

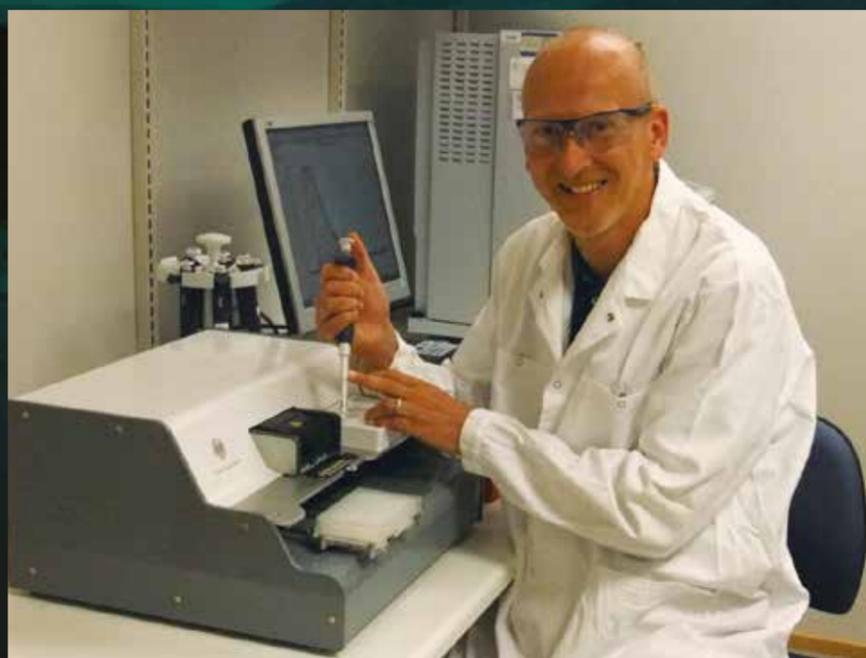
# Imagination knows no boundaries

AstraZeneca scientists engaged in surface plasmon resonance studies are reaping the benefits of a recently acquired HP D300 Digital Dispenser, saving time, enhancing consistency and using significantly less compound for dose-response experiments.



The Structure and Biophysics department at AstraZeneca R&D Mölndal, Sweden, is focused on the application of biophysical methods to determine how compounds interact with drug targets, examining physical parameters such as thermodynamics and binding kinetics. Principal Scientist Stefan Geschwindner explained: "Our department is involved in everything from determining the feasibility of a potential project to supporting lead identification, lead optimization and even characterization of candidate drugs for clinical studies. We aim to understand the driving forces behind compound-target interactions through a range of biophysical approaches, principally surface plasmon resonance (SPR) and nuclear magnetic resonance (NMR), but also technologies such as thermal shift assays and isothermal titration calorimetry."

Stefan continued: "The need for the HP D300 Digital Dispenser was largely driven by a demand for more effective SPR studies and increased flexibility. We have set protocols for structure-activity relationship screening, using 7 and 10 concentration dose-response curves with a fixed range of dilution patterns and starting concentrations. However, there are times when we need the flexibility to use different dilution patterns to correctly describe dose-response curves and determine exact affinity values, for instance when cooperative binding is observed. Primary fragment screening is also a major part of our work; after dissolving the solid compounds in DMSO to prepare 100 mM stock solutions, manual dilutions are typically performed in 96- or 384-well plates, which is very time consuming. We needed to look at alternative solutions, as well as to widen our scope for the usual compound studies."



Stefan Geschwindner setting up a dose-response curve on the HP D300

"We already had an acoustic dispenser, but this was not ideal. As there are peaks and troughs in our work, we needed an economical solution that could accommodate these changing demands, and the HP D300 was an attractive option. We contacted Tecan, who provided an instrument for us to try, and people immediately saw the benefits, realizing that the HP D300 could really change our way of working, helping to generate data more rapidly and shorten lead times."

"The HP D300 is very easy to use and saves us so much time. It gives us the flexibility to use very low concentration stock solutions and perform different dilution patterns, and the instrument does all the calculations for us. Another big advantage is that we save a lot of material, which is particularly important when the amount of compound available is limited; once the 10 mM stock solution has been prepared, there can be very little material remaining. Where we may only have sufficient compound to run one dose-response curve if acoustic dispensing were used, the HP D300 can even recover any solution that has not been dispensed, which is brilliant. The savings are tremendous and, other than manual pipetting, this is probably the only effective way to prepare our dose-response curves."

"It is also much easier to set up SPR experiments, which are very sensitive to variations in DMSO concentrations. Using the HP D300, we have found that, when compounds in DMSO are dispensed directly into a buffer without DMSO, the resulting DMSO content is so low that we can eliminate DMSO from the running buffer in many cases, particularly for very potent drug candidates. We now have a lot of data showing that this is a very straightforward way of preparing dose-response curves and,

without the need to make two buffers or run solvent correction cycles, we save lot of time."

"The HP D300 is also beneficial for thermal shift assays, where a dye is used to monitor protein unfolding. We prepare a matrix of different protein versus dye concentrations, and also test varying volumes. Once we have the optimal volume and ratio of protein to dye, we use the HP D300 to dispense a constant concentration of dye into a 384-well plate. This gives us consistency throughout the lead screening exercise."

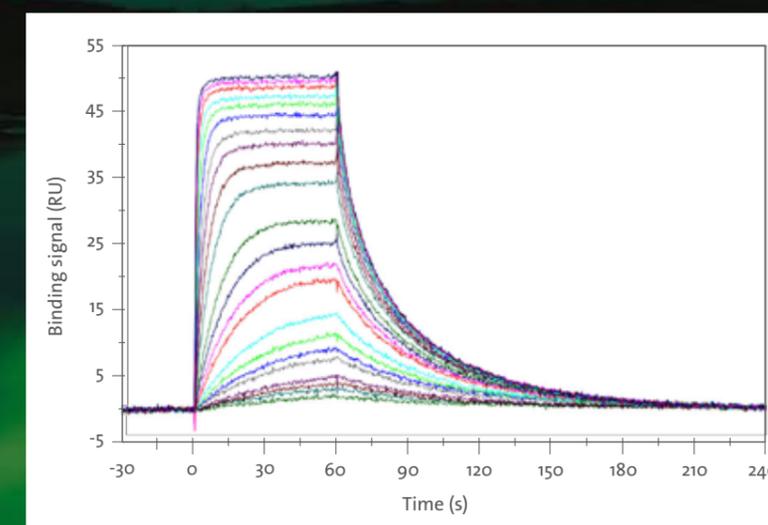
"We've had the HP D300 for about nine months now, and are really pleased with it. It's so intuitive that hardly any training is necessary; even inexperienced users can become proficient in basic operation in as little as five minutes. Originally, it was just intended for our group, but now staff from all departments are using the system, as it is so much easier than doing dose-response

"The limit of the HP D300's capabilities is basically the imagination of the users."

curves with the acoustic dispenser. Everybody says that it is probably the best investment we have made in the last five years. The costs-to-benefits ratio is just brilliant, and it can do so much. The limit of its capabilities is basically the imagination of the user," concluded Stefan.

To find out more about the HP D300 Digital Dispenser, visit [www.tecan.com/digitaltitration](http://www.tecan.com/digitaltitration)

To find out more about AstraZeneca R&D Mölndal, visit [www.astrazenecamolndal.com/more-about-molndal.php](http://www.astrazenecamolndal.com/more-about-molndal.php)



Sensorgrams of a 22 concentration-response experiment prepared with the HP D300 showing the binding kinetics of a small molecule engaging with a protein-protein interaction target