GENERATING BOWEL MOVEMENTS THAT FACILITATE NUTRIENT ABSORPTION
DOI # 10.13034/CYSJ-2014-023

Jan D Huizinga¹, Ruihan Wei², Ji-Hong Chen¹,³, George Wright¹, Berj Bardakjian⁴

1 Farncombe Family Digestive Health Research Institute, McMaster University
2 Hillfield Strathallan College
3 Renmin Hospital at Wuhan University, Wuhan, Hubei, China
4 Institute for Biomedical Engineering, University of Toronto

ABSTRACT
When nutrients enter the intestine from the stomach, the movements of the intestine caused by contractions of the intestinal musculature (“intestinal motility”) have to fulfill the function of mixing the content with digestive enzymes and optimizing absorption by exposing all content to the lining of the gut. Intestinal motility is performed by smooth muscle cells and orchestrated by intestinal pacemaker cells and by a nervous system that is unique to the intestine. Movements to promote mixing are called “segmentation”, and movements that propel content along are called “peristalsis”. Peristalsis and segmentation in the human intestine are rhythmic and are governed by pacemaker cells called “interstitial cells of Cajal” or “ICC”. With peristalsis, a network of pacemaker cells generates a wave of electrical activity that propagates into the musculature and determines the rhythm and propagation of contraction, similar to the pacemaker system of the heart. A recent discovery published in Nature Communications revealed that the segmentation motor pattern is initiated by certain nutrients that activate a second network of pacemaker cells. This second pacemaker activity is an electrical rhythmic signal that interacts with the first pacemaker activity, modifying it in such a way that the musculature responds with a completely different motility pattern; it changes the nature of the contractions from peristalsis to non-propulsive segmentation.

INTRODUCTION
We eat a meal and almost never think about all that the body does to transform it into nutrients. Nutrients can be absorbed into the bloodstream through epithelial cells, which line the inside of the intestine. The nutrients then go to all cells in the body to keep them working. The mixing of food with digestive enzymes to extract the nutrients, and the exposure of the nutrients to the epithelial cells does not happen without proper motility, which occurs through highly organized contraction patterns of the musculature. We need muscle contractions to promote the mixing of food with enzymes for proper digestion (segmentation) and to move the food along the intestine (peristalsis; see box 1). Amongst the organizers of the contractions are specialized nerves and the pacemaker cells of the gut, the so-called interstitial cells of Cajal (ICC; see box 2). In the last decades we have learned a lot about peristalsis, but we still know very little about segmentation. We recently published a paper in the journal Nature Communications titled: “The origin of the segmentation motor activity of the intestine”. Here we will explain what was discovered through this research and some background on pacemaker activity in the gut.

METHODS AND RESULTS
Studying the movements of the intestine
We study the movements of the intestine by removing the whole intestine from a rat or mouse and then placing it in a physiological salt solu-
tion. Thereafter, we record the activities via a video camera. Then we use computer programs to analyze the video images. The computer places dots along the edges of both sides of the intestine in the video and then calculates the distance between opposite dots along the entire intestine, over the full duration of time of the video recording. When the intestinal musculature contracts, the intestinal circumference becomes smaller, the distance between the dots decreases. When the muscle cells relax, the distance between the dots increases. As a result, we get an image that shows all the movements of the intestine, called a “spatiotemporal map”. Figure 1D shows such a map. The diameter changes are shown on a white–black scale, with white being a contracted (narrow) intestine and black being a distended (wide) intestine. The movie shows video recordings of the two dominant motor patterns of the intestine – peristalsis and segmentation.

Measuring electrical activity in the intestinal musculature
Most of us have seen an electrocardiogram taken of our heart. To make this, electrodes are placed on our skin, leading to an image of the familiar heart rhythm, which is a reflection of the electrical activity of the heart. Electrical activity in the gut can be measured using similar principles. Figure 1A1 shows this electrical activity in the mouse at 28 / min, which was measured in vitro with highly specialized glass electrodes and equipment that magnifies the signal so that we can see it. We call this electrical activity in the gut a “slow wave” since it is much slower than the electrical activity of the heart. The slow wave is the pacemaker activity generated by interstitial cells of Cajal (see box 2). Walter Alvarez, a physician from the Mayo Clinic in the United States, recorded the slow wave electrical activity of the gut for the first time in 1911.

