Final Progress Report for Research Projects Funded by Health Research Grants

Instructions: Please complete all of the items as instructed. Do not delete instructions. Do not leave any items blank; responses must be provided for all items. If your response to an item is "None", please specify "None" as your response. "Not applicable" is not an acceptable response for any of the items. There is no limit to the length of your response to any question. Responses should be single-spaced, no smaller than 12-point type. The report **must be completed using MS Word**. Submitted reports must be Word documents; they should not be converted to pdf format. Questions? Contact Health Research Program staff at 717-783-2548.

1. **Grantee Institution:** MPC Corporation

2. **Reporting Period (start and end date of grant award period):** 1/1/2009 – 6/30/2010

3. **Grant Contact Person (First Name, M.I., Last Name, Degrees):** Shannon M. Barnes, MS

4. **Grant Contact Person's Telephone Number:** 412-648-9676

5. **Grant SAP Number:** 4100047641

6. **Project Number and Title of Research Project:** Project 2, High-Throughput Estimation and Modeling of Protein Filament Distributions from Microscope Images

7. **Start and End Date of Research Project:** 1/1/2009 – 6/30/2010

8. **Name of Principal Investigator for the Research Project:** Gustavo K. Rohde, PhD

9. **Research Project Expenses**.

   9(A) Please provide the amount of health research grant funds spent on this project for the entire duration of the grant, including any interest earned that was spent:

   $28,648.29

   9(B) Provide the last names (include first initial if multiple individuals with the same last name are listed) of **all** persons who worked on this research project and were supported with health research funds. Include position titles (Principal Investigator, Graduate Assistant, Post-doctoral Fellow, etc.), percent of effort on project and total health research funds expended for the position. For multiple year projects, if percent of effort varied from year to year, report in the % of Effort column the effort by year 1, 2, 3, etc. of the project (x% Yr 1; z% Yr 2-3).

Last Name	Position Title	% of Effort on Project	Cost
Shariff	Student	38.5%	$23,854.69

9(C) Provide the names of **all** persons who worked on this research project, but who *were not* supported with health research funds. Include position titles (Research Assistant, Administrative Assistant, etc.) and percent of effort on project. For multiple year projects, if percent of effort varied from year to year, report in the % of Effort column the effort by year 1, 2, 3, etc. of the project (x% Yr 1; z% Yr 2-3).

Last Name	Position Title	% of Effort on Project
Rohde	Principal Investigator	10%
Murphy	Professor	10%

9(D) Provide a list of **all** scientific equipment purchased as part of this research grant, a short description of the value (benefit) derived by the institution from this equipment, and the cost of the equipment.

Type of Scientific Equipment	Value Derived	Cost

10. Co-funding of Research Project during Health Research Grant Award Period. Did this research project receive funding from any other source during the project period when it was supported by the health research grant?

Yes_____ No_____X____

If yes, please indicate the source and amount of other funds:

11. Leveraging of Additional Funds

11(A) As a result of the health research funds provided for this research project, were you able to apply for and/or obtain funding from other sources to continue or expand the research?

Yes____X_____ No_____

If yes, please list the applications submitted (column A), the funding agency (National Institutes of Health—NIH, or other source in column B), the month and year when the application was submitted (column C), and the amount of funds requested (column D). If you have received a notice that the grant will be funded, please indicate the amount of funds to be awarded (column E). If the grant was not funded, insert "not funded" in column E.

Do not include funding from your own institution or from CURE (tobacco settlement funds). Do not include grants submitted prior to the start date of the grant as shown in Question 2. If you list grants submitted within 1-6 months of the start date of this grant, add a statement below the table indicating how the data/results from this project were used to secure that grant.

A. Title of research project on grant application	B. Funding agency (check those that apply)	C. Month and Year Submitted	D. Amount of funds requested:	E. Amount of funds to be awarded:
Automated high-throughput estimation and modeling of protein network distributions	☑ NIH ☐ Other federal (specify:_____ _____) ☐ Nonfederal source (specify: _____)	07/09	$ 800,000	$ 800,000
	☐NIH ☐ Other federal (specify:_____ _____) ☐ Nonfederal source (specify: _____)		$	$
	☐NIH ☐ Other federal (specify:_____ _____) ☐ Nonfederal source (specify: _____)		$	$

11(B) Are you planning to apply for additional funding in the future to continue or expand the research?

Yes__X_____ No_____

If yes, please describe your plans:

If our research project is successful, we plan to submit a renewal of our NIH grant when it ends.

