Biophotonics Circle

Biophotonics Initiative

The recently released Research Opportunity Summary of the UBCO Research Task Force identifies clusters of existing expertise around which future growth in faculty and resources might nucleate. Among those identified is one under the rubric of **optimization, image processing and inverse problems**. The present document aims to propose a broad "biophotonics initiative" on which research within this cluster could focus; to explain how our existing expertise could contribute to it in complementary ways; to point out the resultant opportunities for collaboration and synergy with the broader community at both the local and national levels; and to urge adoption of this initiative by UBCO as a strategic priority. The main body of the document outlines the rationale for this initiative; the following appendices present, in slightly more technical detail, two possible research areas for which relevant expertise already exists at OUC, and which would be aided by this initiative.

Biophotonics – definition:

"Biophotonics" is a rapidly emerging constellation of applications for laser, electro-optical and fiber-optic technology in biology and medicine. Developing areas include the manipulation and automatic identification of cell-sized particles (*e.g.* as normal or cancerous); structural imaging at both the micro- and macroscopic levels; "functional imaging" that detects and localizes anomalies in tissue function as opposed to structure; and novel forms of therapy in which, e.g., systemically administered drugs are selectively activated in specific locations by the presence of light.

Comparative advantages

Any new research undertaking vying for a commitment of UBCO's resources should not only be intrinsically worthy, but should enjoy some comparative advantage over other equally worthy proposals, either by fitting the existing capabilities of proto-UBCO better than do competing proposals, or by fitting these capabilities better than it does those of competing institutions. More pithily, not only should it be worth doing, but there should also be a good reason for doing it here. This section enumerates some advantages of the proposed biophotonics initiative, seen from the standpoint of UBCO's circumstances. In the interest of balance, it also acknowledges some difficulties.

1. Emergent versus mature technology:
In the early phases of development, it is easier for a modestly resourced research program to have a significant impact than in the mature phases. The easy things tend to get done first, leaving the relatively difficult and expensive problems for the mature phase. As in economics, a law of diminishing returns applies – less impact, on the margin, from more effort. Also, to improve the state of the art requires that one own or have access to the state of the art, both in terms of material and human knowledge resources. If the state of

the art is quite advanced, this entails the purchase of expensive equipment and the hiring of highly specialized and experienced professionals. This affords a comparative advantage to established institutions already possessing these resources, and constitutes a barrier to entry for smaller, newer institutions seeking to compete in mature areas. Since biophotonics, on the other hand, is an emergent field, it is possible for junior or newly reincarnated researchers to make significant contributions from modestly funded benchtop-scale research.

2. Interdisciplinary connections:
The present proposal would exploit the capabilities of at least two small departments (Physics & Astronomy and Computer Science), which are individually far from achieving "critical mass" in any established research area.

Relevant expertise in the Dept. of Physics & Astronomy includes
- optical design and electro-optics
- inverse problems (deconvolution) and image processing
- signal processing
- computer interfacing (experiment control and data acquisition).

Relevant expertise in the Dept. of Computer Science includes
- optimization theory and practice
- software development
- image processing.

Research opportunities would also arise in applied mathematics. The Dept. of Mathematics & Statistics has relevant expertise in inverse problems and optimization theory, increasing the "bench strength" and depth of available knowledge in those two areas.

If the proposed Faculty of Applied Science becomes a reality, opportunities might arise in electrical engineering (electro-optics; system design). Even if not, New College may possess relevant expertise within the FET or its successor.

If the Biophotonics Initiative were to evolve in the direction of medical imaging or medical monitoring / diagnosis devices, collaborative opportunities might arise in the Dept. of Nursing. If in the direction of, say, super-resolved confocal microscopy, then opportunities would arise in "pure" biological research.

3. Connections in the wider community:
Useful connections outside UBCO/NC might fall into any of several categories:

(a) Outside expertise available for collaborative research:
Within the Okanagan region, there are two other agencies that possess relevant expertise in image processing, namely the Cancer Clinic of the Southern Interior and the Dominion Radio Astrophysical Observatory. The former has already established a working

relationship with faculty in the Computer Science Dept. and with the Dept. of Mathematics & Statistics, and the latter with the Dept. of Physics & Astronomy.

(b) Industrial partnerships for funding and commercial uptake of research:
Here the local scene is bleak, as there are few tertiary industries in the Okanagan, or indeed in B.C. as a whole, of the sort and size to support high-risk investment in extramural R & D. The region is dotted with knowledge-based companies, mainly software cottage industries, which are viable here precisely because of their modest capital requirements. These cannot likely be tapped for significant investment. This dour assessment could brighten considerably if a local startup company were to form with the pursuit of biophotonics as its express purpose rather than as a speculative sideline. (This might conceivably occur in response to UBCO establishing and publicizing the program discussed here, so that the biophotonics initiative could in a sense generate its own local industrial partner.) Fairly generous government subventions are available to support such corporate undertakings (see below). On the other hand, the present attitude of the venture capital community is at best tepid (see below).

