chapel Hill as well as at the MDIBL.

#### Eva and Rolf Kinne

October 1998, Max Planck Institute for Molecular Physiology, Dortmund, Germany and MDIBL, Salisbury Cove, Maine, USA In this undertaking many have helped to get the facts right. Our special thanks go to Susan Fellner and Tom Maren.

#### CENTENNIAL 1998: THE MOUNT DESERT ISLAND BIOLOGICAL LABORATORY 1898-1998

#### A report by the Chairman of the Centennial Committee and Vice Chair of the Board, Rolf K.H. Kinne

The year of 1998 marked the one hundredth anniversary of the founding of the Mount Desert Island Biological Laboratory, an occasion to reflect on the past, to celebrate the present, and to contemplate the future of the Laboratory. In the following, a report on the events of the Centennial celebration is provided - as a memory for those who participated and as a record for those who were not able to be there to share the joy, enthusiasm and dedication with their fellow members.

The activities began with the traditional Fourth of July Picnic at the seashore with the spectacular view of Frenchman Bay and a delicious clambake. Later in July, were the Annual Meeting of the Corporation, the Annual Meeting of the Board of Trustees, and the Centennial Director's Party. These recognized the members of the Corporation, the Officers and the Trustees, who through their generosity in giving time, expertise, and financial support to the MDIBL have maintained this Laboratory as a vivid and successful place of excellence in research and education for a century.

The official opening of the Centennial took place on July 22nd when about 150 people gathered in front of the renovated and restored Dahlgren Hall and the new Maren Auditorium linked together by a shining and graceful connecting building. In the shade of old trees, the Blue Hill Brass Quintet entertained a cheerful crowd before the Director of the Laboratory, David C. Dawson, opened the Ceremonies. Centennial welcome addresses ensued. First spoke Dana Reed, the Town Manager of Bar Harbor, the city that has housed the Laboratory since 1921 and has provided "the fertile soil" for its operation and growth. Then the leaders of the two academic sister institutions, Kenneth Paigen, Director of the Jackson Laboratory, and Steven Katona, President of the College of the Atlantic, extended their best wishes to the Laboratory and highlighted the crucial role of further scientific and intellectual exchange on Mount Desert Island. Finally, Paul Haertel,

endent of the Acadia National Park, recalled the pivotal role the Friends of Acadia, the park's initiators, had played in bringing scientists to the beautiful shores of Frenchman Bay.

In looking into the future James Boyer, Chair of the Board of Trustees of the MDIBL, emphasized the important steps the Laboratory has taken to ensure its future prosperity and success. These steps include the generation of a significant endowment, the finalizing of plans and the procuring of financial resources for construction of a year-round sea water system and a new student dormitory, and, in particular, the completion of a new auditorium which can house scientific and cultural events in every season. In a moving ceremony, Tom Maren, accompanied by his wife Emily and his sons cut the blue ribbon and officially opened the auditorium.

Then a lecture entitled "A Century of Explorations" followed in which the Vice Chair of the Board, Rolf K.H. Kinne, summarized the various phases of scientific explorations at the MDIBL, highlighting them with appropriate examples of paintings and drawings exhibited at Museums of Fine Arts around the world. A summary of the lecture is included in *The Bulletin*.

The celebration extended late into the evening, the sound of the Blue Hill Brass Quintet providing the proper background for a social gathering in the new facilities.

The scientific highlight of the Centennial was the symposium "Gifts from the Sea: Contributions of MDIBL to Basic Science, Biotechnology, and Human Health" organized by David C. Dawson and David H. Evans. The program of presentations is published in this volume of *The Bulletin*. During the congress the seventeenth William B. Kinter Memorial Lecture was presented by Kenneth Olden, Ph.D., Director of NIEHS, who emphasized the importance of "environmental genomics" to scientists and laypeople alike.

In the month of August, the MDIBL exhibited further aspects of its broad spectrum of activities. On August 1, the Pot and Kettle Club housed the Centennial Benefit Banquet, where friends and members of the Laboratory met to enjoy a dinner which reflected the history of the MDIBL by including "Carrot Delight a la Harpswell", Roasted Salmon with Honey Pecan Glaze "New Horizons", and a "Salsbury Cove Blueberry Tart." The guests also listened to introductory remarks of the newly elected Director, John N. Forrest, and to a talk presented by Edward J. Benz, Jr. on the topic "Genomes: What are they and why study them?" With the presentation of commemorative plaques to past presidents and directors of the Laboratory, all present were reminded of fond memories of times past.

The restored Dahlgren Hall experienced its first serious structural test on August, when the Centennial Square Dance drew a cheerful crowd that enjoyed dancing on the new, leveled, and polished floor.