12. Future of Research Project. What are the future plans for this research project?

As our NIH R01 grant was funded, we plan to continue research on this project as described in the aims of that grant.

13. New Investigator Training and Development. Did students participate in project supported internships or graduate or post-graduate training for at least one semester or one summer?

Yes____X_____ No_____

If yes, how many students? Please specify in the tables below:

	Undergraduate	Masters	Pre-doc	Post-doc
Male			1	
Female				
Unknown				
Total			**1**	

	Undergraduate	Masters	Pre-doc	Post-doc
Hispanic				
Non-Hispanic				
Unknown			1	
Total			**1**	

	Undergraduate	Masters	Pre-doc	Post-doc
White				
Black				
Asian				
Other				
Unknown			1	
Total			**1**	

14. Recruitment of Out-of–State Researchers. Did you bring researchers into Pennsylvania to carry out this research project?

Yes_____ No___X_____

If yes, please list the name and degree of each researcher and his/her previous affiliation:

15. Impact on Research Capacity and Quality. Did the health research project enhance the quality and/or capacity of research at your institution?

Yes_____ No____X_____

If yes, describe how improvements in infrastructure, the addition of new investigators, and other resources have led to more and better research.

16. Collaboration, business and community involvement.

16(A) Did the health research funds lead to collaboration with research partners outside of your institution (e.g., entire university, entire hospital system)?

Yes_____ No____X_____

If yes, please describe the collaborations:

16(B) Did the research project result in commercial development of any research products?

Yes_____ No_____X____

If yes, please describe commercial development activities that resulted from the research project:

16(C) Did the research lead to new involvement with the community?

Yes_____ No_____X_____

If yes, please describe involvement with community groups that resulted from the research project:

17. Progress in Achieving Research Goals, Objectives and Aims.

List the project goals, objectives and specific aims (as contained in the grant application's strategic plan). Summarize the progress made in achieving these goals, objectives and aims for the entire grant award period. Indicate whether or not each goal/objective/aim was achieved; if something was not achieved, note the reasons why. Describe the methods used. If changes were made to the research goals/objectives/aims, methods, design or timeline since the original grant application was submitted, please describe the changes. Provide detailed results of the project. Include evidence of the data that was generated and analyzed, and provide tables, graphs, and figures of the data. List published abstracts, poster presentations and scientific meeting presentations at the end of the summary of progress; peer-reviewed publications should be listed under item 20.

This response should be a DETAILED report of the methods and findings. It is not sufficient to state that the work was completed. Insufficient information may result in an unfavorable performance review, which may jeopardize future funding. If research findings are pending publication you must still include enough detail for the expert peer reviewers to evaluate the progress during the course of the project.

Health research grants funded under the Tobacco Settlement Act will be evaluated via a performance review by an expert panel of researchers and clinicians who will assess project work using this Final Progress Report, all project Annual Reports and the project's strategic plan. After the final performance review of each project is complete, approximately 12-16 months after the end of the grant, this Final Progress Report, as well as the Final Performance Review Report containing the comments of the expert review panel, and the grantee's written response to the Final Performance Review Report, will be posted on the CURE Web site.

There is no limit to the length of your response. Responses must be single-spaced below, no smaller than 12-point type. If you cut and paste text from a publication, be sure symbols print properly, e.g., the Greek symbol for alpha (α) and beta (ß) should not print as boxes (□) and include the appropriate citation(s). DO NOT DELETE THESE INSTRUCTIONS.

We have developed and conducted preliminary tests of a model-based procedure for estimating the distribution (including number, length distribution, measure of curvature) of microtubules in live cells from conventional fluorescence-based confocal microscopy images. Details about our prototype method and resulting initial tests are detailed below. Based on this work, conducted by computational biology student Aabid Shariff under the supervision of PI and co-PI, we have:

- *Published one peer-reviewed scientific paper:* A summary of results is found below.
- *Secured NIH R01 funding:* PI and co-PI have been awarded a four-year R01 project proposal on this topic.

Our original proposal contained two distinct aims.

Aim I: Develop methods for automated extraction of quantitative parameters of network distributions from standard fluorescence microscopy images that are amenable to high-throughput proteome-wide studies.

The purpose of this project is to produce a system capable of determining, on average, the statistical properties of network filament distribution for a large population of cells (as observed through high-throughput 3D fluorescence microscopy imaging). Although the ultimate goal of this project is to create a system robust enough to be applied to many different network filament distributions, in this project we seek to test and validate the approach using microtubules. Our progress in this area is detailed below.