However, at the national level, there is considerable industrial interest in photonics. The Ottawa Valley area is home to one of the world's largest clusters of photonics-related companies, many having been spun off from the telecommunications industry after its implosion several years ago. Such companies might serve as platforms for the development and commercialization of basic research, though, since most are small and struggling themselves, they would be unlikely sources of investment capital.

(c) Government partnerships for funding and commercial uptake:
Here the scene is considerably brighter. The national granting councils fund several programs (NRC-IRAP, etc.) that support industrial-academic partnerships, in annual amounts up to about $100,000. Some of the companies in the aforementioned Ottawa Valley cluster are already receiving such support. Anecdotally, such grants are easier to obtain than NSERC funding for traditional curiosity-driven academic research. The former are awarded, to a greater extent, on the perceived utility of the proposed research; the latter, to a greater extent, on the perceived personal merit of the applicant. The biophotonics research theme is currently in favour with the granting councils, affording some advantage in the former arena, and hence some measure of insurance against failure in the latter. Biophotonics is being promoted by the NRC through a series of Vitesse Reskilling Workshops as an employment area to reabsorb knowledge workers displaced by recent convulsions in the telecom sector. A particularly interesting NRC initiative is the establishment of the Canadian Photonics Fabrication Centre (CPFC), in partnership with Carleton University, on the NRC campus in Ottawa. This agency is coming on line at the present moment. According to its own promotional material, its mission is "to support the growth of the Canadian photonics sector by offering companies, universities and others access to fabrication services that will enable these organizations to develop leading-edge photonic devices." Having access to subsidized, state-of-the-art fabrication services would be an immense boon to researchers here, compensating to a great extent for UBCO's initial lack of fabrication facilities and engineering expertise, and for the anticipated lack of local industrial partners. The Ontario government already funds an

agency similar to CPFC, namely Photonics Research Ontario; but its mandate is provincial, so access could be obtained by UBCO only through an Ontario-based industrial partner.

(d) Access to venture capital:
This issue is of course primarily of interest to prospective industrial partners, and only secondarily to UBCO itself. However, the partners' access to capital will clearly affect their willingness and ability to subsidize collaborative research at UBCO, so it deserves some mention. The author cannot pretend to any acquaintance with the venture capital community, but did attend a presentation in November 2003 on the subject of financing Canadian high-tech startups, given by Marc Wickham, who is Vice President, Investments of Ventures West. His assessment of funding prospects for photonics ventures was negative for those in the telecom sector, and neutral for the biophotonic sector. On that guidance, it would appear that biophotonics ventures have about the same funding prospects as other non-telecom-related high-tech ventures.

4. Recruitment possibilities
The present research cluster in optimization, image processing and inverse problems is categorized in the Research Task Force document as one that would benefit from the addition of a senior researcher. What, then, are the prospects for recruiting someone with the credentials required to spearhead a biophotonics program here? There are probably excellent recruitment possibilities at present because

(a) There is still a large overhang of underemployed knowledge workers who came to grief during the dot-com collapse; and

(b) In view of the continuing turmoil within Nortel, there may well be senior personnel still employed there who would welcome a change to a less volatile work environment. Even if candidates in categories (a) and (b) are not exactly what is desired, they increase the overall level of competition among job-hunters throughout the sector, creating a general "seller's market" for the available positions.

5. Scalability
When deciding which research areas to invest in, it is worth asking how outputs will scale with inputs. Is a large threshold investment required before anything at all can be accomplished? Must entire teams of researchers and technicians be hired simultaneously, before any individual can become productive? Would the departure of a key individual, the bankruptcy of an industrial partner, or a change of mood at a granting council, cripple an entire research group? Would completion or abandonment of the original research objectives turn a highly expensive and specialized piece of lab equipment into a white elephant – a stranded investment with no break-up value?

While such questions admittedly take us into the realm of distant speculation, it does seem possible to make a couple of points that favour the biophotonics initiative. As has already been pointed out, this is a young field, and the easy pickings have not yet been exhausted. Thus the investment threshold is quite low - just about any level of investment could produce some appreciable output. For instance,

- $\$10^3$ would buy a neatly lettered sign reading “Biophotonics Institute”, and enough pencils and paper for a solitary mathematician to potter away at multiple-scattering convolution kernels (see Appendix I).
- $\$10^4$ would come close to equipping a time-of-flight light-scattering experiment to test the convolution kernels, if the Biology Department provided the lab rat for free.
- $\$10^5$ would equip a working multi-purpose optics lab that pays for its own rat.