Studying pacemaker activity through calcium imaging
How can we make the pacemaker activity of the interstitial cells of Cajal visible? The rhythmic electrical activity is caused by rhythmic increases in intracellular calcium ions (Ca2+) that activate other ion channels in the ICC cell membrane, which cause the slow wave activity. ICC go from low intracellular calcium to high intracellular calcium in a rhythmic manner in order to achieve rhythmic pacemaker activity. We exposed cells to a dye that enters cells, and this dye becomes fluorescent (which means that it emits light that can be seen by a special microscope) when calcium, Ca2+, binds to it. The origin of the pacemaker activity – the rhythmic changes in Ca2+ – thus show rhythmic flashes of fluorescence. You can see the rhythmic activity of ICC-MP (see box 2) in the first part of movie 1.

The first discovery
The question we had asked ourselves for decades was: how does the intestine switch its motor pattern from peristalsis to segmentation when food arrives from the stomach? We assumed that the nerves of the gut were orchestrating a special program that made the muscle cells contract in a segmentation motor pattern. But one day in Dr. Kunze’s laboratory at McMaster University we witnessed serendipitously that the segmentation motor pattern can occur after all nerve activity is blocked. That discovery made us look to a different possible origin of segmentation - the gut pacemaker cells.

The second discovery
It is likely that many nutrients can induced the segmentation motor pattern; we chose decanoic acid for our experiments, which is a nutrient found in milk and coconut oil. When we studied the effect of decanoic acid on the gut pacemaker activity, we witnessed to our surprise that the pacemaker activity changed from activity with a regular amplitude (or strength of the signal (see figure 1A1 and 1C) to one where the amplitude waxes and wanes (decreases and increases in a rhythmic fashion; see figure 1A2). When we looked closely at the segmentation motor pattern in spatiotemporal maps (see figure 1C), we discovered that the amplitude of the contractions also showed waxing and waning. Simultaneously recording intraluminal
pressure changes (pressure inside the intestine) caused by circumferential muscle contractions also revealed a rhythmic waxing and waning pattern. At this point, we knew that the secret to the origin of segmentation was in the waxing and waning pattern.

What is the consequence of this waxing and waning? Without waxing and waning, a slow wave depolarization travels along the intestine with unaltered amplitude. This means that a circular muscle contraction consisting of a narrowing of the lumen and an increase in intraluminal pressure travels uninterrupted along the intestine, causing peristalsis (Figure 1D). However, when waxing and waning occurs, the slow wave amplitude goes from normal to very low in a rhythmic manner; the low amplitude is low enough to prevent contraction (see box 2). The electrical signal is still propagating but only short-lasting, non-propagating contractions are possible, which is the segmentation motor pattern (Figure 1C).

One way to change an electrical signal is to let it interact with another electrical signal; thus, we hypothesized that the waxing and waning was caused by a second electrical activity interacting with the slow waves. A close look at the electrical activity induced by decanoic acid revealed that the waxing and waning patterns contained two electrical oscillations, the original slow wave activity and another rhythmic activity at a much lower frequency (see figure 1A3), but at the same frequency as the waxing and waning pattern we had observed! We hypothesized that it was a second network of interstitial cells, the ICC-DMP (see box 2), which produced the activity that led to waxing and waning, and subsequently to segmentation. When we let a calcium imaging dye go into the ICC-DMP (see method above), we saw nothing without nutrient input. But when decanoic acid was given, we saw rhythmic changes in calcium, at a frequency that was much slower than the ICC-MP, but at the same frequency as the waxing and waning. Hence the ICC-DMP appeared to be pacemakers as well, but only when something stimulated them, like nutrients.

