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Les Académies des arts, des lettres et des sciences du Canada

BULLETIN DE L'ACADÉMIE III
ACADEMY III BULLETIN

VOLUME: 1 — ISSUE: 1

In This Issue

Introduction to the Bulletin of the Academy of Science, by the President of the Academy

Welcome to the first issue of the Bulletin of the Academy of Science. There has been a long-standing need for some regular means of communication among Fellows, and this Bulletin is intended to provide a channel for exchanging news and views. There have been some important developments in the Academy in the past year, but they are not often manifest to members. This Bulletin will keep you up to date with recent developments and show you how the Academy is contributing to the public life of Canada. We hope that this will be a two-way affair, and encourage you to tell us about Academy-related events or issues at your institution. The Honorary Editor, Betty Roots, will be glad to include your material in subsequent issues of the Bulletin. We expect to be publishing three times annually from now on and invite your suggestions about the kind of material that you think we should cover.

- Dr. Graham Bell, President of Academy III

Note from the Editor

In this first issue of the Bulletin of the Academy of Science, the President of the Academy, Professor Graham Bell, reports on activities of the Royal Society of Canada having particular relevance to the Academy and invites comments and suggestions from Fellows.

By and large we know little of our colleagues' activities and the contributions they make to Canadian society. A recent innovation of Academy III at the Annual General Meeting (AGM) of the Society was to invite some newly elected Fellows to give presentations on their work and interests in non-technical terms. Unfortunately, for a variety of reasons, only a small proportion of Fellows attend the AGM. The Bulletin provides a means of reaching a wider audience thus this issue includes contributions from two new Fellows. One from the Division of Applied Sciences and Engineering and one from the Division of Mathematical and Physical Sciences.

Like Professor Graham, I also urge you to submit suggestions and material to me for inclusion in the Bulletin.

Betty Roots, Hon. Editor

President's Message

The political meeting of the G8+ heads of state is traditionally preceded by a meeting of the G8+ Academies of Science to discuss the themes announced by the host government. In 2010 it was Canada's turn to host the summit, and RSC therefore had the responsibility of hosting the Academies. The two themes chosen by the government were Health of Women and Children, and Innovation for Development. Both had controversial aspects – the former, in particular, aroused a lot of public comment.

We first chose the lead writers for each theme, one Canadian and one foreign, who prepared draft statements that were circulated among the Academies. These were discussed and modified at the meeting in Ottawa on 7-8 April. We then went through them line by line (and in some cases word by word) to get unanimous agreement on a final version. Once both had been signed by everyone they were transmitted to the government as a guide to the current state of informed opinion. The complete joint statements on the Health of Women and Children, and Innovation for Development can be found on the RSC website.

From one point of view this was a very successful operation: the drafts were well-prepared, the meeting was productive and the statements were agreed unanimously and delivered on time. We undoubtedly rose in the estimation of our peers as an Academy that can get things done. From another point of view, we have no idea whether these statements were effective in guiding policy development. There was a general feeling after the meeting that we should establish a procedure for evaluating the statements to find out whether governments take them seriously enough to justify the time, effort and money spent in developing them. We shall undertake this next year, as part of the planning for the next G8+, which will be hosted by the National Academy of Sciences.

IANAS in Ottawa

The other big event of 2010 was the triennial General Assembly of the InterAmerican Network of Academies of Science (IANAS), which consists of all the national Academies of Science of the hemisphere. IANAS is important because it offers the only opportunity for the representatives of almost every country in North, Central and South America to meet face-to-face to discuss issues of common interest. In particular, it has set up four working groups to cover four critical areas: water, energy, women in science and science education. These four groups reported at a one-day symposium held in late August at the International Development Research Centre in Ottawa. The General Assembly itself took place over the next two days. Both events were entirely successful and strengthened the links between the academies.

Expert Panels

One of the most important initiatives of RSC is to set up Expert Panels to report on issues of current concern. These issues are often scientific or technical, so the panels are particularly relevant to the Academy of Science. There are currently four panels in the process of preparing reports.

(1) Environmental and Health Impact of Canada's Oil Sands Industry (chaired by Steve Hrudey, University of Alberta).
(2) Sustaining Canada's Marine Biodiversity: Responding to the Challenges Posed by Climate Change, Fisheries and Aquaculture (chaired by Jeff Hutchings, Dalhousie University).
(3) End-of-Life Decision Making (chaired by Udo Schuklenk, Queen's University).
(4) Early Childhood Development (chaired by Clyde Hertzman, UBC, and Michel Boivin, Université Laval).