The equipment for optics experiments typically consists of several moderately priced modules that can easily be reconfigured for highly various uses, rather than a single expensive and complicated monolith with a highly specific application, a need for a dedicated technician, and a thirst for liquid helium. Thus if the experiment fails or its owner dies, other uses can be found for the equipment and all is not lost.

Conclusion

We submit the biophotonics initiative as a possible strategic focus for interdisciplinary research at UBCO. We feel that it fits the capabilities of an identified research cluster, and could easily involve other researchers as well. It is an emergent field likely to experience major future advances, rather than a mature discipline where one can only tinker at the margins. It is in favour with granting agencies, and has obvious commercial potential.

Appendix I

Sample application – optical imaging of biological tissue:

As an example – just one, it should be stressed, among many and varied possibilities – we briefly describe recent advances in optical imaging. It may seem curious that there should be anything novel about using light to form images. However, because of the relative opacity of biological tissues to ordinary light, there are great challenges in imaging the *interior* regions of biological organisms using visible light. Paradoxically, imaging techniques using X-rays, NMR and ultrasound are far more advanced and better established. While there are good reasons why visible-light imaging has been neglected in the past, there are equally good reasons for a revival of interest from this point forward:

(*i*) One is the advent of two-photon excitation. This helps overcome the relative opacity of biological tissue to visible light. Rather than using a visible light source, the tissue is illuminated with relatively penetrating near-infrared light. Nonlinear polarizability of the illuminated matter causes frequency-doubling of some of the scattered light, which can thus be used to form an image in the visible. Another advantage of multi-photon excitation is that it defeats the Abbe resolution limit, allowing higher-resolution optical microscopy than has been possible hitherto.

(*ii*) A long-standing barrier to the optical imaging of interior tissue has been breached by the exponential advance of computing power. Optical photons are typically scattered several times while traversing a tissue mass. Tracing the scattered light back to form an image of the scattering mass has therefore been a formidable mathematical "inverse problem". Hence the historical preference for X-ray imaging: this radiation is far more penetrating than visible light and, to a good approximation, either travels straight through its target or is removed from the beam by a single scattering event, leaving an image in the form of a simple geometric shadow. With vastly increased computing power, however, the difficulties of optical imaging may be overcome by relentless number-crunching. Work has begun on imaging algorithms for numerically cracking the multiple-scattering problem.

(*iii*) As the medical profession, along with society in general, becomes ever more risk-averse, there is mounting pressure to replace old therapies and diagnostic techniques using dangerous ionizing radiation (X-rays) with more benign, less invasive alternatives. This will provide a strong incentive for the development of photonic imaging methods in the near future.

Appendix II

Sample application – medical X-ray imaging:

Current faculty members from the departments of Computer Science, Mathematics & Statistics, and Physics have competencies in image processing, inverse problems, optimization, and mathematical modeling of cell evolution. Together they can improve the cancer treatment process at several steps (imaging, treatment plan, treatment delivery, QA) bringing together a variety of tools (convex and nonsmooth analysis, optimization, inverse problems, image processing and interpretation, partial and ordinary differential equations, convolution techniques, etc.). The BC cancer for the Southern Interior has provided the medical knowledge and data thereby completing the available skill set.

The radiotherapy treatment of a patient follows several steps. Once the physician has made the diagnosis, some imaging is performed using e.g. a CT scanner. A 3-D image of the patient body is generated from those images. The oncologist outlines the tumour, the organs at risk, and prescribes the doses. The planner then creates a treatment plan. The treatment plan can now be applied to the patient. QA requires additional imaging e.g. to determine whether the target was hit using portal images.

Each of those steps requires expertise in diverse areas. Optimization methods are required to compute the best possible treatment to achieve the prescribed targets. It requires dose computation algorithms, optimization models, inverse problem methods, and modeling the biological behavior of cell evolution. Modeling the biological reaction of cells to radiations is the key to create more efficient plans. Image processing is also key in this process, both at the planning and QA stages to facilitate the detection of the location of the different target areas (tumour, organs at risk, area treated). There is also a growing interest in following the tumour movement in the body of the patient while in treatment. The real-time aspect would require not only mathematical and image processing expertise but expertise in areas such as physics and engineering could also improve the end result. Moreover, less invasive imaging could be performed in the future using bio-photonics.

Current faculty members have already some working relationship with the local BC Cancer clinic (co-op students working at the BC Cancer clinic both in Physics and Computer Science, directed studies courses targeted to the planning process (optimization) and QA (image processing). While focus has been limited to existing treatment models, bio-photonics would be a natural step to expand the actual work.

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