



GEORGIA INSTITUTE OF TECHNOLOGY  
OFFICE OF CONTRACT ADMINISTRATION

NOTICE OF PROJECT CLOSEOUT

Closeout Notice Date 10/19/94

Project No. E-19-564 \_\_\_\_\_ Center No. 10/11-6-P5247-1A0\_  
Project Director YOGANATHAN A P \_\_\_\_\_ School/Lab CHEM ENGR \_\_\_\_\_  
Sponsor DHHS/PHS/NIH/NATL INSTITUTES OF HEALTH \_\_\_\_\_  
Contract/Grant No. 1 F32 HL08972-01 \_\_\_\_\_ Contract Entity GTRC  
Prime Contract No. \_\_\_\_\_  
Title FLUID MECHANICS STUDY OF THE MITRAL VALVE COMPLEX \_\_\_\_\_  
Effective Completion Date 940930 (Performance) 941230 (Reports)

Closeout Actions Required:	Y/N	Date Submitted
Final Invoice or Copy of Final Invoice	N	_____
Final Report of Inventions and/or Subcontracts	N	_____
Government Property Inventory & Related Certificate	N	_____
Classified Material Certificate	N	_____
Release and Assignment	N	_____
Other _____	N	_____

Comments \_\_\_\_\_  
CONTINUED BY E-19-586. \_\_\_\_\_

Subproject Under Main Project No. \_\_\_\_\_

Continues Project No. \_\_\_\_\_

Distribution Required:

Project Director	Y
Administrative Network Representative	Y
GTRI Accounting/Grants and Contracts	Y
Procurement/Supply Services	Y
Research Property Management	Y
Research Security Services	N
Reports Coordinator (OCA)	Y
GTRC	Y
Project File	Y
Other _____	N
_____	N

REVIEW GROUP <b>CLIN-2</b>	TYPE <b>5</b>	ACTIVITY <b>F32</b>	FELLOWSHIP NUMBER <b>HL08972-02</b>
TOTAL AWARD PERIOD			
From: <b>10/01/93</b>		Through: <b>09/31/96</b>	
REQUESTED BUDGET PERIOD			
From: <b>10/01/94</b>		Through: <b>09/31/95</b>	

to be verified by applicant. Check information in Items 1 through 6. If incorrect, furnish correct information in Item 11.  
 . TITLE OF RESEARCH TRAINING PROPOSAL