The third discovery
Many electrical activities move through our body. When we touch a hot object with one of our fingers, a nerve detects the heat, an electrical signal is generated (called a nerve action potential) and this signal travels to the brain through nerves. Because of this signal, the brain becomes aware of the heat and we are compelled to withdraw our finger. An electrical signal, the action potential, is the way the finger communicates with the brain. In the heart there is a pacemaker center in the sino-atrial node, which sends electrical signals out to all the muscle cells. In the intestine, in a network of interstitial cells, similar in principle to the nerve and the heart, the electrical signal is a rhythmic change in the cell membrane potential (called “slow wave” in the intestine). The slow wave is the signal of communication within the ICC network as well as the signal to communicate from the ICC to the millions of muscle cells that generate motility. Interestingly, the intrinsic properties of the ICC make them oscillate at different frequencies. However, they are electrically coupled which forces the oscillations to synchronize, that is, to act in unison. With the creation of a second pacemaker activity, the situation becomes even more complex. Now, pacemaker activities from two independent pacemaker networks (the ICC-MP and the ICC-DMP) travel (propagate) into the musculature where they interact. Hence the musculature experiences coupled oscillators.

Our understanding of the coupling of oscillators has a fascinating history and most likely a more fascinating future. The history starts with Christiaan Huygens, a scientist from the Netherlands who first noticed this phenomenon in 1665. Ill in bed on a ship, with nothing better to do than watch pendulum clocks that he had made, hanging on the wall, Huygens noticed that no matter where they started their individual oscillation, within about half an hour the two pendulums swung towards and away from each other in unison – they synchronized. Many examples exist in nature; a swarm of fireflies flash in unison, and our heart muscle cells contract as if they are one. Mechanical or electrical oscillations, when they are coupled,
will influence each other and will tend to synchronize.

What is the nature of the coupling of the pacemaker activities of the ICC-MP and ICC-DMP? We do not know enough about coupled oscillators to fully understand this, but we figured out that the signals did not simply add up, which would lead to an increase in the amplitude of the electrical signal; when we checked our results with decanoic acid we saw that there was no increase in the amplitude.

Scientists working towards understanding electrical communications in the brain have figured out different modes of communication. The phase of a low frequency signal can influence the amplitude of a high frequency signal. We used the methods the brain scientists have developed to find evidence for this type of coupling. We found that when the ICC-DMP activity is depolarizing (the cell is becoming less negatively charged (figure 1C)), the amplitude of the slow wave decreases, and when the ICC-DMP activity is hyperpolarizing (the cell is becoming more negatively charged (figure 1C)) the slow wave activity increases in amplitude. Thus, phase-amplitude coupling occurs within the musculature. This is the essence of our Nature Communications paper – the discovery of the origin of the waxing and waning nature of the electrical activity. We found that when this pattern is generated, segmentation can occur and we found a good explanation for why it happens.

WRAP UP

In Canada and around the world there are many patients that have problems with gastrointestinal motility. They may have frequent or constant pain caused by contractions; they may have frequent or chronic diarrhea or frequent or chronic constipation. It affects their quality of life very much; their ability to work, and their ability to contribute to society may be strongly diminished. Such patients will visit their family physician, who may send them to a gastroenterologist. The gastroenterologist may not be able to help the patients much since it is difficult (without motility measurements) to diagnose the problem effectively. There are few drugs available and those drugs will only help some, but not all patients, and again without measuring the motility in the patients, it is difficult to predict which drugs will be of benefit. The problem is that we do not know enough about the workings of the small and large intestine and why it does not work properly in some patients. We need more knowledge of how to measure motility in patients and how we should interpret the results of such measurements. Thus, we must gather more basic knowledge; our recent study published in Nature Communications, and many other studies by laboratories and clinics all over the world contribute to this knowledge.

