F-25-X-2 # 2

Cheng Zhu
Mechanical Engineering
GA Tech Res Corp - GIT
Atlanta GA 30332

NATIONAL SCIENCE FOUNDATION
FINAL PROJECT REPORT

PART I - PROJECT IDENTIFICATION INFORMATION

1. Program Official/Org.	John D. Enderle - BES
2. Program Name	BIOENG & RSCH TO AID PERSONS/W DISAB PRO
3. Award Dates (MM/YY)	From: 09/92 To: 02/95
4. Institution and Address	GA Tech Res Corp - GIT Administration Building Atlanta GA 30332
5. Award Number	9210684
6. Project Title	Modeling of Transient Processes in Cell Adhesion

This Packet Contains
NSF Form 98A
And 1 Return Envelope

PART IV -- FINAL PROJECT REPORT -- SUMMARY DATA ON PROJECT PERSONNEL

(To be submitted to cognizant Program Officer upon completion of project)

The data requested below are important for the development of a statistical profile on the personnel supported by Federal grants. The information on this part is solicited in resonse to Public Law 99-383 and 42 USC 1885C. All information provided will be treated as confidential and will be safeguarded in accordance with the provisions of the Privacy Act of 1974. You should submit a single copy of this part with each final project report. However, submission of the requested information is not mandatory and is not a precondition of future award(s). Check the "Decline to Provide Information" box below if you do not wish to provide the nformation.

Please enter the numbers of individuals supported under this grant.
Do not enter information for individuals working less than 40 hours in any calendar year.

	Senior Staff		Post-Doctorals		Graduate Students		Under-Graduates		Other Participants[1]	
	Male	Fem.	Male	Fem.	Male	Fem.	Male	Fem.	Male	Fem.
A. Total, U.S. Citizens					1			1		
B. Total, Permanent Residents	1									
U.S. Citizens or Permanent Residents[2]:										
American Indian or Alaskan Native										
Asian.....	1									
Black, Not of Hispanic Origin.....										
Hispanic										
Pacific Islander										
White, Not of Hispanic Origin					1			1		
C. Total, Other Non-U.S. Citizens										
Specify Country 1.										
2.										
3.										
D. Total, All participants (A + B + C)	1				1			1		
Disabled[3]										

☐ Decline to Provide Information: Check box if you do not wish to provide this information (you are still required to return this page along with Parts I-III).

[1] Category includes, for example, college and precollege teachers, conference and workshop participants.

[2] Use the category that best describes the ethnic/racial status fo all U.S. Citizens and Non-citizens with Permanent Residency. *(If more than one category applies, use the one category that most closely reflects the person's recognition in the community.)*

[3] A person having a physical or mental impairment that substantially limits one or more major life activities; who has a record of such impairment; or who is regarded as having such impairment. *(Disabled individuals also should be counted under the appropriate ethnic/racial group unless they are classified as "Other Non-U.S. Citizens.")*

AMERICAN INDIAN OR ALASKAN NATIVE: A person having origins in any of the original peoples of North America and who maintains cultural identification through tribal affiliation or community recognition.

ASIAN: A person having origins in any of the original peoples of East Asia, Southeast Asia or the Indian subcontinent. This area includes, for example, China, India, Indonesia, Japan, Korea and Vietnam.

BLACK, NOT OF HISPANIC ORIGIN: A person having origins in any of the black racial groups of Africa.

HISPANIC: A person of Mexican, Puerto Rican, Cuban, Central or South American or other Spanish culture or origin, regardless of race.

PACIFIC ISLANDER: A person having origins in any of the original peoples of Hawaii; the U.S. Pacific territories of Guam, American Samoa, and the Northern Marinas; the U.S. Trust Territory of Palau; the islands of Micronesia and Melanesia; or the Philippines.

WHITE, NOT OF HISPANIC ORIGIN: A person having origins in any of the original peoples of Europe, North Africa, or the Middle East.