Model estimation method: We have devised a Monte Carlo-type procedure for generating simulated confocal microscopy images of microtubule patterns. Our procedure takes as input image resolution, information about the point spread function, and information specifying the microtubule pattern (number of filaments, their length distribution, and a measure of curvature and cell geometry) and outputs a simulated image according to specifications. The simulated image is then compared to a real image from which one wishes to obtain information. If the images match (according to a statistical comparison of the images' pixel intensities), then the correct microtubule pattern has been identified. If the match is not of sufficient quality, the parameters describing the pattern are updated using an optimization procedure.

Tests with simulated data: As an initial experiment, we tested the ability of our method to recover known parameters from simulated microscopy images. We used several cell geometries (obtained as described above) and simulated images of microtubule distributions (generated using the generative modeling framework described above) whose parameters were known (and generated at random). Close to 4,000 images were generated for each cell. We then recovered these images with the matching framework discussed above and used a brute force approach to searching for the optimal parameters. We chose the Mahalanobis distance (matching) function computed using Harailck features in order to determine the best match. To quantify a notion of average error between the estimated and known parameters, we used the mean absolute percentage error (MAPE) defined as:

$$MAPE = \frac{1}{400}\sum_{t=1}^{400}\left|\frac{R_t - S_t}{R_t}\right|$$

where R_t refers to the known parameters and S_t refers to the estimated image parameters. The MAPE results for each cell geometry are shown in Table 1.

Table 1 shows surprisingly good results for estimating the number of microtubules and their co-linearity and moderate results for the mean and standard deviation of the length distribution. It is important to note that for the standard deviation results, MAPE errors are expected to be high since these are, essentially, the standard deviation of a standard deviation.

	Cell 1	Cell 2	Cell 4	Cell 6	Cell 10
MAPE for Number of Microtubules	2.7753%	5.4867%	4.0705%	3.8742%	4.9754%
MAPE for Mean of length distribution	27.8212%	52.4988%	50.0152%	56.0101%	44.3871%
MAPE for Std Dev of length distribution	112.8923%	146.1125%	121.4288%	102.7076%	115.5642%
MAPE for Collinearity	4.8050%	5.0460%	4.9169%	4.2038%	4.4762%
Cell morphology					

Table 1. MAPE for parameter recovery (using simulated data) using the generative modeling framework described above

Estimation on real live cells

Here we also show that the generative modeling framework can be used to recover the parameters of a real image (a HeLa cell) and that an image generated from the recovered parameters has the same visual appearance as the real image. Results are shown in Figure 1. While it is certain that the individual tracks of both images do not overlap spatially, these cannot be statistically distinguished as far as the features are concerned. While we naturally expect that for a single instance (cell image) there will be errors in the estimated parameters (as there would be in any procedure), the repetition of the measurement over many cells is expected to yield average properties for a given cell population.

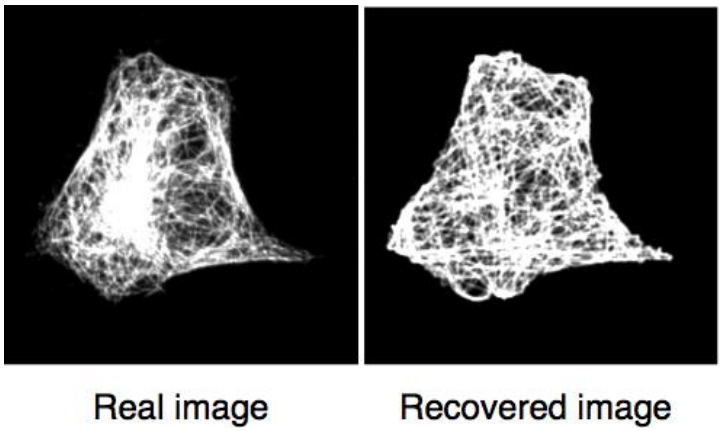

Figure 1. Example of a real image (with tagged alpha tubulin fluorescence) and an example of the image recovered using the approach described above.

Acquisition of image data of NIH 3T3 cells treated with nocodazole

To further test our method's ability to uncover parameters that accurately describe microtubule distributions depicted in confocal microscopy images, we have also acquired an image dataset where the microtubule distribution has been manipulated (disrupted) by adding nocodazole at known concentrations. Sample images are shown in Figure 2. Images were taken at different time points. The data have been analyzed with our methods, and we are in the process of preparing another manuscript for a peer-reviewed journal and will submit it soon.