On August 15 we celebrated with the friends of Leonard Silk, commemorating a cherished and respected Trustee of the MDIBL. The occasion was an Open House at the Causeway Club with tennis and lemonade. This was also the evening for which the many fans of an "old car reborn", the new Volkswagon Beetle, had waited in anticipation. The drawing of the raffle organized by Helmut Weber, Trustee of the MDIBL, took place. To our collective chagrin, the winner was not one of the MDIBL family, but all there enjoyed the suspense of the occasion. The evening concluded with the first concert given in the Maren Auditorium. Under the title "Biorhythms: Music at the MDI Bio Lab" it featured New England folk musicians Cindy Kallet and Bills Staines, who enchanted the audience of junior and senior fans of folk music.

#### Acknowledgments

I would like to take this opportunity to thank all who contributed to the success of the Centennial. A joyful, cooperative spirit made this special event possible and memorable.

#### THE MOUNT DESERT ISLAND BIOLOGICAL LABORATORY 1898-1998: A CENTURY OF SCIENTIFIC EXPLORATION

#### Rolf K.H. Kinne Max-Planck-Institut fur Molekulare Physiologie, 44139 Dortmund, FRG

My assignment today is to summarize past scientific achievements at the Mount Desert Island Biological Laboratory. It is a great honor and privilege for me to do so at an occasion which marks not only a vivid century of education and research but also the dedication of the Maren auditorium and, therefore, bridges the past, present, and future of this unique place. Such a summary is not an easy task since, as already noted by E.K. Marshall "*The Laboratory is made up* of independent workers, each with his own interest; this makes a discussion of the past scientific research much more difficult than for an institution where interests are centered around one or several themes." Thus the story should be told about prominent men and women who worked at the Laboratory, but there were (and still are) so many that it would be difficult to mention only a few without doing injustice to others.

There is only one exception today, Tom Maren. Although Dr. Maren spent 35 years of summer research investigating the biological role of only one enzyme - carbonic anhydrase - his work during these years is characterized by an unusual breadth of disciplines - physiology, pharmacology, and biochemistry - and by the wide range of systems he studied. His investigations on marine models contributed significantly to our current understanding of the role and importance of carbonic anhydrase in the removal of  $CO_2$ , one end product in the oxidation of nutrients such as sugar, from the cells and from the body. Furthermore, he clearly established the pivotal function of this enzyme in the formation of cerebrospinal fluid - the fluid bathing the brain - and aqueous humor - the fluid contained in the eyes. The basic observations on shark eye led to entirely new concepts and drugs for the treatment of glaucoma in humans.

I, therefore, opted in what follows to define major phases of scientific exploration at the Laboratory and to assign names to them, being well aware that such a subjective procedure may stir some controversy, for which I apologize in advance.

ation of Marine Vertebrates and Invertebrates as Model Systems for Understanding the Evolution of Species (1898 - 1921). During this period the main emphasis in teaching and research was placed on comparative anatomy and embryology from which the tree of ancestorship of species and first structure-function relationships were deduced. Major contributors: Ulric Dahlgren, John S. Kingsley, and many others.

The MDIBL, then called Harpswell Laboratory, was founded in 1898 at South Harpswell, Maine. At the end of the nineteenth century, artists and scientists alike were drawn to the Atlantic coast because of its pristine beauty. Another reason for biologists to leave their dusty collections of dead specimens was the interest sparked by Charles Darwin's theory on the evolution of species which was based on the careful observation of wildlife in its natural habitat.

\*Modified from the lecture given in the Maren Auditorium at Salsbury Cove, Maine, on July 22, 1998, on the occasion of the Centennial Celebration Ceremony.

John S. Kingsley, Biology Professor at Tufts College and founder of the Harpswell Laboratory went to the Maine Coast because of the abundance of sea life that could be easily collected, brought back to the laboratory, and then analyzed morphologically. In a Summer School of Biology, Kingsley taught Darwin's research methods to biology professors and students. At that time, Comparative Anatomy was one of the strongholds in the courses held. Embryology added another way to elucidate evolution, since ontogeny, the development of an individual member of a species, reflects phylogeny, the evolution of the species itself.

In 1921, the Harpswell Laboratory under Ulric Dahlgren moved to Salsbury Cove on Mount Desert Island. The Laboratory had accepted the gift of a piece of land donated by the Wild Gardens of Acadia (which later became Acadia National Park), with the proviso that a biological station would be formed which had to function continuously with but one three year interruption permitted, an obligation that the MDIBL fulfilled even in the difficult period of World War II. Thus, Mount Desert Island, one of the most beautiful spots on the Atlantic Coast of the United States became the new base for the Laboratory.

Actually Dahlgren had another choice for relocation, but he hoped that the truly affluent "rusticators" who flocked Mount Desert Island during the summer might be supportive of the Laboratory in the future, which has indeed been the case.