These reports complement those issued by the Council of Canadian Academies, which RSC contributes to. They differ in that they are not commissioned by government, and so give a wholly independent expert appraisal of an issue identified by the membership. Any Fellow may suggest topics for an expert panel, and we welcome any suggestions that you have.

"Young Academy"

An idea that is gaining momentum is to set up an organization within RSC to accommodate scientists in the most active and productive period of their careers, before the usual age of election to Fellowship. The size and composition of this new academy, the procedure for choosing its members and its relationship with the Academy of Science are beginning to be discussed, and the President has set up a working group to investigate such issues. Absolutely nothing has yet been decided – not even the name - and your advice will be very welcome. Please write to say whether you think that the idea is sound, and if so how we should proceed with implementing it.

How to contribute

The Expert Panels and the "Young Academy" are only two examples of activities where we depend on the willingness of volunteers to advance the program of RSC. There are many other examples: nomination and selection committees, divisional officers, international relations, lecture series, university representatives, regional chapters – all of these and more require people willing to serve. If you would like to participate more actively in the affairs of the Academy of Science, please write to us describing where your interests lie. We would love to hear from you.

Medicinal Inorganic Chemistry

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Medicinal inorganic chemistry is the application of inorganic chemistry to the therapy or diagnosis of disease.[1,2] Much of traditional medicinal chemistry is closely focused on organic compounds containing the elements in the top right hand corner of the Periodic Table, the big six freely available elements – carbon, nitrogen, oxygen, phosphorus, sulfur and hydrogen. Because nature uses so many metallic elements to effect chemical transformations *in vivo* and in the environment - about 35% of all enzymes are metalloenzymes - we simply ask the question: Could the metallic elements, about 80% of the Periodic Table, be useful in the chemical design of new diagnostics and therapies? Nature uses such metals as manganese, iron, cobalt, nickel, copper and zinc…why not medicinal chemists?

Many of the afore-mentioned metallic elements are essential for life; molecular design can be employed to optimize the concentration range for optimum physiological response of all compounds, including those that contain metals as ions, even those commonly thought of as toxic.[3] Once the element and oxidation state have been chosen, molecular design can be used to optimize speciation and biochemistry, thereby yielding a new chemical entity of potential as a drug. Indeed, there are many inorganic compounds in clinical use today, compounds such as cisplatin for the treatment of numerous cancers, alone or in combination, Magnevist™ for magnetic resonance imaging (MRI) contrast and two dozen technetium-99m agents for single photon emission computed tomography (SPECT) in nuclear medicine; these incorporate, respectively, the elements platinum Pt, gadolinium Gd and technetium Tc, none of which has known natural biological roles. Why then is there still such resistance to metal-containing compounds in the pharmaceutical industry? The best answer remains the important leadership roles that organic chemists have assumed in that industry over many decades. This has led naturally to a focus on organic chemistry – in the 21st century with so many traditional drugs coming off patent concomitant with the growing innovation gap and the closing/amalgamation of big pharma research centres, the time has clearly come to take a less traditional approach. Inorganic

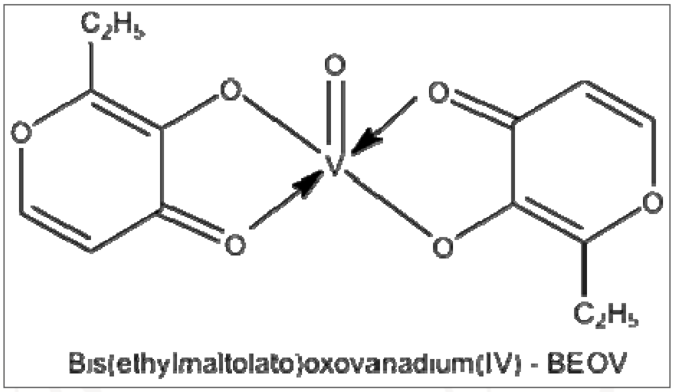


Figure One

compounds, analogues of such stalwarts as cisplatin [*cis*-$Pt(NH_3)_2Cl_2$], the archetypal example containing as it does not one atom of carbon, deserve a closer look as they already occupy an important but often misunderstood role in the pharmacopoeia.