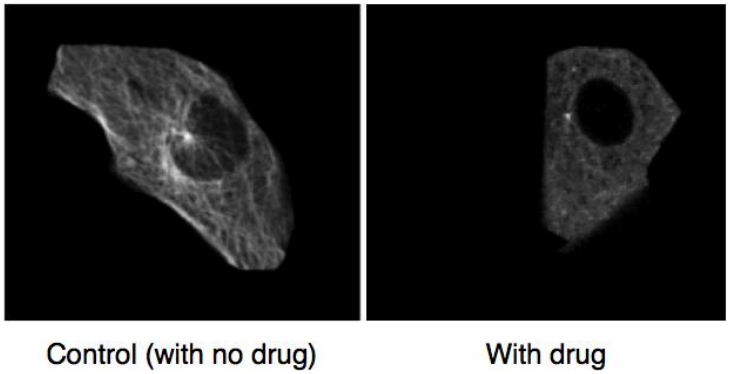

Figure 2 Cell image with and without drug.

Aim II: Develop modeling simulation approaches that will capture cell-level essential statistical characteristics of network filament distributions

Once the distributions of the descriptive parameters (obtained from Aim I above) are available, a filament distribution with identical statistical characteristics can be simulated for any given cell geometry. We are able to produce such simulated structures, given cell geometry information as well as microtubule pattern information. The next step is to do this within the context of modeling a specific type of cell under specific physiological conditions. To accomplish this goal, the filament modeling framework being developed as part of this project will be incorporated with modeling of other organelles in the cell. Both the PI and co-PI have initial results of modeling approaches applied to other cell organelles.

18. Extent of Clinical Activities Initiated and Completed. Items 18(A) and 18(B) should be completed for all research projects. If the project was restricted to secondary analysis of clinical data or data analysis of clinical research, then responses to 18(A) and 18(B) should be "No."

18(A) Did you initiate a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?

_____Yes
__X___No

18(B) Did you complete a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?

_____Yes
___X__No

If "Yes" to either 18(A) or 18(B), items 18(C) – (F) must also be completed. (Do NOT complete 18(C-F) if 18(A) and 18(B) are both "No.")

18(C) How many hospital and health care professionals were involved in the research project?

_____Number of hospital and health care professionals involved in the research project

18(D) How many subjects were included in the study compared to targeted goals?

_____Number of subjects originally targeted to be included in the study
_____Number of subjects enrolled in the study

18(E) How many subjects were enrolled in the study by gender, ethnicity and race?

Gender:
_____Males
_____Females
_____Unknown

Ethnicity:
_____Latinos or Hispanics
_____Not Latinos or Hispanics
_____Unknown

Race:
_____American Indian or Alaska Native
_____Asian
_____Blacks or African American
_____Native Hawaiian or Other Pacific Islander
_____White
_____Other, specify:_____
_____Unknown

18(F) Where was the research study conducted? (List the county where the research study was conducted. If the treatment, prevention and diagnostic tests were offered in more than one county, list all of the counties where the research study was conducted.)

19. Human Embryonic Stem Cell Research. Item 19(A) should be completed for all research projects. If the research project involved human embryonic stem cells, items 19(B) and 19(C) must also be completed.

19(A) Did this project involve, in any capacity, human embryonic stem cells?
_____Yes
___X_ No

19(B) Were these stem cell lines NIH-approved lines that were derived outside of Pennsylvania?
_____Yes
_____ No

19(C) Please describe how this project involved human embryonic stem cells:

20. Articles Submitted to Peer-Reviewed Publications.

20(A) Identify all publications that resulted from the research performed during the funding period and that have been submitted to peer-reviewed publications. Do not list journal abstracts or presentations at professional meetings; abstract and meeting presentations should be listed at the end of item 17. **Include only those publications that acknowledge the Pennsylvania Department of Health as a funding source** (as required in the grant agreement). List the title of the journal article, the authors, the name of the peer-reviewed publication, the month and year when it was submitted, and the status of publication (submitted for publication, accepted for publication or published.). Submit an electronic copy of each publication, listed in the table, in a PDF version 5.0.5 format, 1,200 dpi. Filenames for each publication should include the number of the research project, the last name of the PI, the number of the publication and an abbreviated research project title. For example, if you submit two publications for PI Smith for the "Cognition and MRI in Older Adults" research project (Project 1), and two publications for PI Zhang for the "Lung Cancer" research project (Project 3), the filenames should be:

Project 1 – Smith – Publication 1 – Cognition and MRI
Project 1 – Smith – Publication 2 – Cognition and MRI
Project 3 – Zhang – Publication 1 – Lung Cancer
Project 3 – Zhang – Publication 2 – Lung Cancer

If the publication is not available electronically, provide 5 paper copies of the publication.

