

# An astonishing screening capacity for kinetic studies

The Wellcome Trust Centre for Cell Biology (WTCCB), University of Edinburgh, UK, relies on Tecan's versatile range of microplate readers for kinetic studies to increase understanding of living systems at the molecular level. The WTCCB has a remarkable screening capacity for chemical genetic screens, owning twenty Sunrise™, four Infinite® F200s and one Infinite M200 plate reader.

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The Wellcome Trust Centre for Cell Biology (WTCCB) is one of nine UK-based Wellcome Trust Centres, and aims to advance knowledge of fundamental biological processes. Within the WTCCB, Mike Tyers' group has established an automated screening facility able to perform kinetic studies and track growth rates over time for small molecule screens. To support these studies, the scientists use Sunrise microplate readers to take absorbance readings for kinetic studies and to establish growth curves, which are used to determine parameters such as growth rate, lag phase, time and saturation. The system, referred to as 'The Wall', was inspired by a similar microplate reader system in the Nislow and Giaever laboratories at the University of Toronto, Canada, and enables researchers to take readings over long time intervals with

minimal manual intervention. Advanced temperature control is an important feature of the system, heating every well separately to minimize inter-well variability and prevent condensation.

Michaela Spitzer, a PhD student using the platform for chemical genetic screening, explained how the system is used: "We have libraries of compounds that inhibit yeast growth, for example, and use genetic methods to investigate their mode of action within the cell. Yeast deletion mutants are inoculated with various drugs in a 96-well plate, then absorbance readings are taken at 15 minute intervals. From the resulting growth curves we are able to determine if deletion mutants are more sensitive to a given drug than the control strain. Using a 96-well format increases sample

throughput and allows us to take readings for 24 or even 48 hours, if necessary. Previously this would have required staff to come into the laboratory at late hours to take readings and set up samples. Luckily those days are over, and the system has become increasingly popular with many laboratories within the Institute, for a wide range of applications requiring time resolved quantitative analysis."

Although the WTCCB's Infinite systems have, so far, mainly been used for absorbance readings, they are also equipped for monitoring fluorescence-based inhibition assays. Rachel White, laboratory technician, said: "The optical density (OD) readouts from the Infinite and Sunrise machines are comparable, allowing the instruments to be used interchangeably for absorbance



studies, and we are in the process of optimizing our Infinite readers for our green fluorescent protein (GFP)-based screens. Use of 384-well plates for these studies will allow us to further extend the capacity of 'The Wall', and we also have the NanoQuant Plate™ accessory for low volume quantitation of DNA samples for cloning, microarray and deep sequencing."

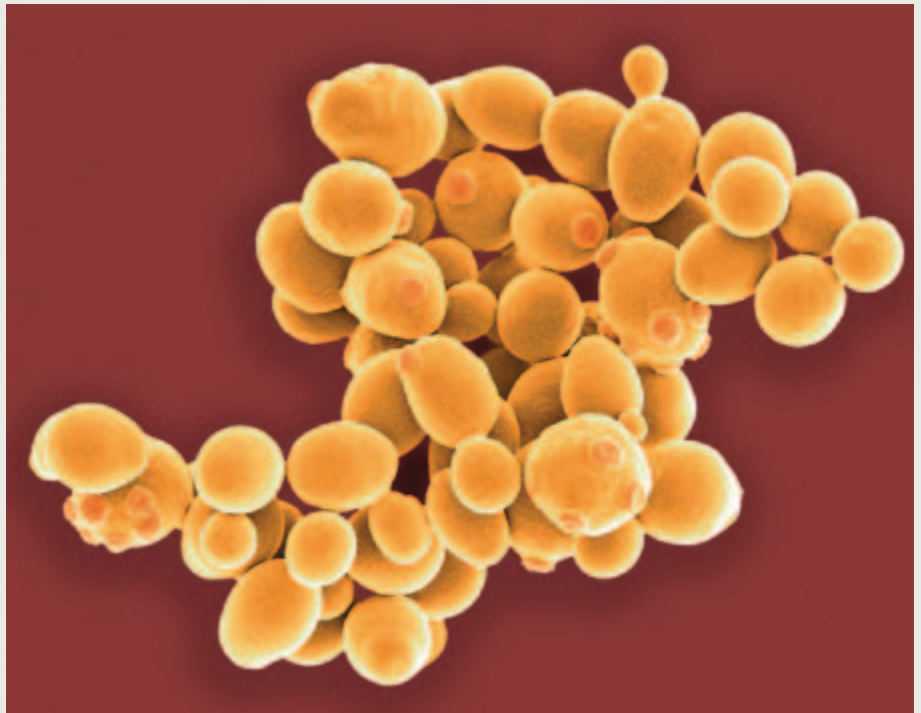
Tecan's Magellan™ software is used to control all the plate readers, simplifying analysis and enabling visualization of growth curves. Hille Tekotte, senior research associate, commented: "Magellan allows you to see the whole plate on the screen, and gives you the ability to overlay individual wells instantly. This allows us to compare different samples to each other, and to control strains during a run, meaning we can tell almost immediately whether an experiment is working or not."

The WTCCB's major concern was fitting all the machines, and the computers to control them, into the available space, as well as the stability of the networked computers and software. To overcome this, 10 Sunrise readers are connected to a single desktop, controlled by one copy of Magellan. Jan Wildenhain, an E-science Data Information & Knowledge Transformation (eDIKT) research associate, explained: "We have purchased cards which enable us to use the Magellan software to control up to 16 plate readers from one PC. The system was straightforward to set up and we had no problems at all. It is very stable and reliable, and gives us the capability to do a lot of parallel reads without any performance issues. This is important to us because we screen large collections of mutants or compounds, and need to be able to do multiple simultaneous reads. The growth curves generated by the Magellan software allow us to study performance differences between screens, which would not be possible with the single reads of a standard plate reader, and we can screen up to 2,500 compounds simultaneously. Overall, Tecan's instruments offer us the broadest range of features, as well as being the most cost-effective solution on the market, and the Company provides good technical support, responding very quickly to our needs."

To find out more on Tecan's detection instruments, visit [www.tecan.com/detection](http://www.tecan.com/detection)



Laboratory technician Rachel White with 'The Wall'.



Proliferating yeast cells.