

Volume 32, Number 1, April, 2001

**PHYSIOLOGY
CANADA**

**PHYSIOLOGIE
CANADA**

Published by the Canadian Physiological Society
for Canadian physiologists and their colleagues

Vol. 32, No. 1
April, 2001
ISSN 0822-9058

EDITOR:

Kenneth C. Marshall, Ph.D.
Department of Cellular and Molecular Medicine
The University of Ottawa
451 Smyth Road
Ottawa, Ontario, Canada K1H 8M5
Fax (613) 562-5434
Email: kmarshal@uottawa.ca

SUBSCRIPTION:

Distributed to members as part of their
membership

MEMBERSHIP:

Enquiries regarding membership in the Society
should be directed first to your Head, Department of
Physiology, and then to:
Dr. Penny Moody-Corbett
Division of Basic Medical Sciences
Memorial University
St. John's NF A1B 3V6
Telephone (709) 737-6890
e-mail pmoody@morgan.ucs.mun.ca

Volume 31, Number 1, June, 2000

**PHYSIOLOGY
CANADA**

**PHYSIOLOGIE
CANADA**

Vol. 32, No. 1
April, 2001
ISSN 0822-9058

INDEX

Index	1
Canadian Physiological Society.....	2
Annual General Meeting – Minutes.....	5
Financial Statements – Fiscal Year 2000.....	8
Report to the Canadian Physiological Society.....	11
2001 Sarrazin Lecture – Richard B. Stein.....	14
2001 Stevenson Lecture – Gerald W. Zamponi	18
Update from Queen’s University.....	22
F.C. MacIntosh Senior Visiting Professorship.....	27
J.A.F. Stevenson Visiting Professorship.....	28

**CANADIAN PHYSIOLOGICAL SOCIETY
SOCIÉTÉ CANADIENNE DE PHYSIOLOGIE**

OFFICERS

- President: Dr. Alvin Shrier, Department of Physiology,
McGill University
McIntyre Medical Centre, 3655 Drummond St.
Montréal, Québec H3G 1Y6
Telephone (514) 398-4318 Fax (514) 398-7452
e-mail: ashrier@med.mcgill.ca
- Past President: Dr. Jim Thornhill, Department of Physiology,
The University of Saskatchewan, Faculty of Medicine,
Saskatoon, Saskatchewan, S7N 0W0,
Telephone (306) 966-6530 Fax (306) 966-8718
e-mail: thornhill@sask.usask.ca
- Vice President: Dr. Quentin Pittman
Dept. of Physiology and Biophysics
University of Calgary, Faculty of Medicine
Calgary AB T2N 4N1
Telephone (403) 220-7383
e-mail : pittman@acs.ucalgary.ca
- Secretary: Dr. Penny Moody-Corbett
Division of Basic Medical Sciences
Memorial University
St. John's NF A1B 3V6
Telephone (709) 737-6890
e-mail: pmoody@morgan.ucs.mun.ca
- Treasurer: Dr. Douglas D. Rasmuson, Department of Physiology,
Sir Charles Tupper Medical Building,
Carlton Campus, Dalhousie University,
Halifax, Nova Scotia, B3H 4H7,
Telephone (902) 494-6520 Fax (902) 494-1685
e-mail: rasmus@is.dal.ca

**CANADIAN PHYSIOLOGICAL SOCIETY
SOCIÉTÉ CANADIENNE DE PHYSIOLOGIE**

COUNCILLORS

Dr. Susan E. Jacobs-Kaufman (2002)
Department of Medicine
University of Alberta
475 Heritage Medical Research Centre
Edmonton, Alberta T6G 2G3
Telephone (780) 492-6612
Fax (780) 492-7522
e-mail: susan.jacobs@ualberta.ca

Dr. Steven Barnes (2002)
Depts. of Physiology & Biophysics
and Ophthalmology
Dalhousie University
Sir Charles Tupper Building
Halifax, N.S. B3H 4H7
Telephone (902) 494-3367
Fax (902)494-6309
e-mail: sbarnes@is.dal.ca

Dr. C. Elaine Chapman (2003)
École de Réadaptation
Université de Montréal
Faculté de Médecine
CP 6128, Succ. A
Montréal, Québec, H3C 3J7
Telephone (514) 343-2304
Fax (514) 343-2111
e-mail: chapmanc@ere.umontreal.ca

Dr. Doug Munoz (2003)
Department of Physiology
Queen's University
Botterell Hall
Kingston, Ontario K7L 3N6
Telephone (613) 533-2111
Fax (613)533-6840
e-mail: doug@eyeml.queensu.ca

Dr. R. David Andrew
Dept. of Anatomy and Cell Biology
Queen's University Medical School
Botterell Hall
Kingston, ON K7L 3N6
Telephone (613) 5452860
Fax (613) 2566
e-mail andrewd@post.queensu.ca

Dr. John F. MacDonald
Department of Physiology
University of Toronto
Medical Sciences Bldg. Room 3318
Toronto, ON M5S 1A8
Telephone (416) 978-1518
Fax (416) 978-4940
e-mail: j.macdonald@utoronto.ca

**CANADIAN PHYSIOLOGICAL SOCIETY
SOCIÉTÉ CANADIENNE DE PHYSIOLOGIE**

COMMITTEES

Nominating Committee:

F. Richmond
A. Ferguson
S. Martin
C. Cheeseman
J. Lund

**CPS Representative to CFBS
Program Committee:**

T. Gordon (1999)

Publications Editor:

K.C. Marshall

Archives:

J. Church
H. McLennan

Science Policy Representative:

A. Krantis

**Executive Committee for J.A.F.
Stevenson Visiting Professorship:**

T. Gordon
A.M.J. Buchan
D.D. Rasmusson

CORPORATE PATRONS

Fine Science Tools

Harvard Apparatus Canada

Lamont Scientific Ltd.

**Canadian Physiological Society
Annual General Meeting**

January 13th 2001

There being 21 members present the meeting was called to order by the chair Dr. J. Thornhill at 4.50 pm.

- 1 Approval of the minutes of the January 2000 Annual General Meeting
Proposed: Dr. D. Jones Seconded: Dr. R. Stein

Carried

- 2 Treasurers' report
For the full report please see the attached document.
Motion for approval of the report:
Proposed: Dr. D. Munoz, Seconded: Dr. K. Marshall
Carried

There continues to be a decline in the number of Regular members. This does not include a group of members who are >2 years in arrears. There was discussion concerning a suggestion that the Treasurer offer a one-time amnesty for these individuals to encourage their remaining within the Society. It was felt that while this may be unfair on individuals who have kept their memberships up-to-date, the possibility of reducing the number of reminder notices required it was worth trying.

