Success Story

AstraZeneca

Taking Drug Discovery to the Next Level

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– Nicklas Hallén
Team Leader, HPC Team, Mölndal

As one of the world's leading pharmaceutical companies, AstraZeneca's business is focused on turning good ideas into innovative, effective medicines that make a real difference in important areas of healthcare.

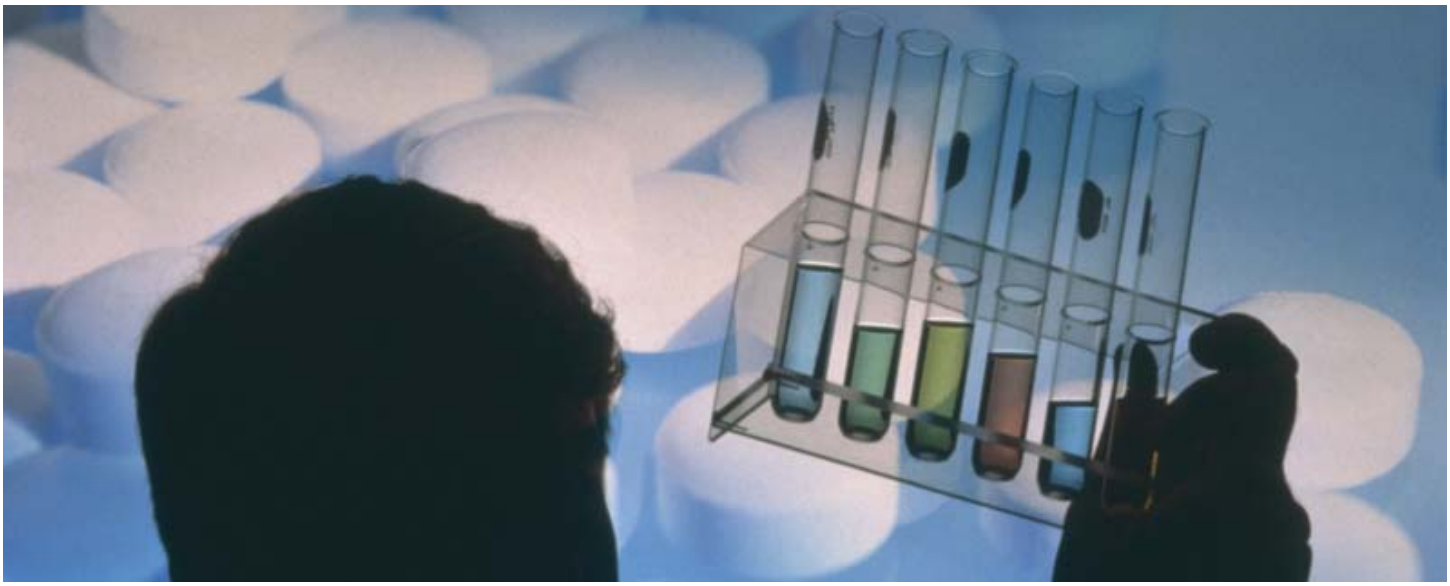
The HPC Team in Mölndal (near Göteborg), Sweden, is a part of the company's Discovery Information organisation, and provides high performance computing (HPC) and visualisation services to support AstraZeneca's Discovery and Development functions. Discovery focuses on pre-clinical work, while Development handles drug formulation, clinical trials etc. The team's goal is to help researchers in both these areas, by providing tools that accelerate and improve the process of developing new drugs.

Making Sick People Healthy

"Our researchers are looking for a combination of speed and quality," explains Nicklas Hallén, HPC Team Leader. "Speed is very important, as it normally takes around ten years to develop a new drug. This starts with identifying a 'target', developing a substance that will remedy the problem, and then registering a patent for the new substance. A patent is valid for 20 years, so the sooner we can bring the new drug to market, the longer we are protected by it.

"The other, even more critical aspect is maximising quality, in order to ensure that the drug has the minimum side-effects, so patients get medicines that are as good as they can be. What we want is to make sick people healthy – that's ultimately why we're here."

The HPC Team primarily supports the pre-clinical phase of drug discovery – where



AstraZeneca's researchers have chosen a disease or condition that they want to address, and are trying to identify the mechanisms in the body that make the condition appear, in order to develop an active substance that prevents this.

Finding a means of preventing hay fever illustrates how this works in practice. Cells have many different structures on their surfaces, which (in layperson's terms) are like keyholes. When something fits into the "keyhole", a process is triggered and the cell starts to behave in a way that can be harmful or uncomfortable. In the case of hay fever, pollen granules trigger a process that produces histamines that make the person start to sneeze, their eyes start to run etc. Preventing this involves developing a chemical substance (a "key") that will fit into the keyhole the histamine locks into and block the possibility for the histamine to trigger the reaction – without the key itself producing any effects.

"Our researchers are highly experienced in identifying the keyholes that are the likely 'culprits' for different types of medical condition, and in finding out what they look like," continues Hallén. "Our job is to support them, by providing the combination of HPC, analysis tools and 3D visualisation they need to develop the chemical substances that are likely to have the most positive effect."

Finding the Key That Fits the Keyhole

The first part of this process involves using a Linux® cluster for "virtual screening" and "virtual docking". AstraZeneca's researchers have access to databases containing the properties of millions of different substances (keys), and use screening and docking software on the cluster to match each of these against the keyhole to see which have a potential fit. The researchers then use this information to discuss the changes they could make to the most promising substances to improve their fit still further, and then work through an iterative process until they have identified a workable solution. This is then passed on to a bench chemist to synthesise the substance, and enable it to be tested to see if it has the desired effect.