**FLUID MECHANICS STUDY OF THE MITRAL VALVE COMPLEX**

a. APPLICANT (Name and address, street, city, state, zip code)		4. SPONSORING INSTITUTION (Name and address, street, city, state, zip code)																
<b>FONTAINE, ARNOLD A</b> <b>GEORGIA INST OF TECHNOLOGY</b> <b>DEPT OF CHEMICAL ENGINEERING</b> <b>778 ATLANTIC DR</b> <b>ATLANTA, GA 30332-0100</b>		<b>GEORGIA TECH RESEARCH CORP</b> <b>225 NORTH AVE</b> <b>ATLANTA, GA 30332</b>																
b. SOCIAL SECURITY NUMBER		5. ENTITY IDENTIFICATION NUMBER																
<b>039-34-5580</b>		<b>1580603146A1</b>																
2c. HIGHEST DEGREE(S)		6. TITLE AND ADDRESS OF OFFICIAL SIGNING FOR SPONSORING INSTITUTION																
<b>PHD</b>		<b>BUSINESS OFFICE</b>																
d. DEPARTMENT, SERVICE, LABORATORY OR EQUIVALENT		<b>CONTRACTING OFFICER</b>																
<b>CHEMICAL SCIENCES &amp; MATERIALS</b>		<b>GEORGIA TECH RESEARCH CORP</b>																
e. MAJOR SUBDIVISION		<b>GEORGIA INST OF TECHNOLOGY</b>																
<b>G A TECH RESEARCH INSTITUTE</b>		<b>ATLANTA, GA 30332-0420</b>																
i. NAME OF SPONSOR		BITNET/INTERNET ADDRESS																
<b>YOGANATHAN, AJIT P</b>																		
complete the following (See instructions)		10a. PERMANENT MAILING ADDRESS (Street, city, state, zip code)																
7. HUMAN SUBJECTS																		
a. <input checked="" type="checkbox"/> NO <input type="checkbox"/> YES { OR Exemption # _____																		
b. Assurance of Compliance # _____																		
8. VERTEBRATE ANIMALS																		
a. <input checked="" type="checkbox"/> NO <input type="checkbox"/> Yes... IACUC Approval Date _____																		
b. Animal Welfare Assurance # _____																		
9. TRAINING SITE(S) (Organizations and Addresses)		10b. APPLICANT'S TELEPHONE INFORMATION																
		<table border="1"> <thead> <tr> <th></th> <th>Area Code</th> <th>Phone number &amp; extension</th> </tr> </thead> <tbody> <tr> <td>OFFICE</td> <td>404</td> <td>894-8121</td> </tr> <tr> <td>FAX</td> <td>404</td> <td>894-2291</td> </tr> <tr> <td>HOME</td> <td>404</td> <td>438-0254</td> </tr> <tr> <td>PERMANENT ADDRESS</td> <td>404</td> <td>894-8121</td> </tr> </tbody> </table>			Area Code	Phone number & extension	OFFICE	404	894-8121	FAX	404	894-2291	HOME	404	438-0254	PERMANENT ADDRESS	404	894-8121
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HOME	404	438-0254																
PERMANENT ADDRESS	404	894-8121																

1. USE THIS SPACE FOR CORRECTIONS TO ITEMS 1 THROUGH 6. INDICATE THE NUMBER(S) WHERE ANSWERS APPLY.

2. APPLICANT CERTIFICATION AND ACCEPTANCE: I certify that the statements herein are true, accurate, and complete to the best of my knowledge, and I agree to comply with Public Health Service terms and conditions if an award is issued as a result of this application. I certify that I have read the National Research Service Award Service Assurance, that I will abide by the Assurance if an award is made, and that the award will not support residency training. Willful provision of false information is a criminal offense (U.S. Code, Title 18, Section 1001). I am aware that any false, fictitious, or fraudulent statement may, in addition to other remedies available to the Government, subject me to civil penalties under the Program Fraud Civil Remedies Act of 1986 (45 CFR Part 78).

SIGNATURE *[Signature]* DATE **6/30/94**

**INDIVIDUAL NATIONAL RESEARCH SERVICE AWARD  
CONTINUATION APPLICATION**

FELLOWSHIP NUMBER

HL08972-02

**13. APPLICANT SUMMARY OF ACTIVITIES (Do not exceed 3 pages.)****A. CHANGES**

Since submission of the last application, have any significant changes occurred in the training program, particularly the research project, academic status, or time distribution of activities (i.e., percentage of time devoted to research project, course work, teaching, etc.)? If so, explain.

**B. PROGRESS REPORT**

Describe concisely the research performed and research training obtained during the past year. List all courses and publications.

**C. RESEARCH TRAINING PLANS**

Describe concisely the research and research training planned for the requested budget period, including any course work.

**13a) No changes since submission of the funded application.**

**13b) New models were designed and constructed, during the first part of the calendar year, to provide the optical and ultrasound access needed to conduct the proposed studies. The models are rigid Plexiglas models with characteristics which will allow the investigations of the transmitral flow fields in the vicinity of the mitral valve leaflets and in the left ventricle. New papillary muscle holding rods have been developed incorporating strain gage force sensors to permit measurement of the forces exerted on the papillary muscles by the mitral valve leaflets. Delivery of the new holding rods is expected in early July. Testing of the new apparatus will begin upon delivery. In addition to the new rigid left ventricular models, a unique compliant left ventricular sack model is being evaluated for use in the proposed study. A natural mitral valve complex can be mounted and tested in this new compliant model.**