Motion in favour of the one time amnesty

Proposed: Dr. A. Shrier, Seconded: Dr. D. Munoz

Carried

- 3 The following new members were welcomed to the Society:

Regular Members: Dr. A. Baer, Queen's University
Dr. G. Kidder, University of Western Ontario
Dr. B. Vanderhyden, Ottawa Regional Cancer Centre
Dr. P. Morley, National Research Council/University of Ottawa

Student Members: Laibaik Park, Saskatoon
Mei Fok, Alberta
Steven Prescott, McGill
Falguni Patel, U of T
Bridgid Murphy, Queen's

Emeritus Status: Arnold Naimark, Manitoba
George Biro, Ottawa
Daniel Osmond, Toronto
William Ross, National Defence, Ottawa

Associate Status: Dr. Mark Bisby, Ottawa
Tyna Paquette, Dream and Nightmare Laboratory,
Montreal
Dr. S. Chowdhury, Dalhousie University

- 4 Report from the Canadian Journal of Physiology and Pharmacology
Dr. S. Jacobs-Kaufman reported that the impact factor has increased from 1.28 to 1.49 mainly due to increased quality of the articles and faster publication rate. Dr. Jacobs-Kaufman requested submission of articles from members as the number of manuscripts received is continuing to decline. All of the NRC journals are available on the web and are linked directly to procite and reference manager programmes.
- 5 Physiology Canada
Dr. K. Marshall reported that the journal has moved to the web site and hard copy versions are no longer available. A number of suggestions were made to increase the visibility of the web version of the journal. Firstly, all Physiology Departments in Canada should have a link to the web page. In addition each Department should be asked to provide the name of an individual who will act as a liason with Physiology Canada providing up-dates on Departmental activities. Dr. Marshall is working on developing the latter.
- 6 Future meetings
2002 University of Alberta: Drs Saunders and Jacobs-Kaufman . The meeting will be held from 30th January to February 3rd 2002 at Silver Star Ski Resort outside Vernon B.C. It will be held jointly with the Scandinavian Physiological Society. There will be 2 symposia “Autonomic control of cardiovascular function” and “Microgravity”. The cost for 1 person (sharing a room) will be \$82 per night including meals. The nearest airport is Kelowna and there are direct flights from Toronto, Calgary/Edmonton and Vancouver.
2003 University of Western Ontario: Dr. D. Jones. The meeting is in the early planning stage. Suggestions for improvements to the present meeting format will be welcome. Possibilities are to hold workshops and change the date/location of the meeting.
- 7 Web site
The CPS web site will remain at UBC for now. CPS will buy the site names cps.ca and physiology.ca and register these to increase availability through general browsers.
- 8 IUPS
Four delegates from CPS will attend the meeting with part of their travel costs paid by NRC. These individuals are currently Drs. P. Moody-Corbett, D. Jones, A. Shrier and A. Buchan.

9 Election Results

Vice-President: Dr. Quentin Pittman

Secretary Dr. Penny Moody-Corbett

Councillors: Drs. David Andrew and John MacDonald

Vote of thanks to the out-going Secretary.

10 Future Perspectives.

Issues to be discussed

Role of council members

How to increase visibility of CPS

Can CPS link to CIHR funding for symposia?

Discussion of ways to involve members in the Society; increase involvement with annual meeting request submissions for symposia topics from members.

Suggestion that a questionnaire be sent out, however one was circulated in 1999.

11 Treasurers' travel to meeting

At last years' annual meeting it was agreed to pay the travel costs for the Secretary to attend the Annual Winter meeting. It is proposed that the same should apply to the Treasurer.

Proposed: Dr. D. Jones Seconded Dr. R. Stein

Carried

12 Dr. A. Shrier took over as President of the Society and thanked the outgoing President Dr. J. Thornhill for all his work on behalf of the Society. Thanks were also extended to the retiring Council members Dr. M. Kelly and B. Van Vliet. Meeting adjourned at 6.00pm.

CANADIAN PHYSIOLOGICAL SOCIETY

Financial Statements - Fiscal Year 2000

General Operating Balance as of 31 December, 1999**\$67,108.1****Revenues:**

Membership Dues	\$	4,681.37	
Late Filing Fees etc.	\$	290.00	
Corporate Patrons	\$	2,100.00	
2000 Winter Meeting	\$	9,734.66	
2001 Winter Meeting	\$	1,865.00	
Physiology Canada Subscriptions Ads and Copy Revenue	\$	73.32	
Interest	\$	89.50	
		Total:	\$ 18,833.85 \$18,833.85

Disbursements:

Physiology Canada	\$	1,625.85	
2000 Winter Meeting	\$	6,603.90	
2001 Winter Meeting	\$	2,000.00	
2002 Winter Meeting	\$	1,000.00	
Student Prizes	\$	300.00	
Sarrazin Lecturer Expenses	\$	1,063.80	
MacIntosh Lecturer () Expenses	\$	-	
Secretary/Treasurer/President	\$	315.07	
Other	\$	119.24	
Bank Charges	\$	-	
		Total:	\$ 13,027.86 \$13,027.86

Balance of Revenues over Disbursements:

\$ 5,805.99 \$ 5,805.9

General Operating Balance as of 31 December 2000**\$72,914.1****Funds Handled for Other Organizations**

Funds Received

CFBS Levies ¹	\$	8,992.93	
CJPP Subscriptions ²	\$	1,229.37	
Subtotal:		\$10,222.30	\$10,222.30

Funds Dispersed

CFBS Levies ¹	\$	8,992.93	
CJPP Subscriptions ²	\$	1,229.37	
Subtotal:		\$10,222.30	\$10,222.30
Balance Owing:			\$0.00

1. CFBS Levy is neither a true revenue nor expense. Funds are collected and transferred to CFBS as they accumulate. Thus these amounts are separated from the general revenues

and expenses.

2. CJPP subscriptions are neither a true revenue nor expense. Funds are collected and transferred to CJPP as they accumulate. Thus these amounts are separated from the general revenues and expenses.

Douglas D. Rasmusson
Treasurer

Auditor

Auditor

Date: January 4, 2001

Date:

Date:

Canadian Physiological Society

Provisional Budget - Fiscal Year 2001

Revenues:

Membership Dues	\$5,000.00	
Corporate Dues	\$1,200.00	
Late Filing Fees	\$300.00	
2001 Winter meeting	\$1,000.00	
Physiology Canada	\$100.00	
Bank Interest	\$3,000.00	
Total:	\$10,600.00	\$10,600.00

Expenses:

Physiology Canada	\$2,000.00	
2001 Winter Meeting	\$3,000.00	
2002 Winter Meeting	\$1,000.00	
Sarrazin lecturer	\$1,500.00	
MacIntosh lecturer	\$1,500.00	
Executive	\$300.00	
Student Prizes	\$300.00	
Bank Charges	\$0.00	
Contingency	\$1,000.00	
Total:	\$10,600.00	\$10,600.00

net: **\$0.00**

J. A. F. Stevenson Visiting Professorship Fund:

Investment Fund 080-1555

Balance as of December 31, 1999	\$20,543.51
Less 1999 Award (Dr. John Greer)	-\$1,367.12
Less 2000 Award (Dr. Gerald Zamponi)	-\$1,459.59

PHYSIOLOGY CANADA

Gain on Investment	\$1,134.00	
	Total: \$18,850.80	
Balance as of December 31, 2000		\$18,850.80

C. P. S. Student Travel Award Fund:	Investment Fund 080-1589	
Balance as of December 31 1999	\$32,451.10	
Less Student travel awards	-\$1,000.00	
Gain on Investment	\$1,877.06	
	Total: \$33,328.16	
Balance as of December 31, 2000		\$33,328.16

Membership Report

Total membership as of January 1, 2000	360
New Members as of December 31, 2000	7
Resignations and deaths	-22
Total membership as of January 1, 2001	345

Membership Category		
Regular	226	(-17)
Associate	21	(-1)
Student	34	(-)
Emeritus	57	(+3)
Honorary	1	(-)
Corporate	6	(-)
Total:	345	(-15)

The Canadian Physiological Society is pleased to include in its 2000 membership the following

Corporate Patrons:

Carl Zeiss Canada
Chromatographic Sciences Company
Fine Science Tools

Harvard Apparatus
HEKA Electronics
Lamont Scientific

By Susan Jacobs-Kaufman, Co-editor

This year marks the second occasion on which I am able to bring good news to the membership of the Canadian Physiological Society. We have maintained the gains made last year with respect to improving service to authors, and our impact factor has risen to its highest level in 10 years and is projected to rise further.