Note: The grant agreement requires that recipients acknowledge the Pennsylvania Department of Health funding in all publications. Please ensure that all publications listed

acknowledge the Department of Health funding. If a publication does not acknowledge the funding from the Commonwealth, do not list the publication.

Title of Journal Article:	Authors:	Name of Peer-reviewed Publication:	Month and Year Submitted:	Publication Status (check appropriate box below):
A generative model of microtubule distributions and indirect estimation of its parameters from fluorescence microscopy images	A. Shariff, R. F. Murphy, G. K. Rohde	Cytometry A	09/09	☐Submitted ☐Accepted X Published
2.				☐Submitted ☐Accepted ☐Published
3.				☐Submitted ☐Accepted ☐Published

20(B) Based on this project, are you planning to submit articles to peer-reviewed publications in the future?

Yes___X_____ No_____

If yes, please describe your plans:

As mentioned above, we have acquired microtubule image data on cells treated with Nocodazole; some of these data have been analyzed, and we plan to submit a manuscript sometime in fall 2010.

21. Changes in Outcome, Impact and Effectiveness Attributable to the Research Project. Describe the outcome, impact, and effectiveness of the research project by summarizing its impact on the incidence of disease, death from disease, stage of disease at time of diagnosis, or other relevant measures of outcome, impact or effectiveness of the research project. If there were no changes, insert "None"; do not use "Not applicable." Responses must be single-spaced below, and no smaller than 12-point type. DO NOT DELETE THESE INSTRUCTIONS. There is no limit to the length of your response.

None

22. Major Discoveries, New Drugs, and New Approaches for Prevention Diagnosis and Treatment. Describe major discoveries, new drugs, and new approaches for prevention, diagnosis and treatment that are attributable to the completed research project. If there were no major discoveries, drugs or approaches, insert "None"; do not use "Not applicable." Responses must be single-spaced below, and no smaller than 12-point type. DO NOT DELETE THESE INSTRUCTIONS. There is no limit to the length of your response.

None

23. Inventions, Patents and Commercial Development Opportunities.

23(A) Were any inventions, which may be patentable or otherwise protectable under Title 35 of the United States Code, conceived or first actually reduced to practice in the performance of work under this health research grant? Yes_____ No___X_____

If "Yes" to 23(A), complete items a – g below for each invention. (Do NOT complete items a - g if 23(A) is "No.")

a. Title of Invention:

b. Name of Inventor(s):

c. Technical Description of Invention (describe nature, purpose, operation and physical, chemical, biological or electrical characteristics of the invention):

d. Was a patent filed for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
Yes_____ No____

If yes, indicate date patent was filed:

e. Was a patent issued for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
Yes_____ No____
If yes, indicate number of patent, title and date issued:
Patent number:
Title of patent:
Date issued:

f. Were any licenses granted for the patent obtained as a result of work performed under this health research grant? Yes_____ No____

If yes, how many licenses were granted?_____

g. Were any commercial development activities taken to develop the invention into a commercial product or service for manufacture or sale? Yes___ No____

If yes, describe the commercial development activities:

23(B) Based on the results of this project, are you planning to file for any licenses or patents, or undertake any commercial development opportunities in the future?

Yes_____ No____X_____

If yes, please describe your plans:

24. Key Investigator Qualifications. Briefly describe the education, research interests and experience and professional commitments of the Principal Investigator and all other key investigators. In place of narrative you may insert the NIH biosketch form here; however, please limit each biosketch to 1-2 pages. *For Nonformula grants only – include information for only those key investigators whose biosketches were not included in the original grant application.*

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Gustavo Kunde Rohde	POSITION TITLE Assistant Professor of Biomedical Engineering Carnegie Mellon University
eRA COMMONS USER NAME Gkunder	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Vanderbilt University, Nashville, TN, USA	BS	1995-1999	Physics/Mathematics
Vanderbilt University, Nashville, TN, USA	MS	1999-2001	Electrical Engineering
University of Maryland, College Park, MD, USA	PhD	2002-2005	Applied Mathematics
Naval Research Laboratory, Washington, DC	Fellowship	2005-2006	Signal Processing