Qualitative studies have been performed on the transmitral flow fields associated with normal mitral valves in both the rigid and compliant left ventricular models. These studies involved standard video planar and 3-D flow visualization, high speed planar and 3-D video at frame rates up to 500 frames/sec, and color Doppler flow mapping. Quantitative measurements of the transmitral flow fields in the near vicinity of and between the valve leaflets have been obtained using Doppler ultrasound velocity mapping in both in-vitro models. In addition, general hemodynamic data (pressure and flow waveforms, pressure drop, etc.) have also been obtained during the qualitative and quantitative experiments. Preliminary qualitative and quantitative studies of the fluid mechanics associated with glutaraldehyde fixed mitral valves are now underway in the compliant left ventricular model. The mitral valves are fixed in the laboratory, which provides the trainee with experience in the various fixation techniques employed clinically. Analysis of the preliminary data obtained to date is currently underway.

I have gained considerable experience in the cardiovascular fluid dynamics field through supervision of and participation in various other research projects within Professor Yoganathan's research group. I have been investigating the effects of currently used chordal sparing techniques on the flow fields of the prosthetic heart valves used in these techniques. The three-dimensional mean flow and turbulent fields associated with commonly used prosthetic heart valves in both steady and pulsatile flow is also under investigation. For these studies, I have developed and currently manage a three-component laser Doppler velocimetry lab in the Georgia Tech Bioengineering Center. These prosthetic valve measurements are the first three component measurements distal to valve prostheses. I have co-wrote a recently sponsored AHA proposal investigating the effects of papillary muscle position and transmitral pressure gradient on the effective coaptation of the mitral valve leaflets and degree of regurgitation in ischemic mitral incompetence in steady and pulsatile flow. These experiments will complement my traineeship proposal by studying the degree of papillary muscle malposition on normal mitral valve function. Preliminary steady flow experiments have already been conducted and results presented at the 1993 ACC meetings in Atlanta Georgia. Professor Yoganathan has also involved me in his right heart research and experimental studies on the quantitation of mitral and aortic regurgitation as part of my training in the cardiovascular fluid dynamics area.

I supervise and provide experimental expertise to PhD and masters degree students within the Professor Yoganathan's research group. Furthermore, I actively interact and collaborate with cardiologists from the Massachusetts General Hospital in Boston, other Georgia Tech Bioengineering faculty and researchers in the Hemodynamics Research Group at the University of Aarhus, Denmark. These interactions have been instrumental in my medical/clinical education.

During the past year, I have audited two graduate courses in the bioengineering program, "Pathology of the Cardiovascular System" and "Biofluid Mechanics". I have also presented several papers at regular weekly group

research meetings, and have attended several bioengineering seminars. My bioengineering research has been presented at the ACC and AHA meetings in Atlanta Georgia. Additionally, I was an invited speaker for a bioengineering seminar at the Penn State University Bioengineering Department. A paper has been submitted for publication to the *Journal of Biomechanics*, and five other papers are currently in process and will be submitted for publication in the following year. The following lists the abstracts, presentations, and publications I have co-authored in the past year.

#### Manuscripts submitted for Journal Publication:

1. Burleson, A.C., N'Guyen, T., Fontaine, A.A., Levine, R.A. and Yoganathan A.P., "A Model Based on Dimensional Analysis for Non-Invasive Quantification of Valvular Regurgitation Under Confined and Impinging Conditions: In-Vitro Pulsatile Flow Validation," Submitted for Publication, *J. Biomechs*.
2. Young, K.H., Walker, P.G., Fontaine, A.A., Panchal S., Ensley A.E., Oshinsky J., Sharma S., Bank S, Ha B, Lucas C.L. and Yoganathan, A.P., "Swirl in Fontan Connections: In-Vitro Experimental Studies," Submitted for Publication, *J. Biomechs*.