Such compounds will consist of one or more metal ions surrounded in the chemical "clothing" of ligands, organic molecules that stabilize the oxidation state and exchange chemistry of the metal ion. BEOV, the ethylmaltol compound of oxovanadium (IV) (VO^{2+}, vanadyl), has completed a small phase 2 clinical trial for type 2 diabetes under our aegis[4] and presents an excellent example. The ethylmaltol anion wraps the oxovanadium(IV) core in an organic "sheath" which is oxygen-rich and imparts to the compound useful properties such as water solubility and high bioavailability, making it an excellent agent for diabetes therapy exploiting the inherent insulin-enhancing properties of vanadyl.

The introduction of such inorganic or coordination compounds (incorporating ligands coordinated to a metal ion) into the human body is fraught with competing reactions. The blood and other compartments contain many small molecules (e.g. ascorbate, citrate, glutathione) and numerous larger proteins (e.g. transferrin, metallothionein, serum albumin) that are capable of stripping a coordination compound of its ligands, binding the metal ion tightly, and altering its biodistribution often towards undesired toxic storage, or elimination. To a medicinal inorganic chemist, the body can be considered as a large soft test tube of competing ligands. Hence, molecular design of coordination compounds is a critical component of inorganic drug design.

Over the last quarter century, I have been involved in many research projects comprising molecular design of metal compounds for medicinal purpose. In addition to the previously noted insulin-enhancing vanadium pharmaceuticals, my group at UBC in recent years has studied, originated and contributed to projects in carbohydrate conjugates of ^{99m}Tc and ^{186}Re (rhenium) for nuclear medicine, ferrocenyl-carbohydrate conjugates in malaria therapy, lanthanide compounds for bone resorption disorders, gallium antimicrobial agents, glycosylated pro-drugs for metal passivation in neurodegenerative diseases such as Alzheimer's and ^{68}Ga (gallium) conjugates in positron emission tomography (PET) with Canada's leading isotope provider Nordion. Imaging (whether radiation in nuclear medicine, or magnetization in MRI) presents unique opportunities in

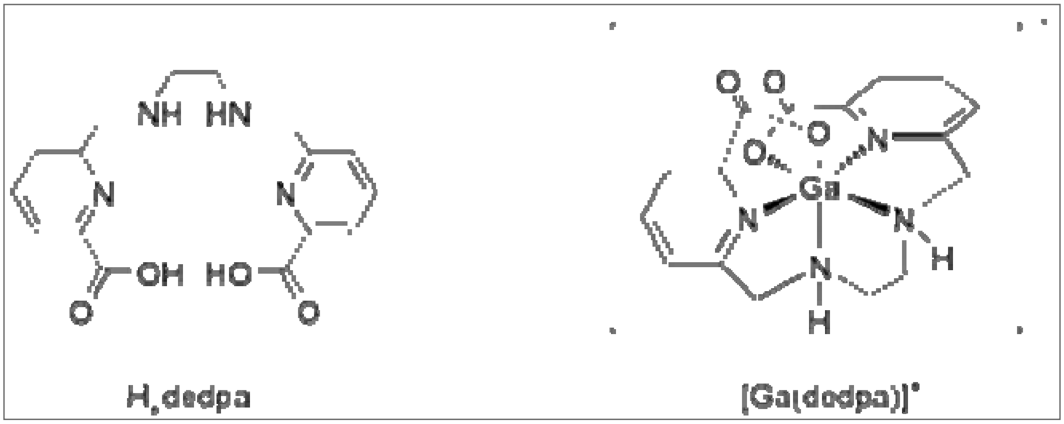
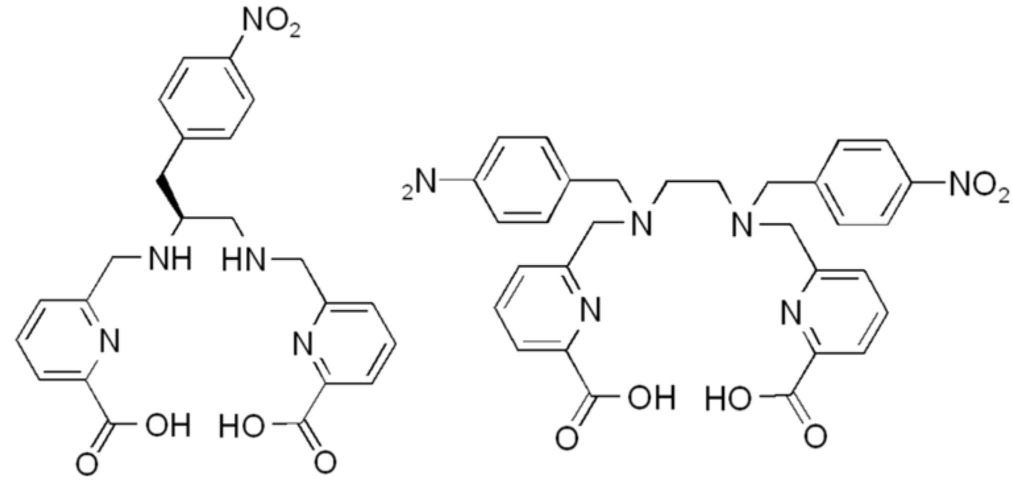