Our study has increased our understanding of a fundamental control system that governs the types of movements of the intestine, which are required for specific circumstances. At night, most of the time the intestine is quiet, but every one and a half hours, peristaltic contractions sweep the intestine clean of remaining content and secretions. After a meal, we need a very different motility; we need to mix the content so that the nutrients are mixed with digestive enzymes and are constantly exposed to epithelial cells for absorption. Nutrients such as decanoic acid induce a pacemaker activity in a subset of interstitial cells of Cajal – the ICC-DMP – and this pacemaker activity interacts with the pacemaker activity that is always present and generated by ICC-MP. It is very likely that the gut nervous system can also induce this ICC-DMP pacemaker activity. The interaction of the two pacemaker activities within the musculature creates a waxing and waning electrical activity, which subsequently leads to a segmentation motor pattern. The strength of these contractions will depend on how much the musculature gets stimulated by the gut nervous system, which is also triggered by nutrients. It is clear that we are influencing the motility of the gut by our diet, so a healthy diet is important for a well functioning intestine. We are not passive bystanders to our health; we are active participants!

FUTURE DIRECTIONS

With every new discovery, many new questions arise! Does the intestine have many ways
to initiate the second pacemaker? Can we find out a way of doing this that might help patients that have problems with nutrient absorption? Is the second set of pacemakers abnormal in patients with motility problems? Can we promote segmentation to combat diarrhea? Does segmentation in the large intestine occur in a similar manner to that observed in the small intestine? Our more recent work found that butyric acid, which is produced by bacteria in the intestine, can also evoke the second pacemaker activity. Is this an essential component? What if the bacteria in the intestine have a composition that does not produce butyric acid? So you see, there are always more questions than answers, and in this way medical research will remain fascinating for medical scientists and physicians. And all this research will slowly but surely find its way to better diagnoses and better treatments for patients with intestinal motility problems.

THE TWO MAJOR MOTILITY PATTERNS OF THE INTESTINE: PERISTALSIS AND SEGMENTATION

Box 1
When we eat a meal, our gut wakes up and responds with thousands of actions that have a clear purpose: to bring nutrients to every cell in the body and to remove waste. Gut motility is crucial for this process. When motility goes wrong, we experience constipation or diarrhea, both of which make us very uncomfortable. As the Chinese philosopher Lin Yutang (1895-1976), who spent years searching for the secret to happiness, wrote: “when our bowels move, we are happy, if they don't move, we are unhappy.”

Peristalsis is the term used to describe the motility pattern that moves content from the oral to the anal end of the intestine, similar to squeezing toothpaste out of a tube. The gut is essentially a muscular tube. Hundreds of muscle cells at one position of the gut contract as a ring around the whole circumference and this contraction moves to the anal end, pushing content in front of it. Pacemaker cells orchestrate this; they determine the frequency and velocity of peristalsis by synchronizing the contractile activity of the muscle cells. The smooth movement of peristalsis occurs because all the thousands of ICC pacemaker cells are coupled oscillators, which synchronize their behaviors. Our laboratories made important contributions to our understanding of the role of ICC in motility using spontaneously mutated mice that do not have ICC-MP. These mice do not produce slow waves and they do not produce normal peristalsis. Clinically, some drugs that promote gut peristalsis are available for patients that move food along too slowly.

Segmentation has been recognized for more than 100 years; however, how the body creates this motor pattern has remained a mystery. We now have solved part of this puzzle. Segmentation is non-propulsive contractile activity. It mixes the content of the intestine with digestive enzymes and brings nutrients into contact with the lining of the intestine for absorption. Many parts of the intestine contract for a few seconds and then relax again. The next moment other parts contract and relax; this all occurs in a rhythmic manner at the frequency of the gut pacemaker activity. The Nature Communications paper provides for the first time, evidence for an elegant hypothesis as to how segmentation is connected to slow wave activity. It is as if the propagating peristaltic movement is chopped up into small parts, so that no effective propulsion is happening. Although it is chopped up, one can still recognize the frequency and organization related to slow waves. The chopping up occurs because a second pacemaker, induced by nutrients, oscillating at a much slower frequency, is interacting with the first pacemaker activity, such that the slow waves are not uniform anymore, but rather they wax and wane in amplitude and create distinct non-propagating contractions. So far, we do not have medications to enhance segmentation for patients with the inability to perform sufficient segmentation.