#### Manuscripts in Progress:

1. Fontaine, A.A., Walker, P.G. and Yoganathan, A.P., "Three-Component Coincident LDA Velocity and Turbulence Measurements Distal to Normal and Stenosed Aortic Valve Prostheses: An In-Vitro Study".
2. Burleson A.C., Fontaine, A.A. and Yoganathan A.P., "A Model Based on Dimensional Analysis for Noninvasive Quantification of Valvular Regurgitation under Confined and Impinging Conditions".
3. Fontaine A.A., Ellis J., Hopmeyer J. and Yoganathan A.P., "In Vitro Comparison of the 3-Component Mean Flow and Turbulence Structure Distal to a Bileaflet Heart Valve Prosthesis: Steady vs. Pulsatile Flow".
4. Ellis J., Fontaine A.A., He S. and Yoganathan A.P., "The Impact of Driving Pressure on Effective Regurgitant Orifice Area in Incomplete Mitral Valve Closure".
5. Stadter R., Fontaine A.A., He S. and Yoganathan A.P., "Influence of Chordal Sparring Techniques on the Hemodynamics of Prosthetic Heart Valves: An In Vitro Study".
6. Walker P.G., Fontaine A.A. and Yoganathan A.P., "Evaluation of Phase Velocity Encoded MRI as a Tool for In Vivo Assessment of Prosthetic Valve Function: An In-Vitro Study".

#### Abstracts/Presentations:

1. Fontaine, A.A., "Heart Valve Research at the Georgia Tech Cardiovascular Fluid Mechanics Laboratory," Invited Seminar, The Pennsylvania State University, Bioengineering Center and Artificial Heart Program, March, 1994.
2. Fontaine, A.A., Levine, R.A., Menendez, M., Williams, K., Reeves, W.F., Pawleikiwz, S.W., Kassel, J. and Yoganathan, A.P., "Mitral Regurgitant Jet Momentum Quantitation through Digital Auscultation: An In-Vitro Study," Abstract presented at the ACC March 1994 meeting in Atlanta, GA.
3. Walker, P.G., Pedersen, E.M., Flepp, L., Heinrich, R., Fontaine, A.A. and Yoganathan, A.P., "A Study of Normal and Stenotic Mechanical Heart Valves using Magnetic Resonance (MR)," Abstract presented at the ACC March 1994 meeting in Atlanta, GA.
4. Schwammenthal, E., He, S., Fontaine, A.A., Nidorf, S.M., Vlahakes, G.J., Yoganathan, A.P., Weyman, A.E. and Levine, R.A., "Impact of Leaflet Geometry on the Severity of Mitral Regurgitation in Mitral Valve Prolapse: Insights from an In-Vitro Model," Abstract presented at the ACC March 1994 meeting in Atlanta, GA.
5. Hopmeyer, J., Yang, S., Fontaine, A.A., Schwammenthal, E., Levine, R.A. and Yoganathan, A.P., "Quantification of Regurgitation by the Proximal Isovelocity Surface Area (PISA) Technique: Detailed Validation by Laser Doppler Anemometry," Abstract presented at the ACC March 1994 meeting in Atlanta, GA.
6. Schwammenthal, E., He, S., Yoganathan, A.P., Levine, R.A. and Fontaine, A.A., "The Impact of Driving Pressure on Effective Regurgitant Orifice Area in Incomplete Mitral Valve Closure," Abstract presented at the ACC March 1994 meeting in Atlanta, GA.
7. Fontaine, A.A., Walker, P.G. and Yoganathan, A.P., "Three Component Coincident LDA Velocity Measurements Distal to Normal and Stenosed Aortic Valve Prostheses: An In-Vitro Study," Abstract to be presented at the 2<sup>nd</sup> World Congress on Biomechanics, July 1994, Amsterdam.
8. Fontaine, A.A., Walker, P.G. and Yoganathan, A.P., "In-Vitro Steady Flow 3-D Turbulence Structure Distal to Normal and Stenosed Aortic Valve Prostheses," Abstract to be presented at the 3<sup>rd</sup> International Symposium on Biofluid Mechanics, July 1994, Munich, Germany.