Our priorities over the past three years since Dr. Nakatsu and I assumed the editorship of the *Canadian Journal of Physiology and Pharmacology*, were better service to authors in terms of reviewing and manuscript processing; publication of the Journal in a timely manner; and enhanced stature. One of the measures by which the stature of journals is judged is based on the impact factor. While the impact factor calculation was not designed for this purpose, it has been used widely to rate journals and also to rate individual papers. This use of impact factor has been the subject of many heated debates, particularly when it has been used by a grant reviewer to rate productivity without thoroughly reading the paper in question. Nevertheless, the fact of the matter is that impact factor continues to be used in a variety of ways, and raising the Journal's score in this regard was considered an important service to its authors.

The ten-year (1990-99) average impact factor for the *Canadian Journal of Physiology and Pharmacology* is 1.282, while the last year's impact factor was **1.493**, the highest number in 15 years, since 1984. This improvement in numerical value may be partially due to the way in which impact factor is calculated and the previous negative effect of our being late in publication. The submission of additional high quality manuscripts to this journal, will improve the content of the Journal and increase the number of published pages. Citing papers published in CJPP will also increase the impact factor. We need the continuing support of Society members to sustain this growth.

Another variable contributing to the increased impact factor may be the rigour with which the referees review the manuscripts. In the last year our rejection rate has risen from 31.8 to 37.8%. The net effect of the endeavours of the last few years is better service for our authors with shortened turnaround times, increasing stature of the Journal, and smaller issues.

The latter is an issue that requires our attention. We have the capacity to publish more pages provided that we receive the appropriate material for publication. It follows that we require more quality submissions describing the fine research of the membership in order to increase the volume of publications. During 2000, there were 1096 pages published, an increase of 111 pages over the preceding year. In addition, the number of new manuscripts submitted increased by 10 papers. These figures are deceiving and disturbing, however, since the net number of regular papers decreased from 211 in 1999 to 183 in 2000. The increase in total number is due to an increase in the number of symposium papers submitted during the year.

Certainly we will not compromise on the quality of published papers to increase volume; if any changes are made, I see us as being more likely to increase the quality of our offerings through enhanced rigour of our reviews.

Our goals for the near future are to further elevate the stature of your journal and to increase the number of published pages. To this end we require the active participation of our membership through submission of manuscripts and service to the Journal.

In response to last year's call for participation, we were gratified to receive letters from individuals saying that they wished to join the editorial board and/or review papers. With more participation by active investigators like these volunteers, the Journal's future looks very much brighter than it did just two years ago.

CONTENTS

During 2000, there were 7 review articles published, and one Rapid Communication, in addition to regular articles and a few Brief Reports. In addition, papers from the following symposia were published:

- | | |
|----------|--|
| February | 5 th International NPY Meeting (full issue, Grand Cayman, April 1999) |
| | October |
| | Trace elements and molecular mechanisms of disease (3 papers, from June 1999 CFBS) |
| November | Neural strategies for complex motor behaviours (4 papers, from the CPS 2000 meeting) |
| December | Brain-Pituitary-Peripheral Axis (full issue, held at Calgary, August 1999) |

The following symposia are scheduled for 2001 issues:

- | | |
|----------|--|
| January | Kinetics of EC Coupling in the normal and diseased heart (4 papers, from the CPS 2000 meeting) |
| February | Radiobiologie fondamentale et appliquée (18 papers in English and French, held at Guadeloupe, France, December 1999) |
| March | New strategies for combating cerebral ischemia (4 papers, from the CPS 2000 meeting) |

Papers from the August 2000 symposium "Natriuretic peptides and vasopeptidase inhibitors" are presently under review. The acceptable papers will comprise one full issue later in 2001.

We have agreed to consider publishing the papers from the forthcoming summer 2001 symposium on "Peptide receptors: from gene to therapy". Papers from this symposium would comprise a full issue in 2002.

We have invited the organizers of the two symposia being presented at the current CPS meeting to invite presenters to submit manuscripts for publication in your Journal. Dr. Krnjevic, who is being honoured at one of the symposia, was the editor of the *Canadian Journal of Physiology and Pharmacology* for a number of years.

Many of you will have already heard that the Government of Canada is working with universities across Canada to solve the problem of increasing journal costs and diminishing library holdings. One approach to this problem is to increase the availability of electronic journals. To this end the *Canadian Journal of Physiology & Pharmacology* and all its sister NRC Research Press journals (14 in total), including *Biochemistry & Cell Biology*, *Canadian Journal of Microbiology*, and *Genome*, are presently freely available to anyone with a Canadian internet address. This service is being provided through CISTI (Canadian Institute for Scientific and Technical Information) and began January 1st.

The composition of the Editorial Board has changed. We would like to extend our sincere thanks to the following Associate Editors who have retired over the past year: Dr. Bernie Bressler, Dr. Diane Finegood, Dr. Anthony Krantis, Dr. Ann Logan and Dr. John Wallace. We would also like to extend a warm welcome to new Associate Editors, Dr. Ghassan Bkaily, Département d'anatomie et de biologie cellulaire, Université de Sherbrooke; Dr. Doug Jones, Department of Physiology, University of Western Ontario; Dr. David Riddick, Department of Pharmacology, University of Toronto; and Dr. Wallace MacNaughton, Department of Physiology and Biophysics, University of Calgary.

It is gratifying to see that progress is being made. It remains for me to thank Dr. Kanji Nakatsu (my co-editor), the associate editors who handle the manuscripts in their areas of expertise, Mrs. Lynda Hendrickson (our editorial assistant), and last but not least everyone at NRC Research Press who have worked so hard to improve our Journal.

Sincerely,
Dr. Susan Jacobs-Kaufman,
Co-Editor

A Personal Odyssey from Physics to Physiology and Prosthetics: The 2001 Sarrazin Lecture



Richard B. Stein, Department of Physiology and Centre for Neuroscience,
University of Alberta, Edmonton T5K 1Y8

People ask kids: "What do you want to be when you grow up?" The assumption is that there is a simple, fairly linear path through school to training for a career and following it through your lifetime. That is becoming less and less true, but my path has been more of a random walk. This article relates briefly some of the events and people that influenced the path that is described in the title of this lecture.

The world was quite different when I was growing up in the 50's in the U.S. There were two superpowers and the U.S.S.R. had shown its technological prowess by putting up the Sputnik satellites. Khrushchev pounded his shoe at the U.N. and threatened to bury the U.S. In that context physics seemed an important and exciting field and I was lucky enough to win a scholarship to study physics at M.I.T. However, as an undergraduate I became more and more disillusioned. Physicists seemed to be building bigger and bigger machines to study smaller and smaller particles that seemed to have less and less relevance to anything on a human scale.