Figure Two

medicinal inorganic chemistry because, in order to achieve specific sets of desirable and detectable properties, the most likely elements will be metallic - the Periodic Table is about 80% metals.

The ideal g-emission properties of ^{99m}Tc have led to its compounds being used in many millions of medical procedures per year around the world – two dozen different products incorporate this isotope into agents for SPECT; however, there is currently a sporadic supply crisis due to the aging National Research Universal (NRU) reactor at Chalk River, and various problems at some of the five other locations outside North America. There is no American source despite the USA being the world's largest medical market. This has sparked interest in other isotopes that might complement or even replace ^{99m}Tc to alleviate the supply problem for an aging population that will require increasing numbers of procedures. Our interest has been drawn to gallium because it has two isotopes of interest in nuclear medicine, ^{67}Ga, a g-emitter, and ^{68}Ga, a b^+ (positron) emitter.

Having a biological chemistry and ionic size analogous to iron Fe^{3+} (without the associated easy reduction to Fe^{2+}), Ga^{3+} coordination chemistry in aqueous solution (water being most relevant to medicinal probes) presents not only an interesting scientific topic, but one with significant application upside. Indeed, in a project funded by Nordion and NSERC (via the CRD programme), we have already made significant headway in discovering a recently reported[5] ligand system (H_2dedpa) that binds Ga^{3+} isotopes[6] to form $[Ga(dedpa)]^+$ and incorporate design elements that allow conjugation to biologically targeting moieities. $[Ga(dedpa)]^+$ is formed in 10 minutes at room temperature with both ^{67}Ga and ^{68}Ga, providing a simple 1:1 compound with a desired symmetric hexadentate coordination environment. Concentration-dependent *in vitro* solution studies show that the ligand labels (binds gallium) at very low concentrations (10^{-7} M) with high radiolabeling yield (>97%) and specific activities up to 9.8 mCi $nmol^{-1}$. These positive results are not surprising in light of the very high thermodynamic stability of the binary compound (log K = 28.11(8)[6]) that results from the perfect fit of this ligand to the Ga^{3+} ion. The ligand's two halves each bind one meridian of the Ga octahedron such that the corresponding bond lengths and angles in each half are identical.



Mono- and bi-functionalized analogues of H_2dedpa

Figure Three

Under more physiologically relevant conditions, $[Ga(dedpa)]^{+}$ also shows strong stability when the ^{67}Ga-labelled complex is challenged with the iron transport protein transferrin, maintaining its integrity even after two hours challenge at 37˚C. Biodistribution data obtained *in vivo* for the labeled compound $[^{67}Ga(dedpa)]^{+}$ (mice) show that it is cleared nicely from all the organs, except the renal excretory system, suggesting that $[Ga(dedpa)]^{+}$ is a "blank canvas" to which we can now apply biologically-relevant functionality in order to drive it to appropriate compartments in the body for imaging purposes.

Indeed, intense chemical synthesis studies are now underway to design robust dedpa-analogues carrying functionality such as a peptide, protein, or small molecule that will direct the Ga-dedpa-conjugate via specific receptor interactions. So far we have successfully functionalized once the ethylene backbone or twice the aliphatic N atoms with nitrobenzyl groups – these nitrobenzyl derivatives are easily synthetic precursors for conjugation to biomolecules in order to make the receptor-specific interactions.

Molecular design is a significant contributor to medicinal inorganic chemistry. The chemistry inherent in the architecture of molecules present fascinating and rewarding intellectual challenges that also may have significant benefit to humankind.