INTERSTITIAL CELLS OF CAJAL (ICC) AS PACEMAKER CELLS OF THE INTESTINE

Box 2
It is fascinating that most movements of the gut occur very rhythmically. The intestinal wall
is made up of many types of cells, including muscle cells that generate contraction or motility, epithelial cells (the lining of the gut) that bring nutrients from the lumen into the bloodstream, and secretory cells that release enzymes into the lumen for digestion. The orchestration of motility is carried out by gut nerve cells, and the pacemaker cells of the gut, which are known as the interstitial cells of Cajal. Think of the workings of a car. The gas tank, the engine, and the steering wheel, each has its own function. All are specialized and sophisticated, but none can perform the function of a car on their own. They need each other to make driving possible. So it is with most organs in the human body that they have specialized cells, each with their own function, and together they make an organ work.

*How were the interstitial cells of Cajal discovered?*

Santiago Ramon y Cajal was a passionate Spanish artist who lived from 1852 to 1934. His father discouraged his artistry and forced him to study medicine. When during his medical studies he looked through a microscope, he became fascinated by what he saw; to communicate his excitement to others he started to draw what he witnessed through the microscope. When Dr. Ramon y Cajal studied the gut nervous system he discovered what later would be called the interstitial cells of Cajal, which are positioned between nerves and muscle cells in the gut (Figure 2). His drawings were extremely insightful and so he combined his passion for medicine with his passion for the arts! Ramon y Cajal received the Nobel Prize in medicine in 1906 for his contributions to our understanding how the nerve cells work. He is now considered the father of neuroscience.

*How did medical scientists working on the intestine realize the importance of ICC?*

This happened when an anatomist from Denmark, Lars Thuneberg, went to a conference of gut physiologists in 1983 and told them about these cells, suggesting that they were the pacemaker cells of the gut. He and Maria Simonetta Faussone Pellegrini from Italy discovered many types of ICC and we are slowly starting to understand their function.

*What are pacemaker cells?*

The pacemaker cells of the heart make the contractions of the heart rhythmic. That is, each contraction is short and followed by muscle relaxation, and this happens over and over again in a very rhythmic manner of about 60 times per minute. The human intestine contracts 12 times per minute, and the mouse intestine 40 times per minute, like clockwork. Both peristalsis and segmentation (box 1) have this rhythm. The peristalsis can be seen in the second part and the segmentation movements in the third part of movie 1. This paper deals with the transition between peristalsis and segmentation; how does our body switch from peristaltic activity to segmentation activity? The pacemaker cells of the gut, the interstitial cells of Cajal, together with the nerves in the gut, orchestrate all of these rhythmic contraction patterns. Unlike the heart, which has a clump of about 500 pacemaker cells, the intestine has networks of these cells throughout the whole gastrointestinal tract. In the intestine there are two networks of interstitial cells of Cajal, which we call ICC-MP (figure 1A1) and ICC-DMP (figure 1A3). ICC-MP are connected to a network of nerves which are called the Myenteric Plexus, hence the abbreviation ICC-MP. ICC-DMP are connected to a network of nerves that are called Deep Muscular Plexus, hence the abbreviation ICC-DMP. A cell body of single ICC is about five thousandths of a millimeter wide, but they are all electrically connected so that they work as a network. Before we conducted our study, there was no evidence that these networks communicated with each other.