What changed my direction was an elective course in my senior year in Communications Biophysics, taught by Walter Rosenblith. Rosenblith had fled Nazi Europe and later became Provost of M.I.T., the highest academic officer in that prestigious Institution. His course introduced me to information theory and its potential application to the nervous system. Estimates at that time suggested that a nerve cell could transmit more than 1000 bits/s [1]. With 1,000,000,000,000 or more neurons the information capacity of the nervous system could be staggering. To try to test this in a senior thesis project I asked subjects to respond as quickly as possible to 1, 2, 4 or 8 choices (0, 1, 2 or 3 bits of information). The reaction time increased about 140 ms with each extra bit, which represented a capacity of 7 bits/s. Clearly, there was an enormous discrepancy that needed further study, but I really had very little background in biology.

Fortunately, I won a scholarship to Oxford and enrolled in a course called PPP (physiology, philosophy and psychology). The letter P has played a prominent role in my career. I enjoyed the Oxford tutorial system which allowed me to fill in many gaps in my knowledge of these broad areas, but I kept thinking about the problem of information in the nervous system. I even developed a theory of information transmission by nerve cells that was later published [2]. However, I needed to get some feedback from a knowledgeable neurophysiologist to see if I was on the right track. I went to see Charles

Phillips, who had written a well known book on the motor cortex [3] and he listened patiently for a half an hour or more. Then, he stopped me and said three things that changed my life: 1) that he wasn't very mathematical and hadn't followed much of what I was saying, 2) that a chap named Denis Noble was moving from London to Oxford. I should go to see him, since he was much more mathematical and 3) that I shouldn't be doing more undergraduate work, but should start a doctorate in Physiology.

I took the train to London to meet Denis and discuss possibilities. Indeed, he was willing to have me as a graduate student, but there was one problem. Denis had never worked on the nervous system, but was well known for applying the Hodgkin-Huxley equations to the heart [4]. However, he wanted to set up a parallel lab doing neurophysiology and was willing to take me as a graduate student. A year later a Rhodes scholar from Australia, Keir Pearson, joined the lab. Keir later followed me to Edmonton so we have been colleagues for over 35 years now. After that brief diversion, Denis continued with his cardiovascular work and never became involved in the nervous system again.

Unfortunately, none of the experiments that I proposed for my thesis in Denis=lab were successful, so again I changed direction and began working with Peter Matthews. Peter's father, Bryan Matthews, had been Professor and head of the Physiological Laboratory at Cambridge and Peter became a Professor at Oxford. His son, Hugh Matthews is now on the staff in Physiology at Cambridge, so there have been three generations of prominent physiologists in the family. Peter spent much of his life studying the muscle spindle [5], whose physiological properties had first been described by his dad [6], so there was an extremely close scientific connection. Muscle spindles proved to be an excellent choice to test some of the theories of variability and information transmission that I was developing, so it was a fortuitous choice [7].

By this time I was a post-doctoral fellow. I liked some aspects of Britain and some aspects of the U.S. and asked "What country in the world combines most of the good features of both without too many of the problems of either?" Canada seemed a good possibility and I moved with my family to Edmonton. There was promise, but very little neuroscience at the University of Alberta, so it has been rewarding seeing neuroscience grow and flourish here. I also came to agree with the U.N. which has consistently rated Canada the best place in the world to live. In Edmonton I continued some of the work I had been doing in Oxford, but also developed methods using cuff electrodes to record neural activity chronically [8]. I was helped greatly by a technician, Dean Charles, who built the cuffs and the electrical systems to amplify the very small signals we recorded. Dean was also an accomplished pianist, who played professionally for many years.

After the technique worked well in experimental animals, we considered whether it could help amputees, who had lost muscles, but still had the nerves that formerly innervated the muscles. An orthopedic surgeon, Lyle Davis, worked with us and implanted cuffs and EMG electrodes into an amputee, Bert Sankey, who had lost an arm below the elbow in Italy during the second World War [9]. Dean built the electronics to allow him to control an electric hand and wrist. However, the connector for bringing the wires through the skin gradually worked out of the skin and had to be removed to avoid infection. This was in 1980 and it would be another 15 years before some of the technical problems were overcome and cuff electrodes were used again in human nerve recordings.

This occurred in Denmark to control functional electrical stimulation (FES), which I will discuss later [10].

About that time we also had a visit from a saxophone player, Hank DeMarco, who had lost a limb to cancer. He wasn't too interested in having implanted cuffs controlling an electric hand, but he wanted to play the Sax again. Dean really liked this project since it combined his two loves, music and electronics. He was able to build a device that allowed Hank to play professionally again without requiring surgery. The TV program >That's Incredible< did a segment on Hank and we got calls from other saxophone players across the country. We were able to help a number of them play the saxophone again, which was rewarding.

Another event around that time changed the course of my research. Terry Fox, who had lost a leg to cancer, decided to run across Canada. He showed tremendous courage and determination, but the cancer returned when he was only half way across the country. Looking at him hobble on his artificial limb, Kelly James, a mechanical engineer in my lab, decided he could build a better above-knee prosthesis. He developed an innovative mechanical design and we added sensors and a microprocessor to run a rule base. One can think of the rules as artificial reflexes that change the properties of the mechanical system at different phases of the gait cycle. In some phases the leg needs to swing freely whereas in others it needs to be rigid to support the body's weight. The design was patented [11] and sold to Otto Bock Orthopedic Industries who are now successfully selling it around the world.

Another Canadian hero, Rick Hansen, decided to wheel completely around the world to raise awareness and money for spinal cord injury. We were already working in the area of electrical stimulation but were motivated to provide practical devices that would improve the mobility and fitness of people who were disabled as a result of a spinal cord injury and stroke. In the last few years we have worked to perfect a foot-drop stimulator for people who can't flex their ankle adequately. As a result the foot drops and may drag on the ground during the swing phase of the gait cycle. The foot-drop stimulator, known as WalkAide, uses a tilt sensor to measure the orientation of the leg with respect to gravity and a rule base to turn on stimulation of the common peroneal nerve to lift the foot [12]. The rules are now hybrid reflexes with signals from an artificial sensor triggering contraction of muscles. These FES systems have been tested in clinical trials across Canada [13] and the trials are being extended now to other countries.

One final device is a leg-propelled wheelchair. The motivation for this device comes from the fact that when someone begins to use a wheelchair for whatever reason the leg muscles atrophy, the bones weaken and other adverse physiological changes occur. As the muscles atrophy, the wheelchair becomes more necessary and a vicious cycle results. We have shown that muscle atrophy [14] and osteoporosis of the bones [15] can be reversed by electrical stimulation of about 1 hour/day. The electrical stimulation can be used to propel the wheelchair to increase mobility at the same time as building up the muscles and bones. If people have residual voluntary activity in the legs, this can also be used to propel the wheelchair and produce the physiological changes. In either case, propelling the wheelchair with the legs only requires about half the effort of propulsion with the arms and about 30% less effort than for an able-bodied person to walk the same distance at the same speed [16]. We are hopeful that this device, which we call LegPro, will help a number of people to improve mobility and fitness.

Are there any general conclusions that can be drawn from what has obviously been a very personal journey? I think there are three general conclusions: 1) Go where your curiosity and your dreams lead. There are always lots of reasons to say no, but if you are determined enough, you may just succeed. 2) Be receptive to good ideas from whatever source. Many of the ideas I discussed came from technicians, students and even the media. Seize the opportunities from whatever source. 3) Don't be afraid of practical applications. I continue to do basic neurophysiology, and could easily have decided that I didn't have the clinical expertise or the business knowledge to pursue many of these applications. However, the clinicians and business people are lacking the physiologists' expertise, so it's necessary to work together if the results are going to be positive. There is great satisfaction in seeing an idea that starts as a laboratory curiosity become a product that can benefit large numbers of people. It takes a lot of work and money, but it's worth the effort.