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Biography

Chris Orvig was born and raised in Montréal. He received his Hons. B.Sc. in chemistry from McGill University in 1976 and subsequently completed his doctorate (as an NSERC of Canada scholar) in technetium chemistry at MIT supervised by Prof. Alan Davison, FRS. After an NSERC postdoctoral fellowship with Prof. Kenneth N. Raymond at the University of California, Berkeley (1981-83) and one year with the late Prof. Colin J. L. Lock at McMaster University, he joined the Department of Chemistry at the University of British Columbia in 1984 as an NSERC URF, where he is now Professor of Chemistry and Pharmaceutical Sciences, and Director of the Medicinal Inorganic Chemistry Group, as well as graduate advisor. His scientific interests are firmly based in the areas of medicinal inorganic chemistry and coordination chemistry – he has been involved over the years with radiopharmaceutical chemistry, metal ion decorporation, and metal ion neurotoxicology, as well as chemotherapeutic metal complexes and ligands. Orvig chairs the editorial board of *Dalton Transactions,* has received various research and teaching awards, has published more than 200 research papers, and is a co-inventor on many issued patents; he is also a certified ski instructor.

Multimedia Data: Problems and Research

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Introduction

This short paper summarizes some issues of multimedia data and focuses on two areas of current research, the area of content based image retrieval and 3-D filtering.

Multimedia Signal Processing

Multimedia is often defined as "media and content that use a combination of different content forms". Usual content forms include text, audio, still images and video. Multimedia Signal Processing is an area of rapid growth, which applies signal processing tools to multimedia content, in order to enable efficient representation, interpretation, encoding and decoding. Typical multimedia applications include among others, GPS navigation, 3D-TV, scalable video streaming, telepresence, e-commerce, cellular telephony and iPad-type of devices.

The usual multimedia application goals include improvement of interpersonal communications, promotion of the understanding of ideas, increase in interactivity of media and increase of accessibility to data.

The recent and rapid expansion of internet usage (Table 1) [1] has resulted in a dramatic increase of different types of multimedia data, which are transforming the entertainment industry. Such data are used in applications, such as business communications, medical imaging, video games, high-definition TV, 3-D imaging and video, while the proliferation of social network technologies are impacting society through the introduction of new methods of marketing and socializing and are often resulting in social revolutions.

Present trends indicate that users (society) demand increased mobility, ease-of-use, personal customization, device flexibility and a high level of collaboration with peers. In addition devices tend to mutate and become multi-functional, effortlessly portable and ubiquitously networked.

While new generations of such devices are contributing to the evolution of our society and occasionally are causing revolutions, they are presently being transformed and their evolution leads to convergence. This refers to the unification under

WORLD REGIONS	CURRENT USERS	% WORLD USERS	GROWTH (2000-2010)	PENETRATION
NORTH AMERICA	266,224,500	13.5%	146.3%	77.4%
EUROPE	475,069,448	24.2%	352.0%	58.4%
ASIA	825,094,396	42.0%	621.8%	21.5%
MIDDLE-EAST	63,240,946	3.2%	1,825.3%	29.8%
AFRICA	110,931,700	5.6%	2,357.3%	10.9%
LATIN AMERICA & CARIBBEAN	204,689,836	10.4%	1,032.8%	34.5%
OCEANIA & AUSTRALIA	21,263,990	1.1%	179.0%	61.3%
WORLD	1,996,514,816	100%	444.8%	28.7%

Table 1. World Internet Usage (June 30, 2010)

the concept of multimedia of different technologies, which developed independently and were unrelated only ten years ago.

Content Based Image Retrieval (CBIR)

The recent flood of digital media, caused by the rapid increase of internet usage, the proliferation of different types of devices and content has led to the realisation that there is a great need for efficient Content Based Image Retrieval (CBIR).

A digital camera, for example, allows a person to save thousands of pictures on a hard drive, while a digital camcorder requires gigabytes of space to store hours upon hours of footage and, as if that was not enough digital audio compression has turned computers into super juke-boxes. As exciting as these applications might be, it is becoming increasingly evident that an increasing effort should be spent in maintaining, organising and storing this large amount of digital data.

Since we are experiencing a device function convergence, which is caused by the fact that data are generated by many types of devices, while the internet acts as a global transport for the data to be consumed by many different devices on demand, there is an increasing need to efficiently store, accurately index and easily retrieve image, video and audio data.

A simple model for a CBIR system can be described as follows: "For a given query (example image, rough sketch, explicit description, colour and texture content) return all similar images within a set of existing images." More complex demands on data retrieval and organisation are found in "automatic albuming", which refers to the automatic creation of artistically satisfactory albums containing the images and sounds belonging to a superset of data. Such albums should satisfy complex human requirements.

For these reasons CBIR is a rapidly expanding area, which combines high-tech elements from a number of well developed disciplines, such as multimedia signal/image processing, computer vision/pattern recognition, computer sciences and more traditional concepts originating from psychology/human perception, aesthetics and information sciences.

