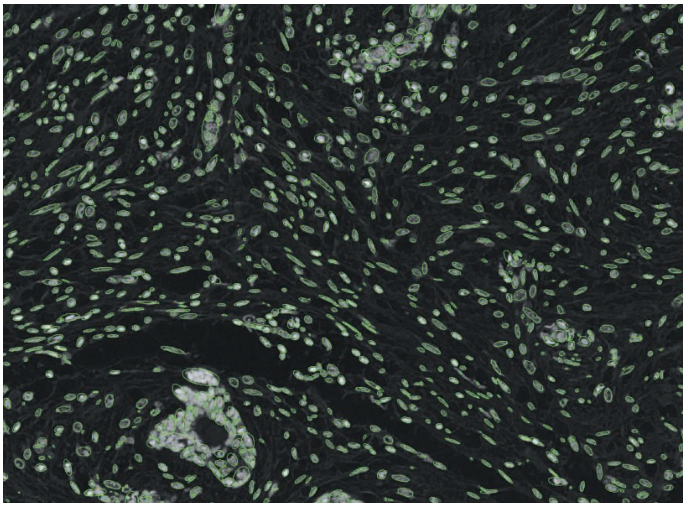

NEWS

Is There an Astronomer in the House?

With biomedical researchers analyzing stars and astronomers tackling cancer, two unlikely collaborations creatively solve data problems

IN 2004, ALYSSA GOODMAN HAD A PROBLEM. An astronomer at Harvard University, she and her colleagues had just wrapped up a project called COMPLETE, a survey of star-forming regions; now they had to analyze massive amounts of data that were tricky to visualize in only two dimensions. Goodman wanted a three-dimensional view of the regions, but the tools available to astronomers weren't up to the task. So she went in search of the answer elsewhere.

Goodman presented her problem at a workshop called Visualization Research Challenges, held at the headquarters of the U.S. National Institutes of Health (NIH) in Bethesda, Maryland. In the audience was Michael Halle, a radiologist at Brigham and Women's Hospital in Boston, who recognized that the technology Goodman needed already existed in medicine. His department had previously developed a piece of visualization software, called 3D Slicer, for use with medical scans such as MRIs. Halle thought it could handle Goodman's astronomical data set as well.

His hunch was right. And the unusual collaboration that formed between his team and Goodman's still exists today at Harvard in a data-analysis project called Astronomical Medicine.

It's not the only odd pairing of astronomers and biomedical researchers motivated by the need to deal with data. At the University of Cambridge's Institute of Astronomy (IoA) in the United Kingdom, Nicholas Walton uses sophisticated computer algorithms to analyze large batches of images, picking out faint, fuzzy objects. When he isn't looking for distant galaxies, nebulae, or star clusters, the astronomer lends his data-handling skills to the hunt for cancer.

From stars to biomarkers

Walton and his colleagues work on a project called PathGrid in which image-analysis software developed for astronomy is being used to automate the study of pathology slides. Pathologists stain tissue samples to identify various biomarkers that indicate a cancer's aggressiveness. Currently, they must inspect each slide personally with a microscope, but PathGrid aims to improve on this time-consuming and subjective endeavor.

The key behind the project is the surprising similarity between images of tissue samples and the cosmos: Spotting a cancerous cell buried in normal tissue is like finding a single star in a crowded stellar field. "There's a natural overlap in astronomy and medicine for needing to identify and quantify indistinct objects in large data sets," says oncologist James Brenton of the Cancer Research UK Cambridge Research Institute, who, with Walton, leads the PathGrid project.

When deciding on the best course of treatment for a person with breast cancer, pathologists look for different biomarkers—specific proteins—in the patient's cancerous tissue. For example, an overexpression of the biomarker human epidermal growth factor receptor 2 (HER2) indicates a more aggressive form of breast cancer with a poorer prognosis. To spot such biomarkers, pathologists use a technique called immunohistochemical (IHC) screening. First they treat the tissue with antibodies that bind to targeted proteins, such as HER2; then a secondary antibody highlights the binding by undergoing a chemical reaction that produces a colored stain.

At present, however, there are only a handful of well-validated biomarkers for cancer, and even fewer that reveal how a patient is likely to respond to a specific treatment, says Brenton. "That's because there's a bottleneck between new biomarker discoveries and being able to put them into clinical practice," he says. "Discoveries are made with relatively small groups of tens to a few hundred patients, but their usefulness needs to be validated on sample sizes of hundreds or several thousands of patients."

Initial discovery studies are small-scale because pathologists must manually assess images in the IHC screening process, qualitatively scoring them for the abundance of a particular biomarker as well as the intensity of the staining. What was needed, Brenton thought, is a way of automating this time-consuming task: a computer algorithm that could accurately pick out stained tissue of varying shapes and sizes in cluttered images.

That's when Walton came on the scene.

CREDITS (LEFT TO RIGHT): EUROPEAN SOUTHERN OBSERVATORY/VISTA AND CASU; WALTON & IRWIN, UNIVERSITY OF CAMBRIDGE

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Surprisingly similar. A picture of the center of our galaxy and a slide of stained cancerous tissue show a common need to pick out indistinct objects in both types of images.

"We've been developing algorithms to extract information from large telescope surveys at the IoA for years. The algorithms are robust to various backgrounds, such as stars, galaxies, and gas," says Walton.