*What exactly is pacemaker activity?*

The pacemaker activity is an electrical activity that orchestrates the rhythmic muscle mechanical contractions. The intestinal wall contains a thick layer of muscle cells oriented circumferentially that all work together (the musculature) to create contractions. A network of ICC-MP (see box 2) generates electrical pacemaker activity, in the form of a repeating electrical oscillation of the cell membrane potential, also
called a “slow wave”, occurring at around 12 oscillations per minute in humans. Normally the inside of every cell is negatively charged compared to the solution that surrounds the cell. This gives the cell a membrane potential, which is the difference in potential between the inside and outside of the cell. The normal membrane potential is about -60 mV. The slow wave brings the membrane potential of the muscle cells, for a few seconds, from about -60 mV to -20 mV; it does this 12 times per minute in the human intestine. How does the slow wave cause rhythmic contractions? At -60 mV, calcium ion channels in the cell membrane are closed; they open up at -20 mV and when calcium ions rush into the cell, the muscle cell contracts. Hence the pacemaker cells force the musculature to contract in a rhythmic manner. Also, the slow wave propagates from the proximal to the distal end of the intestine; hence, the pacemaker activity also determines the direction and velocity of propagation of the muscle contraction. The slow wave causes a depolarization of a ring of circular smooth muscle cells, causing a local ring contraction, which leads to a narrowing of the lumen. Then this depolarization travels uninterrupted along the intestine, creating an uninterrupted wave of the narrowing of the lumen, which pushes the content distally.

A second network of interstitial cells of Cajal, the ICC-DMP, has been known to exist but their function has been unclear. Our recent Nature Communication paper provides evidence that the ICC-DMP generate a second pacemaker activity that changes the nature of the slow wave activity. The ICC-DMP activity is instrumental in determining whether the intestinal contractions are propulsive (moving content along) or whether they produce segmentation (to promote mixing and absorption of nutrients), as explained in the main text.

ACKNOWLEDGEMENTS
Financial support for all the work discussed came from the Canadian Institutes of Health Research (CIHR) and the Canadian National Science and Engineering Research Council (NSERC).

Figure 1  Structure and electrical activities of interstitial cells of Cajal and the segmentation motor pattern
A. Here you see images of the structure of interstitial cells of Cajal (see box 2), ICC-MP (top image), the layer of muscle cells (middle image) and the ICC-DMP (bottom image). The size of a cell body is about 0.01 mm. Superimposed on these images you see a recording of the electrical pacemaker activity of ICC-MP, of the waxing and waning of the pacemaker activity (middle image) and of the pacemaker activity of the ICC-DMP.
B. A still image taken from a video recording of the movements of the intestine, showing segmentation with several contractions occurring simultaneously along the intestine.
C. A schematic drawing of slow wave activity. Slow wave activity is a repeating electrical oscillation of the cell membrane potential. It has a strength or amplitude expressed in millivolts (mV). The upstroke causes the cell to depolarize (become less negative inside) (D) and the downstroke causes the cell to hyperpolarize (become more negative inside) (H). D. A “spatio-temporal map”, showing contractions (white) and relaxations (black) of the intestine.
changing over time. This is segmentation, short rhythmic contractions occurring all along the intestine. The black box shows that there are no uninterrupted waves of contractions that can push content in front of it; we see contraction, relaxation, contraction, relaxation. This allows for mixing but not propulsion.

E. A “spatio-temporal map”, showing contractions (white) and relaxations (black) of the intestine changing over time. This is peristalsis – long uninterrupted contractions that travel along the intestine. The black box shows that each wave of contraction is uninterrupted so that the resulting narrowing of the lumen can push content in front of it.

**Figure 2  Interstitial cells of Cajal, drawn by Santiago Ramon y Cajal in 1911**

The Spanish neuroscientist Ramon y Cajal discovered a cell type in the gut that connected gut nerve cells to the gut muscle cells. Later these cells were called “interstitial cells of Cajal”, abbreviated to ICC. Ramon y Cajal drew this picture of an ICC network after observing it through a microscope from preparations made from the rabbit small intestine. The black cells are ICC, and the large trunks in the background are bundles of nerves.