References

- 1 Rapoport, A. and Horvath, W. J. (1960) *Information and Control* **3**, 335-350
- 2 Stein, R. B. (1967) *Biophysical Journal* **7**, 797-826
- 3 Phillips, C. G. and Porter, R. (1977) *Corticospinal neurones: their role in movement: Monographs of the Physiological Society*, vol. 34, Academic Press, London
- 4 Noble, D. (1962) *Journal of Physiology* **160**, 317-352
- 5 Matthews, P. B. C. (1981) *Journal of Physiology* **320**, 1-30
- 6 Matthews, B. H. C. (1933) *Journal of Physiology* **78**, 1-53
- 7 Stein, R. B. (1970) in *The Neurosciences, Second Study Program* (Schmitt, F. O., ed.), pp. 597-604, Rockefeller University Press, New York
- 8 Stein, R. B., Charles, D., Davis, L. A., Jhamandas, J., Mannard, A. and Nichols, T. R. (1975) *Canadian Journal of Neurological Sciences* **2**, 235-244
- 9 Stein, R. B., Charles, D., Hoffer, J. A., Arseneault, J., Davis, L. A., Moorman, S. and Moss, B. (1980) *Bulletin of Prosthetic Research* **17**, 51-62
- 10 Haugland, M. and Sinkjaer, T. (1995) *IEEE Transactions on Rehabilitation Engineering* **3**, 307:317
- 11 James, K. (1995) U.S. Patent # 5,383,939
- 12 Stein, R. B. (1997) U.S. Patent #5,643,332
- 13 Wieler, M., Stein, R. B., Ladouceur, M., Whittaker, M., Smith, A. W., Naaman, S., Barbeau, H., Bugaresti, J. and Aimone, E. (1999) *Archives of Physical Medicine and Rehabilitation* **80**, 495-500
- 14 Stein, R. B., Gordon, T., Jefferson, J., Sharfenberger, A., Yang, J., Totony de Zepetnek, J. and Belanger, M. (1992) *Journal of Applied Physiology* **72**, 1393-1400
- 15 Belanger, M., Stein, R. B., Wheeler, G. D., Gordon, T. and Leduc, B. (2000) *Archives of Physical Medicine and Rehabilitation* **81**, 1090-98
- 16 Stein, R. B., Chong, S. L., James, K. B. and Bell, G. J. (2001) *Archives of Physical Medicine and Rehabilitation*, in press

The Stevenson Lecture

Structure, Function and G-Protein Modulation of Neuronal Voltage-gated Calcium Channels



Gerald W. Zamponi, Ph.D.

Department of Pharmacology & Therapeutics, University of Calgary

The entry of calcium ions into excitable cells via voltage-dependent calcium channel mediates a wide range of cytoplasmic responses, including calcium dependent gene transcription, muscle contraction and neurotransmitter release. Most neurons express multiple types of calcium channels, including L-,P-,Q-,R-T- and N-types which can be distinguished by their pharmacological and biophysical properties. With the exception of the T-types, voltage-gated calcium channels are heteromultimers which are comprised of a pore forming α_1 subunit which defines the calcium channel subtype, plus ancillary β , α_2 - δ and possibly γ subunits. Molecular cloning has identified ten genes for different α_1 subunits which correspond to the known native calcium channel isoforms and which display highly specialized subcellular localization patterns. Each α_1 subunit is comprised of four highly homologous transmembrane domains which are connected via large cytoplasmic linker regions and which contain six membrane spanning segments (termed S1 through S6) each (see Fig. 1). Over the past four years, the major thrust of my laboratory has been the identification of α_1 subunit structural determinants which govern calcium channel function, and the elucidation of regulatory mechanisms which modulate calcium channel activity.

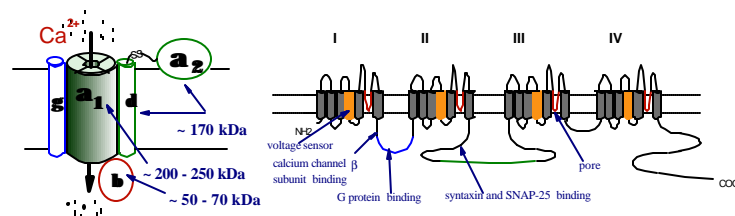


Figure 1 Subunit composition of high voltage-activated calcium channels, and proposed transmembrane topology of the calcium channel α_1 subunit.

Structural determinants of calcium channel inactivation

Over the past decade, the structural basis for a number of important aspects of calcium channel function has been elucidated. However, it has remained a major challenge to identify the molecular determinants which govern calcium channel inactivation (i.e., the entry into a non-conducting state following channel opening). In order to address this issue we decided to take advantage of the notion that L-type (α_{1C}) and R-type (α_{1E}) calcium channels exhibit diametrically different inactivation properties: L-type channels inactivate very slowly whereas R-type channels display very rapid inactivation kinetics. By generating a series of chimeric calcium channels which combined the four major transmembrane domains of L-type and R-type calcium channels, expressing them in human embryonic kidney tsA-201 cells, and examining their inactivation profiles, we were able to determine that all four domains contribute to the voltage dependence of inactivation, and that domains II, III and IV are important factors controlling the rate of inactivation with domains II and III mediating the bulk of the effects in each case. Based on these results, we hypothesized that calcium channel inactivation might involve a pore collapse mediated by the four S6 segments similar to what has been proposed to occur during slow inactivation of certain types of potassium channels. To test this hypothesis, we generated a series of additional chimeras in which the S6 segments in domains II and/or III were exchanged between the two wild type channels. Indeed, we found that the insertion of the domain IIS6 or IIIS6 region of the R-type channel into the non-inactivating L-type channel was sufficient to confer rapid inactivation kinetics. A series of point mutations in the domain IIS6 region of the L-type channel demonstrated a critical role of two single amino acid residues in this process. However, our work also revealed a key role of the cytoplasmic linker region between domains I and II in the inactivation process, and hence, we propose that calcium channel inactivation may involve a docking of the domain I-II linker region to a site comprised in part of the domain II and III S6 segments, which ultimately leads to a blockade of current flux through the channel. It may be noteworthy that the interaction between L-type calcium channels and dihydropyridines (DHPs) occurs in part in the domain III S6 region, and hence, our data may provide a molecular basis for the well established notion that inactivated L-type calcium channels display a dramatically increased affinity for DHP antagonists. Key contributors to this work were Renee Spaetgens (former M.Sc. student), Dr. Jawed Hamid (PDF) and Stephanie Stotz (Ph.D. student).