A fundamental question that often arises in the development of such methods "Why not simply index using text?" This type of approach, although intuitive has been tried in the past and is both simple and simplistic, time consuming, inflexible, highly subjective (user dependent), time consuming and difficult to automate, as well as being susceptible to translation problems.

The primary CBIR application areas are:

- Medical Imaging
- Art and Cultural Heritage applications
- Design and Visual Arts
- Entertainment industries
- Industrial applications
- Government and Security related applications

Improved methods that are being developed by our University of Toronto research group at the Multimedia Signal Processing Laboratory are more powerful, being able to address effective queries in colour, texture and shape, simple hybrid queries (descriptor super-vectors, weighted averages of dis/similarities) and are also able to utilize "relevance feedback", which is provided by a user placed in the loop, statistical approaches, and apply/adjust feature weights to relevant/irrelevant elements. An example of such a system developed is shown in Figure 1.

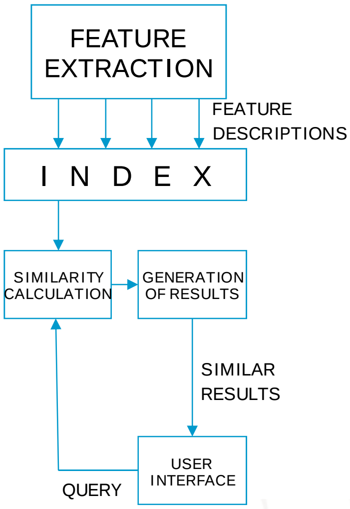

Figure 1. CBIR Basic System

Three-Dimensional (3D) Filters

In recent decades we have seen transitions in imaging going from black and white to colour, and now from two-dimensional (2D) to stereoscopic (3D). As content and technology becomes widely available, we will be seeing an increasing amount of stereoscopic images. Some of the technology that is currently available includes 3D cinema (ex. IMAX 3D), 3DTV, 3D games on the PS3, and 3D digital cameras. In the future an increasing number of applications will evolve into 3D, including but not limited to medical, telepresence and advertising.

Today, 3D image processing is a busy area of research because it is commercially promising and a large number of problems remain to be solved. The simple way to approach the solutions of these problems is to revert back to the methodology developed in the solution of 2D problems. However 2D solutions cannot always be generalised for 3D.

Stereoscopic images are preferable in most applications because they are more "life-like", since they encompass depth. The way that the human observer perceives depth is by seeing two different views of the same scene. When seeing these two images, the brain fuses them together, creating a sense of depth in a process called "stereopsis". The greater the disparity between the left and the right images, the greater the amount of depth perceived.

In image processing, many of the successful techniques operating in 2D can't be directly applied to 3D because they do not directly consider the depth in the image. Even elementary operations such as linear filtering and edge detection (which are the main building blocks of many larger imaging systems/processes) need to be extended to 3D in order to produce effective results that will preserve the appearance of depth. This extension can be made possible by taking advantage of the additional depth information that is available.

Some of these imaging techniques are currently being investigated by our image processing group at Ryerson University. Our research interests include the extension of 2D filters into 3D, and the design of 3D filters for general stereoscopic image processing applications [3]. We envision that the impact of this research will not only lead us towards new tools that can be used in future stereoscopic image processing systems, but also lead to a better understanding of the useful depth information in stereoscopic images. This will contribute to the design of more efficient filtering techniques, and to potentially help us reduce viewer discomfort of 3D technology by producing images that appear more natural to the human visual system.

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Biography

Anastasios (Tas) Venetsanopoulos received the Bachelors of Electrical and Mechanical Engineering degree from the National Technical University of Athens (NTUA) and an M.S., M.Phil. and a Ph.D. in Electrical Engineering from Yale University, New Haven, Connecticut.

Professor Venetsanopoulos has a long career in research, education, and university administration. Over the last four decades he has established himself as an expert in the worldwide biometrics, telecommunications and signal/image processing communities, as an outstanding researcher, scholar, professor and consultant. He has made contributions to biometric signal/image processing, system modeling, computational system design, telecommunications, digital signal/image processing and multimedia research, by authoring and coauthoring more than 8 books and 830 journal and conference papers. His work has been cited in over 400 books and 7,000 research papers. he has been a mentor to over 160 postdoctoral fellows and graduate students.

His present research interests are computational cell biology, biometric signal/image processing research, system modeling, telecommunications, nonlinear and adaptive filtering, knowledge based processing and recognition, digital signal/image processing, 3D vision and multimedia.