A. Positions and Honors

<u>Positions and Employment</u>

1999-2001 Research Assistant, Vanderbilt University, Nashville, TN.
2001-2005 Self Employed Scientific Consultant:
- Section on Tissue Biophysics and Biomimetics, Laboratory of Integrative and Medical Biophysics, NICHD, National Institutes of Health, Bethesda, MD
- Systems Planning Corporation, Arlington, VA

2005-2006 NRC Postdoctoral Associate, Naval Research Laboratory, Washington, DC
2007-present Assistant Professor of Biomedical Engineering, Carnegie Mellon University, Pittsburgh, PA

Professional Memberships
1999-2005 Student Member, IEEE
2005-present Member, IEEE
2008-present Member, ISAC

Honors
2005-2006 NRC research associateship

B. Selected peer-reviewed publications (in chronological order).

Journal publications
1. **Rohde GK**, Aldroubi A, Dawant BM., The adaptive bases algorithm for intensity-based nonrigid image registration. IEEE Trans Med Imaging. 2003 Nov;22(11):1470-9.
2. **Rohde GK**, Barnett AS, Basser PJ, Marenco S, Pierpaoli C., Comprehensive approach for correction of motion and distortion in diffusion-weighted MRI. Magn Reson Med. 2004 Jan;51(1):103-14.
3. Assaf Y, Freidlin RZ, **Rohde GK**, Basser PJ., New modeling and experimental framework to characterize hindered and restricted water diffusion in brain white matter. Magn Reson Med. 2004 Nov;52(5):965-78.
4. **Rohde GK**, Dawant BM, Lin SF., Correction of motion artifact in cardiac optical mapping using image registration. IEEE Trans Biomed Eng. 2005 Feb;52(2):338-41.
5. **Rohde GK**, Barnett AS, Basser PJ, Pierpaoli C., Estimating intensity variance due to noise in registered images: applications to diffusion tensor MRI. Neuroimage. 2005 Jul 1;26(3):673-84.
6. Marenco S, Rawlings R, **Rohde GK**, Barnett AS, Honea RA, Pierpaoli C, Weinberger DR., Regional distribution of measurement error in diffusion tensor imaging. Psychiatry Res. 2006 Jun 30;147(1):69-78.
7. Evans, A.C. and the Brain Development Cooperative Group (2006). The NIH MRI study of normal brain development. NeuroImage, *30* (1), 184-202.
8. Almli C.R., Rivkin M.J., McKinstry R.C. & Brain Development Cooperative Group (2007). The NIH MRI study of normal brain development (Objective-2): Newborns, infants, toddlers, and preschoolers. NeuroImage, *35* (1), 308-325.
9. Waber, C.P., deMoor, C., Forbes, P.W., Almli, C.R., Botteron, K.N, Leonard, G., Milovan, D., Paus, T., Rumsey, J., and the Brain Development Cooperative Group (2007). The NIH MRI Study of Normal Brain Development: performance of a population based sample of healthy children aged 6 to 18 years on a neuropsychological battery. Journal of the International Neuropsychological Society, 13, 1-18.
10. **Rohde, G.K.**, Nichols, J.M., Dissinger, B.M., Bucholtz, F., Stochastic analysis of recurrence plots with applications to the detection of deterministic signals. Physica D 2008, 273, 619-629.
11. **Rohde, G.K.**, Ribeiro, A., Dahl, K.N., Murphy, R.F. Deformation-based nuclear morphometry: capturing nuclear shape variation in HeLa cells. Cytometry, 2008, 73A, 341-350.
12. **Rohde, G.K.**, Nichols, J.M., Bucholtz, F., Chaotic signal detection and estimation based on attractor sets: Applications to secure communications. Chaos, 2008, 18, 013114.

13. **Rohde, G.K.,** Aldroubi, A., Healy Jr., D.M., Interpolation artifacts in sub-pixel image registration. IEEE Transactions on Image Processing, 2009, 18(2):333-345.