"To support this process, since 2000 we've been using Silicon Graphics® Onyx® systems, together with two Reality Centres™ which we recently consolidated into a single installation," says Hallén. "The Reality Centre has one analogue and four digital projectors, and until very recently these were connected to the Onyx and a standard Windows laptop PC.

"When our researchers wanted to discuss an interesting protein, target or keyhole, they would use the Onyx to display a stereo 3D model of it, and the laptop for PowerPoint presentations, etc. Typically they would use the Reality Centre's entire screen for the stereo 3D model; and switch to the PC if they wanted to look at other types of material as well. SGI also developed a special control system to make all the five projectors much easier for our researchers to operate, and overall the solution worked well.

"We can drive everything from a single keyboard and mouse, and display PowerPoint presentations, etc, at the same time as our stereo 3D models. This really solved all our problems and improved the situation very, very much."

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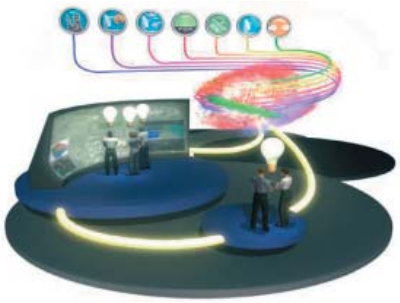
"When SGI said that they were moving to Linux and away from IRIX®, we decided that we wanted to standardise on Intel-based code throughout our three sites in Sweden, and started looking for a replacement for the Onyx. We wanted a visualisation server that could connect to the Reality Centre and run our installed x86 applications, and looked at a number of other suppliers to see if they could help us – but without success.

SGI® pixel fusion server Provides the Answer

"We then spoke to SGI Professional Services, who introduced us to SGI® pixel fusion server and the company's latest visualisation technology. They explained that our researchers would be able to use this as a display engine to connect multiple graphics streams (including the laptop PC) to the Reality Centre, and pixel fusion server to display them in different windows – all in a single 3D space. Other benefits were that we could utilise our x86 software, and migrate the control system for the projectors from the Onyx to the new solution. Rather than having separate keyboards and mice for the graphics system and laptop, we could also drive everything from a single keyboard and mouse, and display PowerPoint presentations, etc, at the same time as our stereo 3D models. This really solved all our problems and improved the situation very, very much."



With the new solution, the web interface used to drive the installation has been simplified considerably, and now provides just two distinct modes: pixel fusion server (on the main simulation display), and laptop / DVD / VCR on a separate central presentation projector. When the user chooses pixel fusion server mode, the main two-channel stereo simulation display is started, and the user can then select from all connected sources and compute resources via a custom graphical user interface – and without the need to enter any complex commands, Linux shell scripts etc.

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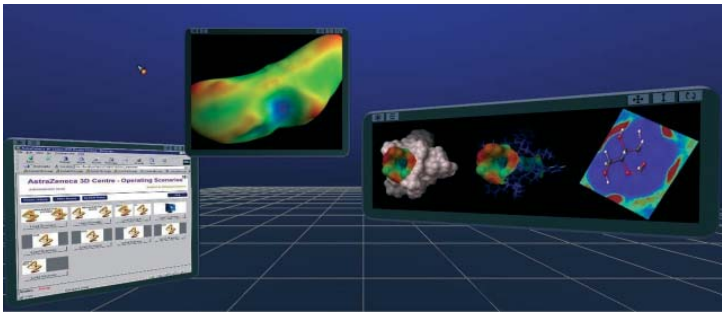
life inspiring ideas



"Although we're only just starting to use pixel fusion server, we're confident it will aid and simplify

our researchers' discussions, and we're already thinking about how we could expand its use in the future," concludes Hallén. "One way would be to add a videoconferencing stream so that our researchers could open up a window and interact with a specialist at another site; and we've also thought about using OpenGL Vizserver™ to enable people in multiple Reality Centres to work together – all sharing and interacting with the same data.

"We have quite a history of working with SGI, first with IRIX-based servers and workstations, and more recently with several SGI® Altix® systems ranging up to 32 processors, which are used for quantum mechanics, molecular dynamics and computational fluid dynamics – the latter to support our Development organisation with improving the manufacturing processes for their drug formulations. One of the things that made us choose SGI is that the company always delivers and its quality of service is excellent. Compared to some of the other, larger companies that do similar things, I don't think I've ever heard SGI say 'no, we can't do that'. SGI always say 'we'll see what we can do', and are very flexible in the way they handle AstraZeneca as a customer. SGI are really outstanding in that respect."

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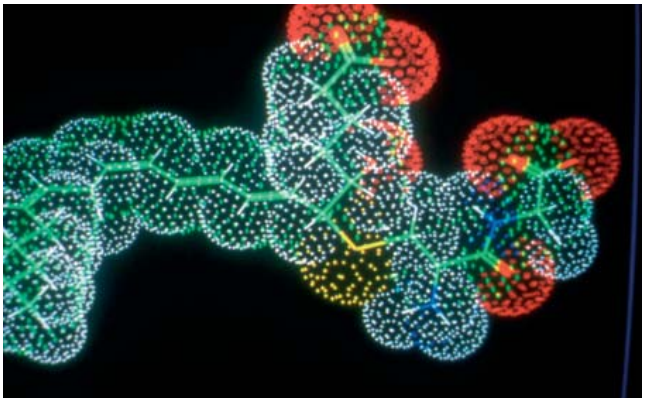

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