Interactions between N-type calcium channels, second messengers and SNARE proteins Calcium channels can be extensively modulated by activation of cytoplasmic messenger molecules. In view of the key role of N- and P/Q-type calcium channels in triggering neurotransmitter release at fast synapses, the modulation of these channels has been a key area of interest to us. In particular, their direct interaction with, and inhibition by, G protein $\beta\gamma$ subunits has been a major focus of my laboratory. Our work has revealed that $G\beta\gamma$ binds directly to the domain I-II linker region of presynaptic calcium channels in 1:1 stoichiometry. Phosphorylation of a single threonine residue in the $G\beta\gamma$ binding region by protein kinase C antagonizes $G\beta\gamma$, and this crosstalk between PKC and G protein inhibition of the channel may serve fine tune the release of neurotransmitters. Our work has also shown that N-type and P/Q-type calcium channels are differentially modulated

by different G protein β subunit isoforms, and that the PKC crosstalk occurs selectively for the $G\beta 1$ subunit isoform. Further complexity is added by our key finding that syntaxin 1A, a protein of the presynaptic vesicle release complex which interacts with the domain II-III linker regions of the N-type and P/Q-type calcium channel $\alpha 1$ subunit, promotes G protein inhibition of N-type calcium channels by mediating a colocalization between the channels and $G\beta\gamma$. In contrast, the structurally related syntaxin 1B isoform is ineffective. We also show that other types of vesicle release proteins such as SNAP25 can modulate the action of syntaxin 1A. Finally, PKC dependent phosphorylation of two separate serine residues within the syntaxin 1A binding region on the N-type calcium channel antagonizes the action of syntaxin 1A. Hence, there are complex interactions between second messengers, presynaptic calcium channels, and vesicle release proteins which ultimately provide immense potential for the fine tuning of calcium entry into the presynapse, and thus, neurotransmission. In that regard, the using molecular approaches to elucidate these interactions will provide valuable clues towards our understanding of mechanisms which regulate calcium homeostasis. This work was carried out by Scott Jarvis (M.D./Ph.D. student), Dr. Michelle Arnot (PDF), Dr. Jawed Hamid, Dr. Zhong-Ping Feng (PDF), Conan Cooper (Ph.D. student), Stephanie Stotz, and my collaborator Dr. Jan Braun (University of Calgary).

Acknowledgments:

I would like to thank the Canadian Physiological Society for awarding me the J.A.F. Stevenson visiting professorship, and Dr. Alvin Shrier (McGill University) for kindly nominating me. This work would not have been possible without the tremendous commitment and efforts of my graduate students and postdoctoral fellows, and the support and understanding of my wife. Financial support was provided by the Alberta Heritage Foundation for Medical Research, the Canadian Institutes of Health Research, the Heart and Stroke Foundation, the Savoy Foundation, and the EJLB Foundation. Finally I would like to thank Dr. Terry Snutch (University of British Columbia) for his generous donation of wild type calcium channel subunits.

Key publications from my laboratory:

Inactivation project:

Stotz, S.C., and Zamponi, G.W. 2001. Structural determinants of fast inactivation of high voltage activated calcium channels. Trends. Neurosci. *In press.*

Stotz, S., Hamid, J., Spaetgens, R.L., Jarvis, S.E., and Zamponi, G.W. 2000. Fast inactivation of voltage-dependent calcium channels: A hinged lid mechanism? J. Biol. Chem. 275: 24575-24582.

Spaetgens, R.L., and Zamponi, G.W. 1999. Multiple structural domains contribute to voltage-dependent inactivation of rat brain α_{1E} calcium channels. J. Biol. Chem. 274: 22428-22436.

G protein project:

Jarvis, S.E., and Zamponi, G.W. 2001. Distinct molecular determinants govern syntaxin 1A mediated inactivation and G protein inhibition of N-type calcium channels. J. Neurosci. *In press.*

Cooper, C.B., Arnot, M.I., Feng, Z.-P., Jarvis, S.E., Hamid, J., and Zamponi, G.W. 2000. Crosstalk between G protein and PKC modulation of N-type calcium channels is dependent on the G protein β subunit isoform. J. Biol. Chem. 275: 40777-40781.

Magga, J.M., Jarvis, S.E., Arnot, M.I., Zamponi, G.W., and Braun, J.E.A. 2000. Cysteine string protein regulates G-protein modulation of N-type calcium channels. Neuron. 28: 195-204.

Arnot, M.I., Stotz, S.C., Jarvis, S.E., and Zamponi, G.W. 2000. Differential modulation of N-type α_{1B} and P/Q-type α_{1A} calcium channels by different G protein β subunit isoforms. J. Physiol. 527: 203-212.

Jarvis, S.E., Magga, J.M., Beedle, A.M., Braun, J.E.A., and Zamponi G.W. 2000. G-protein modulation of N-type calcium channels is facilitated by physical interactions between syntaxin 1A and $G_{\beta\gamma}$. J. Biol. Chem. 275: 6388-6394.

Hamid, J., Nelson, D., Spaetgens, R., Dubel, S.J., Snutch, T.P., and Zamponi, G.W. 1999. Identification of an integration center for crosstalk between PKC and G protein modulation of N-type calcium channels. J. Biol. Chem. 274: 6195-6202.

Zamponi, G.W., Bourinet, E., Nelson, D., Nargeot, J., and Snutch, T.P. 1997. Crosstalk between G proteins and protein kinase C mediated by the calcium channel complex. Nature. 385: 442-446.

Update from Queen' University Department of Physiology

There is a widespread belief in the 'real world' (and sometimes within a university community) that academic departments are climax forests, full of tall, sometimes dead, trees that stifle new growth. This, to paraphrase Conrad Black, is a vile calumny; at least at Queen's.

Turnover within our department has been nothing short of remarkable. Over the last six years, six full-time faculty have retired or left. Vivian Abrahams retired in 1995, his legacy being a strong department and a prize in his name, awarded annually to the most meritorious graduate student completing his or her doctoral program. A year later, Peter Zarzecki retired, apparently deciding that early retirement afforded him an ideal opportunity to explore that interesting phase between solids and gases by sailing inland and coastal waters, depending on the season, accompanied by appropriate comestibles (in port, of course). In 1997, Mark Bisby, then into his second term as Head, left to help run the MRC and transform it into the CIHR. Mark was a superb administrator, teacher (he had double the load of anyone else), and researcher, running a laboratory that produced not just many papers but many gifted graduate students. MRC's gain of a 'turbo-bureaucrat' was our (and Queen's) loss. Last, in 1998 UBC (and the attractions of the west coast) lured away David Fedida, an outstanding young researcher.

Fran Richmond has gradually reduced her commitments as she transfers her interests cross-continent as Research Professor in the School of Pharmacy and the Faculty of Medicine, University of Southern California, and Director of Regulatory and Clinical Science at the Alfred E Mann Institute for Biomedical Engineering. She accompanied Gerry Loeb, a cross-appointee and Director of the Biomedical Engineering Unit, who now is Professor of Biomedical Engineering at USC and Director of the Device Development Facility at the AE Mann Institute. More power to them! Several of their graduate students have joined the Mann Institute, which develops early stage technologies for the health-care field, including cochlear implants and the 'Bion,' an implantable electrode for muscles. Also going with them, at least for the time being, is their innovative "Beyond Academia," a course which prepared students for jobs in, among other things, regulatory affairs in both industry and government. It has now been expanded to a MS Program in Regulatory Science, directed by Fran.

Don Jennings, one of the early recruits to the Department back in the 50s, took 'early' retirement too but that meant only that he put in 6-hour days and didn't have to ask anybody's permission to head off into the woods or lakes when the urge (i.e., deer or ducks) hit him. Don continues to publish, his papers representing a synthesis of modern acid-base and hormonal (renin-angiotensin) physiology related to control of breathing. Only this year did he decide not to apply for any more funding, a decision welcomed by those who no longer had to compete with him.