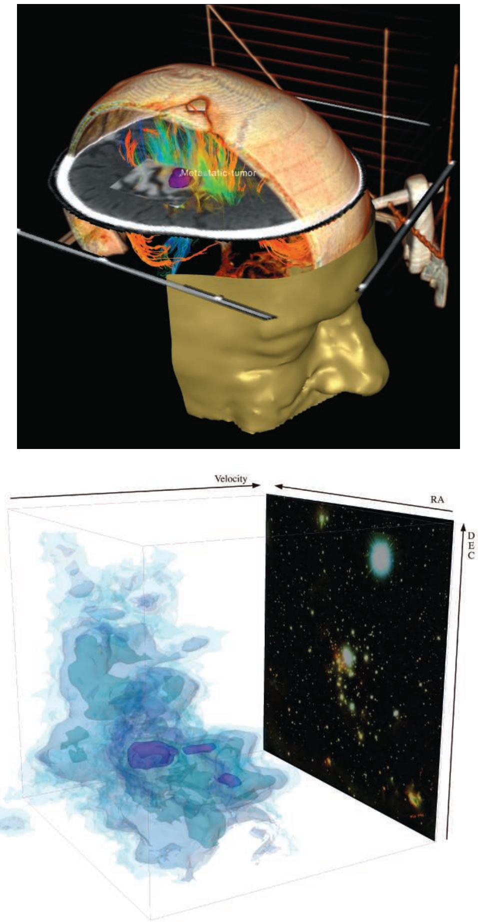
He and Brenton met at the first Cambridge eScience Centre Scientific Forum held in 2002. The scientists, along with colleagues from their respective fields, talked at length about the possibility of using astronomy algorithms in cancer-screening image analysis. Walton and his IoA colleague Mike Irwin found that transferring those algorithms to medical use was painless. "In a pilot scheme to investigate the feasibility of the project, we found that we had to make virtually no changes at all, just tweaking the odd parameters here and there," says Walton.

PathGrid has performed well in tests, Walton and Brenton say. In a study that checked 270 breast cancer images for a biomarker called estrogen receptor (ER), PathGrid agreed with pathologists' scorings for 88% of the positive slides and 93% of the negative ones. (An ER-positive tumor has a better prognosis than an ER-negative one and is treated by suppressing the production of the hormone estrogen.)

A larger test, which looked for the biomarker HER2 in more than 2000 images, yielded even more impressive success rates of 96% and 98%, respectively. Walton says he thinks the results would have been even higher if not for "the subjective manner in which pathologists rate images." PathGrid is consistent yet speedy, says Walton. To analyze a batch of a few hundred images for one specific biomarker would take PathGrid only a few minutes, he says, compared with about 3 hours for a pathologist.

PathGrid is just one of several "virtual pathology" projects now under way, notes Laoighse Mulrane of the University College Dublin School of Biomolecular and Biomedical Science, a cancer researcher who recently reviewed this area. Yet its "novel" use of astronomy-based techniques makes it stand out from the pack, he says: "The collaborative efforts of the groups involved should be applauded."

PathGrid is now ready to undergo trials within a hospital environment in the United Kingdom. "Hopefully, if everything goes well, it could be used as routine, automated screening in hospitals within 3 years," says Walton.



Stellar views. 3D imagery can give a clearer picture of the inner workings of the human body (*top*), and astronomers are using related visualization software to study distant star-forming regions (*bottom*).

CREDITS (TOP AND BOTTOM): ANDRÁS JAKAB/UNIVERSITY OF DEBRECEN, HUNGARY

Adding another dimension

The partnership between astronomy and medicine works both ways, as Goodman and her colleagues have shown with the Astronomical Medicine project. For the COMPLETE survey, Goodman already had algorithms capable of handling enormous data sets. But they were geared toward dealing with 2D images, whereas she also wanted to see how the velocity of gas in star-forming regions changed along the line of sight—essentially treating velocity like a third dimension. "COMPLETE contained the largest 'position-position-velocity' maps of star-forming regions that had been made to date, and we wanted to see and understand this data all at once," she says.

Analyzing 3D images has been an important part of diagnostic medicine for many years, but until Halle heard Goodman's plea for help, nobody had considered adapting the technique to astronomy. After the NIH workshop, the pair quickly began working together and soon brought Michelle Borkin, a Harvard Ph.D. student in applied physics, on board the project.

Borkin was instantly hooked. "The very first time that I saw our astronomical data come to life in 3D Slicer was amazing," says Borkin. "Viewing the data in 3D is far more intuitive to understand than looking at it in 2D. I was instantly able to start making new discoveries that are incredibly difficult to do otherwise, such as spotting elusive jets of gas ejected from newborn stars." While continuing to research star-forming regions using 3D Slicer, the Harvard team is currently working on projects that will give back to the medical world, developing tools based on algorithms used in astronomy to visualize, for example, coronary arteries.

The way in which these two interdisciplinary projects have been able to share tools are special cases, cautions Stephen Wong, a biomedical informatics scientist at the Methodist Hospital Research Institute in Houston, Texas. In general, Wong says, using secondhand algorithms is not a good idea: "To be effective, image-processing algorithms and analysis tools have to be customized and specific to the particular problems under investigation."

Working in interdisciplinary research is also demanding on scientists' already hectic work schedules and has to be fitted around their traditional career duties. "I spend about 10% of my time working on PathGrid and the rest on my day job as part of the European Space Agency's Gaia spacecraft science team," says Walton.

Yet for the scientists involved in both projects, taking on this supplementary work is a labor of love. "Usually, you become an expert in just one field," says Goodman, "but I've had the opportunity to learn something completely new in my 40s. I think people should go into interdisciplinary research, not just because the world might learn something, but because you will too."

As for the astronomers on the PathGrid team, they're able to make a boast that few of their stargazing colleagues can match. "It's great to think that something I'm doing is going to have an impact on how a cancer patient is treated and help to improve their chances of survival," says Walton.

–SARAH REED

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