**MOBILE LEGEND**

*Rhythmic gut pacemaker activity, peristalsis, and segmentation*

The discoveries described here were reported on by the Canadian Broadcasting Corporation. The CBC also made a movie to illustrate the story based on material we provided. In the first part you see the rhythmic activity of the intestinal pacemaker cells of the mouse small intestine the ICC-MP (see box 2) shown through calcium imaging (see main text). The second part of the movie shows peristalsis, the third part of the movie shows segmentation (see box 1).

**RESOURCES**

1. The original research
   a. This manuscript is an explanation of the major features of a recent discovery on how the intestine creates contraction patterns (motility) to facilitate absorption of nutrients.

2. Understanding coupled oscillators.
   a. The origin of our thinking about coupled oscillators, the Christiaan Huygens story.
   b. The paper we used for the method to proof
Q&A WITH PROFESSOR JAN D. HUIZINGA

How would you describe your scientific approach?

I am trying to find the most clinically relevant questions in the field of gastroenterology that are linked to my scientific expertise and to the methodologies available in my laboratory. When the resulting research demands techniques or expertise outside my area, I will seek collaboration. In my first Nature paper, I knew that my idea to find proof of interstitial cells of Cajal being pacemaker cells was good, but I needed and found colleagues at the Universities of Copenhagen and Toronto to make it happen. In the study published in Nature Communications, I worked together with Wuhan University in China. In addition, I did not know enough about the science of interacting electrical activities and so I sought collaboration with Professor Bardakjian at the University of Toronto.

What is your day-to-day work life like as a medical research scientist?

I spend most time of the day in the laboratory. One typical day would proceed as follows. I would discuss with a student a technical problem, then I would discuss with a post-doctoral fellow a new research approach to a problem that we have difficulty solving. Next, I would spend a few hours writing a proposal for further research in order to get money to make the research possible (most of the money I need is for paying salaries for the people in my lab). This would be followed by preparing a talk that I would have to give in a few weeks time, and then I would organize some teaching that would occur in the Honours Biology Pharmacology Coop Program at McMaster University, since I am the director of that program. Finally, I would write for a few hours to make progress on a manuscript related to the latest project that we would submit to a scientific journal. I usually work on 3 or 4 manuscripts at the same time, dealing with different topics and having different people working on them.

What is the most fulfilling aspect of working in your research field?

The most fulfilling aspect is to see a student becoming very exciting when an experiment that we designed together shows success and we...
feel that we eventually will solve the problem we identified.

What are the biggest challenges faced by your field of research today?

It is always a challenge to obtain financial support for basic research and to find the right people to help with conducting the studies. Despite all the challenges, my field of research moves in the right direction by increasing the collaborations between physicians and scientists.

What are some of your research goals?

My research goals are to understand the properties of interstitial cells of Cajal, the pacemaker cells of the gut. My goal is to understand this from a basic science point of view as well as its clinical relevance. No cell in the body acts alone so in understanding the physiology of ICC one aspect of my research will always deal with how the ICC interact with their partners, the smooth muscle cells, the nerve cells and other cells such as fibroblasts.

Many patients have problems with the movements of the gut. For example, chronic constipation is a big problem in Canada. We know very little about what exactly is not working in the small and large intestine. I want to make McMaster University a centre of excellence in measuring and interpreting the movements of the intestines in patients and thereby advising on therapy, and I want to work towards better understanding the underlying mechanisms of the disease.

In what direction do you see your field moving?

I want to strengthen international collaborations and promote collaborations between basic scientists and physicians all interested in the same topic – making Canadians healthier with respect to bowel function.

What advice would you give to high school and undergraduate students interested in medical research?

To high school students I would suggest participating in science fairs, and exploring your school library for physiology textbooks. If one of your friends or a family member becomes ill, explore the internet for more information. Try to understand how the human body works and take good care of your body.

To undergraduate students I would suggest trying to get into a program that gives you work experiences in the academic world and in the industry to get real life experience in research. After graduation, try to get into health sciences, biomedical sciences, biomedical engineering or biophysics. Or try to get into a MD / PhD program to become a physician and a scientist.