**Exploration of Fish Kidneys as Model Systems for Human Kidney Function** (1926 - 1939). Studies on fish with kidneys which lack glomeruli showed that urine formation is a result of filtration and reabsorption as well as secretion. Furthermore, methods were developed to quantify each of these processes separately. This had an enormous impact on the understanding of kidney function in general and in particular on the role of the kidney in salt and water balance in health and disease. Major contributors: Eli K. Marshall, Robert F. Pitts, James A. Shannon, Homer W. Smith, and many others

Here August Krogh's principle "there is always a species where a particular (organ) function can be studied best" came to full fruition. Kidneys without the filtering apparatus for the blood, such as from goosefish, separated filtration from other processes. Moreover, the struggle of fish living in sea water to excrete salt and to preserve water made them ideal models for investigations on salt and water balance.

At that time the MDIBL was indeed the center of modern renal physiology, where application of physico-chemical laws and quantitation of the various processes resulted in the first solid hypothesis on renal function and provided the basis and the impetus for further definitive experiments.

This flurry of activity was interrupted by World War II, when the Laboratory was even closed for two years, but in 1945, mainly due to the heroic efforts of Roy Forster, the Laboratory soon entered into another very productive phase, namely the exploration of dissected tubules and isolated cells for studies of cell growth and transport.

Exploration of Dissected Tubules and Isolated Cells as in vitro Model Systems for Growth of Normal and Cancerous Cells and for Epithelial Transport Functions (Since 1945). The removal of functional elements from complex whole organs or organisms made way for studies defining the basic chemical requirements for cell replication and characterizing physico-chemically transport processes across cell membranes and cell layers. Cell culture is nowadays a major instrument for the development of new drugs, for studies on the mechanisms underlying diseases, and for the elucidation of basic questions of cell life and cell death. Major contributors: Roy P. Forster, Philip R. White, and many others. Again, the choice of the right species, cold-blooded fish, such as flounder or later killifish (both sturdier than mammalian cells that live at 37°C), or plant cells made the difference. In addition, knowledge of the chemistry and biochemistry of intermediary metabolism had been advanced and the choice of the right salts for osmotic survival and of the right substrates for metabolic survival and cell replication was possible. The various cell types compressed into one organ in humans could now be studied separately under well-defined conditions and thus their exact role in the concert of total organ function could be defined with much more precision in an artificial, stable environment.

**Exploration of Non-Renal Salt Transporting Organs in Marine Species as Model Systems for Sodium and Chloride Transport (Since 1950).** The discovery of salt transport in the rectal gland of the dogfish, the operculum of the killifish, flounder intestine, and flounder urinary bladder provided new models for investigations on the function of salt transporting epithelia. The cellular mechanisms for the coupled transport of sodium and chloride were elucidated and two hitherto unknown transport systems, the Na-K-2Cl cotransporter and the NaCl cotransporter, were discovered; they are essential targets for treatment of heart failure and other ailments by diuretics. Major contributors: J. Wendell Burger, William D. Doyle, Franklin H. Epstein, Michael Field, Raymond A. Frizzell, Adrian Hogben, Karl Karnaky, George W. Kidder, Stanley G. Schultz, Patricio Silva, John B. Stokes III, Jose Zadunaisky, and many others

This phase of scientific exploration started in 1956 with the discovery by Knut Schmidt-Nielsen that certain sea birds have above their beak a "nasal" salt gland which enables them to get rid of the salt that they engulf when fishing for prey. In 1959 a similar organ, the rectal gland, was discovered at the MDIBL by Wendell Burger in the spiny dogfish. The rectal gland has remained one of the favorite organs studied in this Laboratory. Fish gills, flounder intestine, and flounder urinary bladder joined the ranks. Again MDIBL became a leading international center for studies on salt and water transport in intact animals, perfused organs, isolated cells, and separated subcellular organelles with biophysical and biochemical techniques.

At that time it became evident that the basic principles of cellular function and the molecules involved are very similar in species as far removed evolutionary as dogfish and man and that biological diversity is mainly achieved by small modifications of identical molecules according to the specific needs of the various cells and/or species.

Exploration of Marine Species as Model Systems for the Role of Nitrogenous Osmolytes in Fluid and Acid-Base Homeostasis and in Cell Volume Regulation (since 1957). Urea, trimethylamines, taurine, and ammonia have been of considerable interest for many years at MDIBL. New pathways for ammonia secretion have been discovered, novel transport mechanisms for urea have been described, and the role of nitrogenous osmolytes in cell volume regulation has been characterized. This has led to a better understanding of liver, kidney and brain function under physiological and pathophysiological conditions. Major contributors: David H. Evans, Leon Goldstein, Arnost Kleinzeller, Gregg A. Kormanik, Bodil Schmidt-Nielsen, and many others

Homer W. Smith and others had observed very early that shark and man behave differently in their treatment of urea. Based on these observations, a new era of exploration started. This scientific era is characterized by cyclic reactions: at the cellular level, the urea cycle, at the organ level, the cycling of urea in the medulla of the kidney and at the whole animal level, the cycling of ammonia through various organs such as liver, kidney, and where applicable gills, concepts that demonstrate a repetition of general principles at increasing levels of organization.