9. Kim, Y.H., Fontaine, A.A., Walker, P.G. and Yoganathan, A.P., "Swirl in Fontan Connections: Flow Visualization and LDA Studies," Abstract to be presented at the 3<sup>rd</sup> International Symposium on Biofluid Mechanics, July 1994, Munich, Germany.
10. Walker P.G., Oyre S., Fontaine, A.A. and Yoganathan, A.P., "Magnetic Resonance: A New Method for Studying the Hemodynamics of Artificial Heart Valves? A Comparison with LDA," Abstract to be presented at the 3<sup>rd</sup> International Symposium on Biofluid Mechanics, July 1994, Munich, Germany.
11. Erhorn A., Vetter H.O., Fontaine A.A., Reichart B. and Yoganathan A.P., "Hydrodynamic Characteristics of a New Stentless Mitral Valve Allograft: In-vitro Results," Abstract to be presented at the 3<sup>rd</sup> International Symposium on Biofluid Mechanics, July 1994, Munich, Germany.

- 13c) **Research Plan:** Continue with planned research on normal and fixed mitral valves in physiologic in-vitro models.
- Complete high speed video analysis of normal and fixed mitral valves in both rigid and compliant left ventricular models.
  - Perform 2-component and 3-component laser Doppler velocimetry measurements of the transmitral and left ventricular flow fields associated with natural and fixed mitral valves.
  - Doppler ultrasound velocity mapping in areas inaccessible to laser Doppler anemometry and flow visualization.
  - Measurement of forces exerted on the papillary muscles by the mitral valve leaflets in normal and abnormal mitral valve geometries. Study the effect of papillary muscle position on the coaptation of the mitral leaflets and the resulting forces exerted on the left ventricular wall transmitted through the papillary muscles.
  - Analyze data and prepare journal publications and conference presentations.

**Research Training Plan:**

- Continue gaining expertise in the use of state of the art clinical tools such as Doppler ultrasound and MRI.
- Continue training in the many facets of cardiovascular fluid dynamics through supervision of and participation in other research projects within Professor Yoganathan's research group. These projects involve detailed studies of the flow mechanics associated with heart valve prostheses, quantitation of mitral and aortic regurgitation, and right heart studies.
- Auditing courses in the Georgia Tech Bioengineering program. These involve medical imaging, and cellular biology.
- Guest lecture in Georgia Tech course taught by Professor Yoganathan.

**INDIVIDUAL NATIONAL RESEARCH SERVICE AWARD  
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*(To be completed by sponsor—follow instructions)*

FELLOWSHIP NUMBER

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14. SUPPLEMENTATION OF FELLOW:  NO  YES — If "yes," specify the amount(s) and dates on which supplementation occurred, and the source of the funds.
- \$12,500 (10/1/93 - 9/30/94): Funds used were unrestricted Industrial Fellowship money for Cardiovascular Fluid Mechanics research in my group.

15. COMMENTS OF SPONSOR *(Use additional page, if necessary)*

A. Evaluate the quality of the training (including academic work) and research progress made by the fellow during the past year. Include performance on cumulative and qualifying examinations, if applicable.

B. Human subjects and vertebrate animals *(see instructions)*.

**15A: Evaluation**

Dr. Arnold Fontaine has been making very good progress on his NRSA postdoctoral training in Cardiovascular Fluid Mechanics and Biomedical Engineering research. He started his fellowship on October 1, 1994. He has started work on all aspects of the specific goals as outlined in his original application.

**Goal 1:** Built two separate apparatuses/models to conduct studies to investigate transmitral flow fields in the immediate vicinity of the mitral valve (MV) leaflets and in the left ventricle (LV) during diastole and systole. For this study he has designed a unique system of strain gauges that will be mounted on the MV complex in order to measure the forces exerted on the MV. We are currently awaiting delivery of these gauges. This study will yield quantitative information not obtained previously, in vitro or in vivo.