Our last retirement will occur this summer when Seon Shin steps down after 29 years.

Seon's distinguished career in endocrinology was recognized by his receipt in 1997 of a plaque for continuous funding from MRC for 25 years. Rumours abound (not really, but this will start it) that his retirement will be devoted to the cultivation of Canadian kim-chee as an anti-oxidant to prevent neurodegenerative disorders.

The department focuses its research efforts in two primary areas: neuroscience and cardiorespiratory physiology.

In Neuroscience, Ken Rose, the last person left from the 70s, integrates techniques from physiology, anatomy, pathology and engineering in order to better understand how spinal neurons convert inputs to outputs and how, and if, they form new connections following injury. He headed up the (re)formation of the MRC/CIHR Group in Sensory-Motor Neuroscience, which merges the expertise of seven PIs from three departments. The group was recently re-funded at increased levels of support, a tribute to Ken's organizational acumen and 'grantspersonship.' Ken continues to attract a steady stream of students, both undergraduate and graduate, which relieves him of the task, increasingly onerous at his age, of staring at computer-generated images of neurons. His collaborators, outside the group, include Robert Fyffe of Wright State, a graduate student of Alan Brown (Edinburgh) who was Ken's post-doctoral supervisor.

Doug Munoz arrived in 1991, followed by Greg Ross (1999) and Martin Paré (2000). Doug, a specialist in eye movement behaviour in non-human primates, normal humans and patients with a variety of neurological and psychiatric disorders, rapidly ascended the academic food chain. Now professor, he holds a Canada Research Chair in Neuroscience and is the Director of the Centre for Neuroscience. He collaborates widely and his success is measured not just by his own achievements but by those of his intellectual progeny. For example, Michael Dorris and then Brian Corneil won the Governor General's Gold Medal in 2000 and 2001, respectively, as the top graduate student at Queen's. Brian now holds a Human Frontiers award. Greg Ross focuses on mechanisms responsible for neurodegenerative diseases like Parkinson's and Alzheimers, including such environmental causes as heavy metals (Greg does use aluminum cookware). He also is Coordinator of Graduate Studies. Martin's research involves determining the neural mechanisms that guide and control visual behaviour. This involves presenting visual search targets (the non-human primate equivalent of "Where's Waldo") to monkeys, recording the responses of neurons in the parietal cortex, and monitoring subsequent saccades. These studies are supplemented by others to establish neuronal connections. Collaborators include other members of the CIHR group as well as Jeff Schall (Vanderbilt) and Stefano Ferraina (La Sapienza, Italy).

An additional focus within neuroscience is neuroregulatory control, represented by Alastair Ferguson and Dean Van Vugt (Obstetrics and Gynecology). Al, who was appointed Head in 1998, concentrates on two main areas: understanding how vasoactive peptides influence circumventricular neurons and, in turn, central cardiovascular control (baroreceptor reflex gain); and how differences in membrane conductances and NMDA receptor subunits in paraventricular neurons affect their resistance to excitotoxic cell damage. The eventual goal of the latter study is the design of clinically useful anti-stroke

agents. This work also forms a nice bridge to the cardiorespiratory focus of the department (see below). Al's collaborators include Quentin Pittman (Calgary), Rick Samson (St. Louis) and Dave Murphy and Julian Paton (Bristol, UK). He produces a steady stream of well-trained graduates who have distinguished themselves. Jaideep Bains, for example, obtained CIHR funding while still a post-doc and is now at the University of Calgary. In addition to running a well-funded and very productive lab, Al serves on multiple institutional, provincial and national committees. Dean's research centres on how, in non-human primates, various endogenous opioid peptides affect the menstrual cycle through regulation of hormonal secretions. In addition to classical endocrinology, Dean uses *in situ* hybridization histochemistry to examine the influence of ovarian steroids and stress on gene expression of hypothalamic neuropeptides. His most recent work examines the potential effects of ovarian steroids on leptin receptor gene expression in the monkey.

Cross-Appointees in Neuroscience include Barrie Frost and Randy Flanagan (Psychology), Mel Roberson (Biology), and Jeanette Holden (Psychiatry). Barrie is widely acknowledged as a leader in many fields, including processing of auditory and visual stimuli in birds, and his current web page lists 13 ongoing research projects, along with his many awards, both national and international, and collaborators. Mel's research, typically in insects, focuses on neural circuit function during thermal or hypoxic stress; collaborators include Virginia Walker (Queen's), Harold Atwood (Toronto) and Jan Ramirez (Chicago). Last year, during his sabbatical, he taught neuroethology at Cornell and received a DSc from the University of St. Andrews in Scotland for his contributions to that same field. Randy's research involves studies of how hand movements are controlled in normal subjects and those with neurological impairments, object manipulation, hand-eye coordination, and motor development in children. Jeanette's area of expertise is the genetic basis of autism and that expertise was recently recognized by CIHR by one of its largest grants ever to a Queen's faculty member, \$4.3M. Her list of collaborators is too long (more than 15 at last count) to be included here but includes individuals as far afield as Indonesia.

The second major focus in the department is cardiorespiratory. The group, which still enjoys Don Jennings' contributions, is composed of Chris Chapler, Steve Iscoe, John Fisher, Jenny Van Eyk and Chris Ward. Along with cross-appointees like Alison Froese, Cheryl King-VanVlack, Denis O'Donnell, Barry Smith, and Larry Wolfe, the members constitute the finest group of cardiorespiratory investigators between Montreal and Toronto. Chris Chapler still appears, without protective gear, in 'his' laboratory but otherwise occupies his time as Associate Dean, Faculty of Health Sciences. Steve, here since 1977 and still funded (!), has recently, in collaboration with Jenny Van Eyk, shifted his focus away from the neurophysiology of abdominal muscle control to the molecular basis for respiratory muscle fatigue. Collaborators include Jeremy Road and Darlene Reid (UBC) and Sabah Hussain (Royal Victoria Hospital, Montreal). With Joe Fisher (Anesthesiology, Toronto) and his team, Steve develops research and clinical applications of their simple circuit which maintains isocapnia regardless of ventilation. John Fisher's studies of control of the airways, particularly receptor afferents, now extend to physiological genomics, using knockout mice (muscarinic receptors or specific kinases).

Many of these studies are done in collaboration with Julia Walker and Marc Caron at Duke. (Julia, a former graduate student of Don Jennings has, despite her northern roots, decided to remain at Duke.) John also collaborates with Jenny Van Eyk in evaluating the role of calcium-independent activation of airway smooth muscle. Jenny joined the department in 1996 and, like Doug Munoz, is one of our rising stars. Aside from her many Queen's collaborators, she has also developed an extensive network of international ones (Eduardo Marban, Stephen Vatner, and Franco Di Lisa), reflecting her prominence in her area of expertise, myocardial stunning. One of her publications was recognized as one of the ten most important papers published in *Circulation Research* in 1999. Jenny just received offers of career scientist awards from both OHSF and CIHR, has received a Chancellor's Award for Excellence, and holds numerous grants, institutional, national (CIHR, OHSF) and international (NIH). The most recent member to join the group is Chris Ward, a Research Scholar of the Heart and Stroke Foundation of Canada, whose OHSF grant was just renewed. Chris focuses on the electrical and mechanical properties of cardiac myocytes isolated from various regions of the heart, and characterization of the effects of oxidants on cardiac ion channels, intracellular calcium regulation and cellular contractility. His recent CFI award is being used to acquire a high-speed imaging system for determination of intracellular calcium concentrations. When not in his lab or office, Chris helps support the local economy by patronizing the nearest chip truck; his one regret that it is closed in winter, when he needs it most.