The scientists working at the MDIBL, however, not only took advantage of the usefulness of marine species for the elucidation of basic phenomena in biology and medicine but also

considered how the scientific achievements of the Laboratory could be utilized to protect these marine models against the hazardous effects of increasing human exploitation of nature.

**Exploration of the Effect of Hazardous Human Activities on Marine Ecology** (since 1969). Combining laboratory studies with extensive field studies on the effect of DDT pollution, the reason for the population decline of many species of birds of prey, such as bald eagles, was unraveled. It was found that the known eggshell thinning was caused by a DDTinduced defect in the calcification reaction. In addition, small amounts of crude oils were shown to reduce growth of young sea birds and to disrupt salt and water balance. Major contributors: William B. Kinter, David S. Miller, David Peakall, John B. Pritchard, David Rall, and many others.

These activities - triggered by the alarming observation that the population of predators that prey on fish had declined precipitously - were initiated at the MDIBL predominantly by Bill Kinter and his associates. Bill Kinter and Bodil Schmidt-Nielsen were also instrumental in establishing MDIBL transiently as a year-round Laboratory.

Toxicological studies continue today at the MDIBL in the Center for Membrane Toxicity Studies funded by the National Institute of Environmental Health Sciences. The members of the Center, such as Ned Ballatori, James L. Boyer, David C. Dawson, Evamaria Kinne-Saffran, Rolf K.H. Kinne, Robert Preston, and others use the wealth of experimental approaches to and depth of knowledge of the normal function of marine model systems accumulated at MDIBL during the last century to investigate the effects of environmental pollutants on processes basic for cellular reproduction, growth and specialization.

These studies will help to delineate the causes of health disturbances in man by environmental pollutants as well as to explain and to prevent the effect of hazardous human activities on marine ecosystems, the ultimate aim being that mankind and the marine ecosystem will live in harmony in the future.

**Exploration of the Cell .** Specific cell functions depend on an extremely high degree of order at the exterior as well as in the interior of the cell. Thus, the exploration of the cell interior was also of central interest in studies of mitosis and cytokinesis. The same holds for contraction of cardiac myocytes and signal transduction within the cell. Progress in this field was fostered by the use of simple, homogenous marine models and development of optical techniques, state of the art being today three-dimensional confocal microscopy. Disruption of intracellular complexity is currently considered as one of the main causes for cancer. Major contributors: Abigail Conrad, Gary W. Conrad, John H. Henson, Margaret Reed Lewis, Warren Lewis, Martin Morad, Raymond Rappaport, and many others.

One other major area of research that has been pursued with great vigor at the MDIBL is the exploration of the cell interior. Due to advances in optical techniques specific functions can be observed in living cells at high resolution in space and time. This allows scientists to understand complex chains of events leading, for example, to the contraction of a muscle or the division of a cell, in terms of the specific reactions involved, their timing and their subcellular localization. Thereby, not only local events can be monitored but also their temporal and special interactions can be delineated.

Finally, the era of molecular biology has added a new and unique facet to explorations at MDIBL.

Marine Molecular Biology (Since 1990). Conformation and structure are key elements for the function of biologically active molecules. Although biochemical and biophysical methods had tackled these problems quite successfully, it was the advent of molecular biology that provided the essential information for structure-function relationships. These techniques have already led to an unprecedented level of insight into the marine models used at MDIBL. Currently many investigators, including Edward J. Benz, Gloria V. Callard, Ian P. Callard, J.B. Claiborne, Bliss Forbush, John N. Forrest, Steven Hebert, David Towle, and many, many others are using this scientific approach. In concentrating on applying these techniques to marine organisms, we are on our way to become a Center for Marine Molecular Biology, thus far unique in the world.

#### Epilog

During the last century the book of knowledge on the function of the human body in health and disease has been opened further and further and the characteristic letters of its components have been deciphered. The Mount Desert Island Biological Laboratory has played a significant role in this process. Let us all hope that the positive aspects of this progress prevail and that they help to preserve the uniqueness of the MDIBL and the pristine beauty of its surroundings.

#### Acknowledgments

This presentation owes its quality in execution to the excellent secretarial experience of Daniela Magdefessel. The inspiring knowledge and thoughtful criticism of my wife Evamarina Kinne-Saffran enriched and improved the lecture.

#### Sources:

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The Mount Desert Island Biological Laboratory Bulletins

## **REPORT TITLES**

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