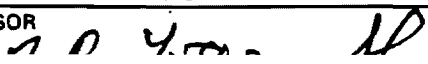


**Goal 2:** Has begun to conduct qualitative and detailed quantitative flow studies on unfixed and glutaraldehyde-fixed MVs in a realistic LV model. He is also investigating the effects of chordal sparing techniques (as utilized by cardiac surgeons) on the flow fields downstream of the MV complex, and investigating the 3-D mean flow and turbulence characteristics of commonly used prosthetic heart valves. These 3-D measurements are unique to the heart valve community.

**Goal 3:** To provide the applicant with training opportunity in the cardiovascular fluid dynamics area. Dr. Fontaine has been exposed to state of the art ultrasound Doppler, including spectral and color Doppler, techniques and MRI velocity mapping techniques. He is thereby supplementing his already acquired

Provide the number of subjects enrolled in the study to date according to the following categories (see Page 6 for definitions).

	American Indian or Alaskan Native	Asian or Pacific Islander	Black, not of Hispanic Origin	Hispanic	White, not of Hispanic Origin	Other or Unknown	TOTAL
Female		NOT APPLICABLE					
Male							
Unknown							
TOTAL							

16. CERTIFICATION. We, the undersigned, certify that: (a) the information herein, including involvement of Human Research Subjects, Recombinant DNA Research, and Vertebrate Animals, are true, accurate, and complete to the best of our knowledge; (b) if this application results in an award, appropriate training, adequate facilities, and supervision will be provided; and (c) we will comply with the Public Health Service terms and conditions of award. A willfully false certification is a criminal offense (U.S. Code Title 18, Section 1001). We are aware that any false, fictitious, or fraudulent statement may, in addition to other remedies available to the Government, subject us to civil penalties under the Program Fraud Civil Remedies Act of 1986 (45 CFR Part 78).

SIGNATURE	TYPED NAME	OFFICE TELEPHONE	DATE
	Ajit P. Yoganathan, PhD	(404) 894-2849	6/30/94
	R.W. Rousseau, PhD	(404) 894-2848	6/30/94
	Janis L. Goddard	(404) 894-4817	7-07-94

expertise in laser Doppler and flow visualization measurement techniques. He has the opportunity to audit needed graduate level courses in Bioengineering, such as biofluid dynamics and medical imaging. He will in the coming year be given the opportunity to guest lecture in courses in order to develop his teaching skills.

In his various research projects Dr. Fontaine has worked closely with MS (one) and PHD (three) students in my Group. He interacts with them daily and also supervises their research activities. He also on a daily basis interacts with two other research fellows in my Group. He and I meet frequently, at least once a week, to discuss his progress and that of the various projects he is involved with. He also interacts closely with Drs. Robert Levine and Ehud Schwammenthal of the Cardiac Ultrasound laboratory at Massachusetts General Hospital in Boston. Dr. Levine is our major collaborator on the various mitral valve projects, and visits Georgia Tech once every quarter for about a week to review progress. Arnie has also had the opportunity to interact with other Bioengineering faculty at Georgia Tech and Emory University School of Medicine, and with the Hemodynamics Research Group at the University of Aarhus, Denmark. These interactions with cardiologists and cardiac surgeons have been very good for his education and have given him the much needed medical perspective to problems associated with the mitral valve.

He has presented some of his preliminary results at the American College of Cardiology meeting held in Atlanta in March. In addition he will be presenting three papers at two international congresses in Amsterdam, The Netherlands and Munich, Germany in July. These meetings will give his research career in cardiovascular fluid mechanics good exposure. During this summer he plans to write at least two major articles, that will be submitted to major biomedical journals. He has already co-authored an article with one of my senior graduate students on mitral valve regurgitation.

In summary, I am very pleased with his research training and progress. I feel that when he leaves my laboratory at Georgia Tech, he will be well qualified to conduct independent research in the field of cardiovascular fluid mechanics (Biomedical Engineering). If you need any further information please do not hesitate to contact me (404 894-2849).

15B: Human Subjects and Vertebrate Animals:

None