* Dr. **Rohde** is part of the Brain Development Cooperative Group

Peer-reviewed conference proceedings

14. **Rohde, GK**, Pajevic, S, Pierpaoli, C, Basser, P.J. A comprehensive approach for multi-channel image registration. Proceedings of the Second International Workshop on Biomedical Image Registration (WBIR03), pp. 214-223, 2003.
15. **Rohde, GK**, Pajevic, S, Pierpaoli, C. Multi-channel registration of diffusion tensor images using directional information. Proceedings of the IEEE Int. Simp. on Biomedical Imaging, pp. 712-715, 2004.
16. **Rohde, GK**, Healy, Jr., DM, Berenstein, CA, Aldroubi, A, Rockmore, D., Stochastic analysis of geometric image processing using B-splines, Proceedings of IEEE ICASSP, pp. 1017-1020, 2006.
17. **Rohde, GK**, Healy, Jr. DM, Berenstein, CA, Aldroubi, A, Measuring image similarity to sub-pixel
accuracy, Proceedings of the IEEE Int. Simp. on Biomedical Imaging, pp. 638-641, 2006.
18. Healy Jr., DM, and **Rohde, GK**, Fast global image registration using random projections. Proceedings of the IEEE Int. Simp. on Biomedical Imaging, pp. 648-651, 2007.
19. **Rohde, GK**, Healy Jr., DM, Berenstein, CA, Aldroubi, A, Interpolation artifacts in biomedical image registration. Proceedings of the IEEE Int. Simp. on Biomedical Imaging, pp. 476-479, 2007.
20. Hallock, C.A., Ozgunes, I., Bhagavatula, R., **Rohde, G.K.**, Crowley, J.C., Onorato, C.E., Mavalankar, A., Chebira, A., Tan, C.-H, Pueschel, M, Kovacevic, J., Axonal bouton modeling, detection and distribution analysis for the study of neural circuit organization and plasticity. Proceedings of the IEEE Int. Simp. On Biomedical Imaging, pp. 165-168, 2008.
21. Cebira, A., Ozolek, J.A., Castro, C.A., Jenkinson, W.G., Gore, M., Bhagavatula, R., Khaimovich, I., Ormon, S.E., Navara, C.S., Sukwani, M, Orwig, K.E, Ben-Yehudah, A., Schatten, G., **Rohde, G.K.**, Kovacevic, J., Multiresolution identification of germ layer components in teratomas derived from human and nonhuman primate embryonic stem cells. Proceedings of the IEEE Int. Simp. On Biomedical Imaging, pp. 979-982, 2008.
22. **Rohde, G.K**, Wang, W., Peng, T., Murphy, R.F., Deformation-based nonlinear dimension reduction: applications to nuclear morphometry. . Proceedings of the IEEE Int. Simp. On Biomedical Imaging, pp. 500-503, 2008.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Robert F. Murphy	POSITION TITLE Ray and Stephanie Lane Professor of Computational Biology
eRA COMMONS USER NAME (credential, e.g., agency login)	

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Columbia College, Columbia University	BA	5/1974	Biochemistry
California Institute of Technology	PhD	5/1980	Biochemistry (J. Bonner)
Columbia University	Postdoc	1979-1983	Biophysics (C. Cantor)

A. Positions and Honors

Positions and Employment

1983-1989 Assistant Professor of Biological Sciences, Carnegie Mellon University
1983-1991 Founding Member, Center for Fluorescence Research in Biomedical Sciences
1989-2003 Associate Professor of Biological Sciences, Carnegie Mellon University
1998-2003 Faculty of Biomedical Engineering, Carnegie Mellon University
1999-2005 Director, Merck Computational Biology and Chemistry Program, Carnegie Mellon University
2005-2008 Founding Director, Center for Bioimage Informatics
2005-2009 Founding Director (w. Ivet Bahar), Joint CMU-Pitt Ph.D. Program in Computational Biology
2003- **Professor of Biological Sciences and Biomedical Engineering**
2006- **Professor of Machine Learning**
2007- **Director (Department Head), Ray and Stephanie Lane Center for Computational Biology**

Honors: Damon Runyon-Walter Winchell Cancer Foundation Fellowship, 1979
Presidential Young Investigator Award, 1983
Fellow, American Institute of Medical and Biological Engineering, 2007
Senior Member, IEEE, 2007
Honoree, Alexander von Humboldt Foundation Research Award, 2008