TECHNICAL INFORMATION

We have analyzed the adhesion of a cell to another cell or to a surface and its detachment from that cell or surface by micrompipette aspiration or by centrifugal forces. The objective is to evaluate the histories of adhesion force and energy during the entire processes of conjugation and detachment. Based on the idea that the cell itself can be used as a mechanical transducer, we seek a scheme to simultaneously calculate the adhesive properties, such as binding force and energy, and the mechanical properties, such as the viscoelastic constants, from the observed cellular deformation under controlled applied loading. The cortical shell-liquid core model has been adapted for the cell as indicated in the proposal. A sequence of constitutive equations with increasing order of approximation and level of complexity are employed in the analysis. For the cortical shell, these include a uniform and isotropic prestress tension, the shear and area elasticity, and the bending elasticity. For the liquid core, these include incompressible inviscid fluid and incompressible Newtonian fluid. Depending on the complexity of the governing equations, the boundary value problems have been solved using an exact analytical method, an approximate analytical method based on small strain linearization, and a regular perturbation method based on the difference between the shear and area elastic moduli.

The major findings include the appropriate rheological model for nucleated cells in the cell-cell adhesion experiment using micropipette manipulation. The adhesion force and energy to be evaluated are scaled by the mechanical properties of the cell, since it is the cell that is being used as the mechanical transducer to measure the adhesive properties. For this reason, it is critical to used a proper rheological model and eveluate from experimentally measured cellular deformations the intrinsic mechanical properties and adhesive properties simultaneously. We found that the deformed shape of the cell can be predicated extremely well by a simple model of a quasi-static liquid core enclosed in a cortical shell with a uniform and isotropic prestress tension. We showed that the inclusion of cytoplasmic flow is not necessary for the accurate prediction of the cell shape. We demonstrated that the friction between the cell and the pipette mount is critical and can significantly affect the model prediction. We also found in our system the increase of adhesion strength during the process of detachment, is in consistent with the published results in other systems.

Not only do the experimental results provide a validation, and point to the limitations of the theory, but the mathematical models also suggest new experiments. We have already identified a lipid vesicle system as an ideal model for studies of the diffusive molecular behavior described in one of the PI's mathematical models for transient cell adhesion. Experiments with this new design is underway.

Some of the work has been published (see list below). Others are at various stage of preparation. One Ph.D. student and one undergraduate student have been working under the support of this grant.

Publications Resulted from This Project

1. Zhu C, Williams TE, Delobel J, Xia D and Offermann MK, "A cell-cell adhesion model for the analysis of micropipette experiments," in *Cell Mechanics and Cellular Engineering*, pp. 160-181, VC Mow, F Guilak, R Tran-Son-Tay and RM Hochmuth, eds, New York, Springer-Verlag, 1994.
2. Zhu C, "Biomechanics and thermodynamics of cell adhesion," in *Principles of Cell Adhesion*, pp. 23-39, M Steiner and PD Richardson, eds, Boca Raton, FL, CRC Press, 1995.
3. Williams TE, Delobel J, Xia D and Zhu C, "A cell deformation model for analysis of adhesion experiments," Carolina Conference in Biomedical Engineering, Chapel Hill, NC, February 4-5, 1994.
4. Zhu C, Williams TE, Delobel J and Xia D, "Mechanical analysis of cell adhesion in micropipette experiments," Keystone Symposium on Biology of Physiochemical Interactions at the Cell Surface, Taos, NM, February 20-26, 1994.
5. Zhu C and Williams TE, "A mechanical analysis of cell-cell adhesion as applied to the micropipette experiment," Annual Fall Meeting of the Biomedial Engineering Society, Tempe, AZ, October 14-16, 1994.
7. Zhu C, Williams TE and Xia D, "A mechanical analysis of cell-cell adhesion for the micropipette experiment," Biophysical Society Annual Meeting, San Francisco, CA, February 12-16, 1995.