Cross-appointees to the group include Alison Froese (Anesthesiology), Cheryl King-VanVlack (Rehabilitation Therapy), Denis O'Donnell (Respirology), Larry Wolfe (Physical Health and Education), and Barry Smith (Paediatrics). Alison still serves as a research consultant but otherwise concentrates on her clinical responsibilities. However, her research achievements were recognized in 1999 by an award from the Canadian Anesthesiologists' Society. Alison has struggled over the years to correct—successfully!—the inadequacies of a flawed NIH trial of high frequency oscillatory ventilation for infants, a technique which she helped introduce. Cheryl, a former student of Chris Chapler, studies endothelin-1 modulation of microcirculatory control in muscle and gut. Her work, done with Chris Chapler, their technician, and Hugh MacDonald (Surgery), was identified as a “Poster with Distinction” for the May 2001 meeting of the American Gastroenterology Association. Cheryl also has multiple responsibilities in various organizations (e.g., Ontario Respiratory Care Society). Denis O'Donnell, an Ontario Ministry of Health Scientist, receives considerable support from pharmaceutical companies for his research on the pathophysiology of exercise and mechanisms of dyspnea in patients with chronic obstructive lung disease, and serves on multiple national and international study committees. Larry Wolfe, whose research resulted in published guidelines for exercise in pregnancy, now uses pregnancy as a model for the study of physicochemical approaches to acid-base analysis and chemical control of ventilation as well as cardiac autonomic responses to exercise. He just completed a major 3-year research project for the US Army. Larry also has extensive editorial and service responsibilities at the national and international level. Last, Barry Smith, after retiring two years ago as Dean of Medicine for health reasons, became involved in helping to establish family care services in the Balkans.

Our other major unit works out of the Gastrointestinal Diseases Research Unit at Hôtel Dieu. Kerry Hill is our only full-time appointment, the others being cross-appointees. Kerry's main research interest, funded by CIHR and NSERC, is the study of mechanisms generating bile; she uses molecular, cellular and whole-organ approaches to identify the proteins that maintain the osmotic pressure required for water flow and bile production.

Bill Paterson, a specialist at both the clinical and research levels, in the physiology and pathophysiology of the esophagus, replaced Ivan Beck (retired) as Director of the unit. Bill recently received awards recognizing his research excellence from both the Canadian and American Associations of Gastroenterology. Other members include Stephen Vanner (control of blood flow and gland secretion in the digestive tract) and Mike Blennerhassett (enteric innervation, control of gut smooth muscle growth, and inflammation). The group's status was recently recognized in the form of a CFI grant which, with matching funds, will exceed \$2.5M.

Over the past 20 years, graduate student enrolment has approximately tripled. This year, 36 students (six of whom graduated) are enrolled. As in other physiology departments, many of our graduates pursue professional degrees (particularly medicine) but more are shifting to academia as retirements start to increase; selected examples are noted above.

Within the Faculty of Health Sciences, members of this department are at the forefront of change. We have often initiated and always embraced the development of cross-disciplinary research and teaching programmes that we feel will ultimately enhance the impact of physiology through the basic medical sciences. Over the next few years, we expect to shift away from the traditional discipline-based graduate degrees to ones based on such areas of strength as neuroscience and cardiorespiratory science, encompassing the multiple approaches provided by individuals in traditional departments. These efforts are not restricted to Queen's. 2001 saw the start of a joint undergraduate program in Respiratory Therapy in collaboration with the Michener Institute in Toronto, as well as the initiation of formal links between the educational programs of our department and the Department of Physiology and Biophysics at the University of Calgary. These initiatives promise to lead to further changes that will ensure the enhancement of Physiology in a dynamic, exciting multi-disciplinary setting for learning at all levels.

Further information is available at our website: <http://meds.queensu.ca/medicine/physiol/>

**Contributed by our correspondent at Queen's,
Dr. Steve Iscoe**

F.C. MacIntosh Senior Visiting Professorship of the Canadian Physiological Society

Each year the Canadian Physiological Society offers a Senior Visiting Professorship to an outstanding senior Canadian physiologist. This senior Visiting Professorship is named after Dr. F.C. (Hank) MacIntosh and is sponsored by the Corporate Patrons of the Canadian Physiological Society. The purpose of the Visiting Professorship is to promote collaboration and exchange between physiology departments and investigators at Canadian universities. The Visiting Professor is to be encouraged to visit two or more departments within the same region of the country so nominations can come from a single department or jointly from two or more. The Visiting Professor would be expected to spend several days at each institution giving seminars, meeting with other investigators and holding sessions with the department's graduate students.

The selection of the senior Visiting Professor will be the responsibility of the Council of the Canadian Physiological Society and will be based upon the scientific achievements of the candidates. Nominees for this award should be members of the Canadian Physiological Society and have made a contribution to the Society. Normally the Visiting Professorship will not be awarded to candidates before the tenth year from receiving their highest degree.

Nominations should be sent to the Secretary of the Society at the address given below. Each nomination must include a letter from the sponsor/s setting out the proposed itinerary, and a curriculum vitae of the candidate.

Individuals who wish to be considered for the F.C. MacIntosh Visiting Professorship are encouraged to approach departments for sponsorship, but they cannot apply directly. Letters of nomination and supporting documents should be sent to:

Dr. Penny Moody-Corbett
Division of Basic Medical Sciences
Memorial University
St. John's NF A1B 3V6
Telephone (709) 737-6890
e-mail pmoody@morgan.ucs.mun.ca

J.A.F. Stevenson Visiting Professorship of the Canadian Physiological Society

Each year the Canadian Physiological Society offers a Visiting Professorship to an outstanding young Canadian physiologist. The purpose of the Visiting Professorship is to promote collaboration and exchange of information among investigators at Canadian universities and to strengthen graduate training programs in physiological research.

The Society will provide travel expenses for the Visiting Professor; living expenses will be the responsibility of the host department. Nominations for the award are to be made normally by the Chair of the host department of physiology to enable a distinguished young investigator from another Canadian institution to spend two to seven days at the host department giving lectures and graduate seminars. The host department of physiology can be any one of the sixteen in Canadian university faculties of medicine.

The candidate chosen to receive the Visiting Professorship will also present a lecture at the Annual Winter meeting of the Society. Partial reimbursement of expenses to attend the Annual Winter Meeting will be the responsibility of the Canadian Physiological Society.

The selection of the Visiting Professor will be the responsibility of the Council of the Canadian Physiological Society and will be based on the scientific achievements of the candidate. Nominees for this award should be a member of the Canadian Physiological Society and in good standing for at least one year and should have contributed to the Society. Normally, the Visiting Professorship will not be awarded to candidates after the tenth year from receiving their highest degree. In the event that more than one host University has requested the chosen recipient, the University which first placed the request will be given preference.

Nominations should be sent to the Secretary of the Society at the address given below. Each nomination should include a letter from the sponsor setting out the proposed itinerary and include the curriculum vitae of the candidate.

Dr. Penny Moody-Corbett
Division of Basic Medical Sciences
Memorial University
St. John's NF A1B 3V6
Telephone (709) 737-6890
e-mail pmoody@morgan.ucs.mun.ca