I. Overview

The transduction of forces in biology plays an essential role in a wide range of phenomena, from cell division to response of tissues to gravity. An unusual feature of these forces is that they often are transmitted over multiple length scales. However, biological force transduction problems are normally discussed within the context of relatively narrow disciplinary meetings, characterized by a particular scale, such as a molecule, cell, etc. The impetus for the Workshop was the realization that, owing to recent developments, important problems of biological force transduction over multiple length scales could be usefully discussed within a single venue. This Workshop aimed to explore recent advances, particularly at the molecular and cellular level, and to make special efforts to bridge the discussion to important problems of interest to workers at the tissue and organ level. Over 100 scientists representing a range of disciplines attended the Workshop. The attendees gathered over a three day schedule, with the following objectives: (1) To present recent advances in research on biological force transduction, (2) To identify new, interdisciplinary or synergistic interactions that could speed progress, and (3) To make recommendations about resources or mechanisms needed to realize these opportunities.

A number of major points emerged during the Workshop discussions:

A. Importance of problems involving Force Transduction:

Force transduction in biology clearly impacts a very wide range of phenomena, ranging from single molecular events to large organ response, and with important effects occurring at all intermediate scales. This essential conclusion became clear from the talks presented and from the wide ranging discussions at the workshop. The study of problems involving force transduction in biology has become sufficiently widespread that there is a now a critical mass of researchers involved in this area. While progress is being made, there is unmet need and opportunity for yet greater progress. Force transduction problems are not just a set of biochemical issues, but span the molecular to the macroscopic, with new tools and concepts needed across the spectrum.

B. Emerging research Themes:

The relationship between force transduction in biology and the biological material itself represents an important stand-alone topic. Thus, the study of force transduction has significant potential for development of new types materials, as the mechanisms for force transduction are

better understand. Indeed the “materials and mechanical” properties of biomolecules are major determinants in their biological function. This is qualitatively different from the traditional view of chemical reactivity as the primary “mode d'emploi” of biomolecules. This represents a new frontier for research, one in which the NSF is ideally poised to make a major contribution.

Force transduction problems require new engineering tools and models at the macro end of the spectrum. Engineering models that accurately represent the complex mechano-structural elements in tissues and organs are currently not available. At the molecular end, the properties and function of mechano-sensitive channels are poorly understood, this includes the relation between the mechanical stress or shear state of a molecule and its functionality. While the mechanical function of the cytoskeleton and related molecules is widely studied, a fundamental or predictive understanding of its biological function remains on the horizon.

A unifying concept, that is somewhat difficult to quantify, is the fact that 'biological force' is typically a cascade of events, some chemical, some physical, some genetic. The “Grand Challenge” is to determine this ‘cascade’ for important examples: Morphological adaptation to stress, chemical reaction to stress and gravitropism. These issues need to be further clarified by experts in the field.

C. Communication between disciplines:

The complexity and multidisciplinary nature of the problems involved in force transduction demand extensive interdisciplinary interaction. A full understanding of the vast majority of the crucial problems will require the participation of chemical, biological and physical sciences. However, there is currently difficulty in communication between disciplines, and, unless this is overcome, it will continue to impede progress in the field. There is a strongly perceived need for cross-training at the post-doc level. It was felt that targeted post-docs in this area of research were an immediate need. These post-docs would encourage and promote interdisciplinary research, and provide leadership for the future in the field. There are unrealized opportunities for collaboration between and theory and experiment. In general, theoretical efforts lag experiment largely due to issues of complexity. Again, this represents a significant arena for new research.

D. Research Training in Force Transduction in Biology:

Other means to encourage interdisciplinary interactions that were discussed include the organization of a Gordon Conference on this topic, a lab course taught at the Marine Biology Lab, and application to the NIH for support of a large scale project focussed on force transduction in biology. Each of these suggestions has both advantages and disadvantages. A Gordon conference has the advantages of being low cost, informal, and stimulating direct contacts, and flexible types of connections. It has the disadvantage of providing little in the way of direction, having a slow timetable, having no funding component, and no direct peer-reviewed involvement. A course at MBL has the advantage of being relatively low in cost, helping to train the next generation, and stimulating meaningful interactions between labs. It has the disadvantage of providing little in the way of direction, having a slow timetable, and being elective and possibly exclusionary. A large NIH project has the advantage of stimulating meaningful interactions between labs around problems, providing a way to direct research to specific problems, and involving peer review to help ensure quality. It has the disadvantage of requiring someone to organize a good group, of possibly excluding young faculty because of tenure concerns, and of being expensive, although the NIH has funded large projects such as this in the past.

E. Participation of Young Scientists

Participants in the workshop included about 15 graduate students and postdocs, all of whom actively engaged in the discussion. Their disciplines were as varied as were those of the more senior participants. This afforded them the opportunity to experience first hand the breadth of the interdisciplinary nature of the research required to make progress in this field. Their participation was one of the most positive aspects of the Workshop.

F. Funding Issues:

There was a sense that many problems of mechano-transduction at the cellular level could be solved in the near future, provided sufficient resources are directed to this field of research. However, new initiatives are required for the simple reason that many topics in the field of biological force transduction fall between current areas of emphasis at the major Federal funding agencies, NSF and NIH. Some topics would benefit from a group approach: Understanding mechanotransduction at the molecular level involves understanding of the physical and biochemical processes involved, and requires a battery of experimental and

theoretical skills. It is therefore critical to develop alliances between researchers who know how to manipulate cells and researchers who know how to make and interpret physical measurements at the cellular level. These points were noted in discussions between conference participants and representatives from NIH, NASA, and NSF. Finally, there was also a consensus that closer coordination and development of joint programs between the NSF and the NIH in the area of biological force transduction would be highly productive.