Service: Member, National Science Foundation Advisory Panel for Cell Biology, 1989-1992
Member, NIH Biological Sciences 2 Study Section, 1993-1997
Chair, Cytometry Development Workshop, November 1998-October 2006
Chair, NIH BDM-A Study Section (Computational Biology), June 2004-June 2006
Member, Editorial Advisory Board**,** *Journal of Proteome Research*, January 2006-December 2008
Member, Editorial Board, *Cytometry Part A*, May 2007-
President, International Soc for Advancement of Cytometry, May 2008-May 2010
Member, National Advisory General Medical Sciences Council, January 2009-December 2012

Area Chair for Bioimaging (with Eugene Myers), Intelligent Systems for Molecular Biology, 2010

B. Selected peer-reviewed publications (selected from 132 peer-reviewed publications)

Most relevant to the current application:

1. M. V. Boland and R. F. Murphy (2001). A Neural Network Classifier Capable of Recognizing the Patterns of all Major Subcellular Structures in Fluorescence Microscope Images of HeLa Cells. *Bioinformatics 17:*1213-1223.
2. S.-C. Chen, T. Zhao, G. J. Gordon, and R. F. Murphy (2007). Automated Image Analysis of Protein Localization in Budding Yeast. *Bioinformatics 23:*i66-i71
3. J. Newberg and R.F. Murphy (2008). A Framework for the Automated Analysis of Subcellular Patterns in Human Protein Atlas Images. *J. Proteome Res. 7:* 2300-2308.
4. T. Peng, G.M.C. Bonamy, E. Glory-Afshar, D. R. Rines, S. K. Chanda, and R. F. Murphy (2010) Determining the distribution of probes between different subcellular locations through automated unmixing of subcellular patterns. *Proc. Natl. Acad. Sci. U.S.A. 107*:2944-2949.
5. L. P. Coelho, T. Peng, and R. F. Murphy (2010) Quantifying the distribution of probes between subcellular locations using unsupervised pattern unmixing. *Bioinformatics 26*:i7-i12.

Additional recent publications of importance to the field (in chronological order)

6. M. V. Boland, M. K. Markey and R. F. Murphy (1998). Automated Recognition of Patterns Characteristic of Subcellular Structures in Fluorescence Microscopy Images. *Cytometry 33*:366-375.
7. T. Zhao, M. Velliste, M.V. Boland, and R.F. Murphy (2005). Object Type Recognition for Automated Analysis of Protein Subcellular Location. *IEEE Trans. Image Proc. 14:*1351-1359.
8. T. Zhao and R.F. Murphy (2007). Automated Learning of Generative Models for Subcellular Location: Building Blocks for Systems Biology. *Cytometry 71A*:978-990.
9. S.-C. Chen, G. J. Gordon, and R.F. Murphy (2008). Graphical Models for Structured Classification, with an Application to Interpreting Images of Protein Subcellular Location Patterns. *J. Machine Learning Res. 9:*651-682.
10. A. Shariff, G. K. Rohde and R. F. Murphy (2010) A Generative Model of Microtubule Distributions, and Indirect Estimation of its Parameters from Fluorescence Microscopy Images. *Cytometry 77A:*457-466.

C. Research Support

<u>Ongoing Research Support</u>

R01 GM075205 Murphy 6/15/07-5/31/11

Building and Validating Location Proteomics Databases

Supports CD-tagging, imaging, pattern analysis and modeling, and image databasing for 3T3 cells.

U54 RR022241 Waggoner 9/30/05-7/31/10

Fluorescent Probes & Imaging for Networks & Pathways

Role is to direct the informatics core (Core 1C). Support limited to salary for one postdoctoral fellow.

R21 AI081209 Mitchell 6/1/09-5/31/11
Protein-protein interaction test in *Candida albicans*
Software development to analyze images from the vesicle capture interaction assay.
R21 GM088816-01 Rohde 9/1/09-9/1/11
Title Deformation-Based Computational Morphometry for Cell Biology Applications
Provides biological and machine learning expertise.
R01 GM075205-03S1 Murphy 10/1/09-5/31/11
Building and Validating Location Proteomics Databases (Competitive Revision)
Use active learning and robotics to determine how subcellular locations of 94 CD-tagged proteins in NIH 3T3 cell cultures change in presence of 94 compounds. To extend to *pairs* of compounds.
RC2 GM092708-01 Kane 10/1/09-9/30/11
The Cell: An Image Library
Provide an interface between the library and our SLIF and PSLID databases.
R01 GM090033-01A1 Rohde 1/1/10-12/31/12
Automated high-throughput estimation and modeling of protein network distributions
Assist in image analysis, estimation, and modeling and supervise image collection.