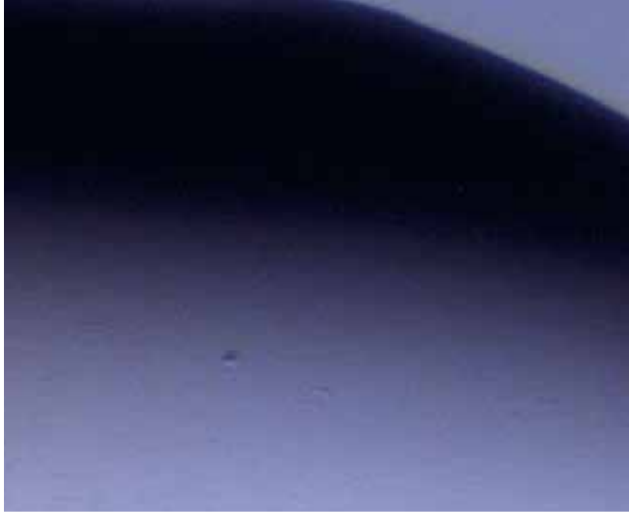
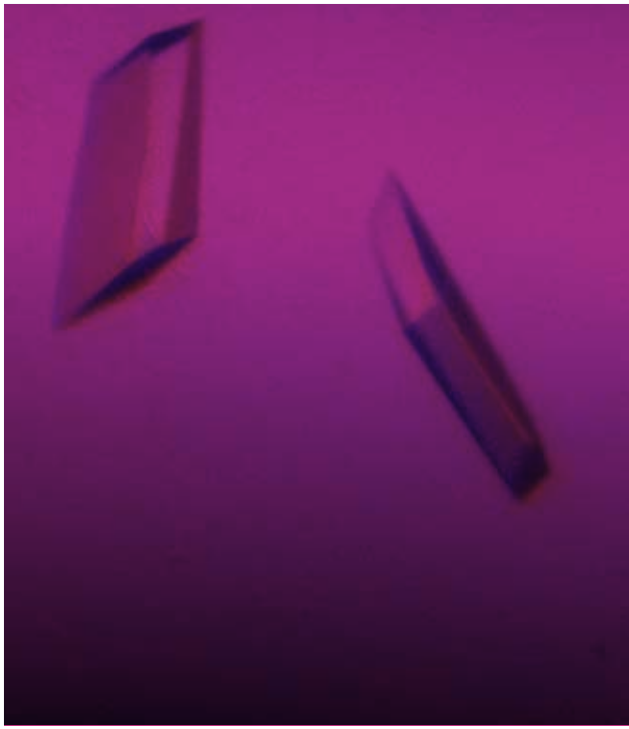
labCrystal

news from the world of protein crystallography

2015





overcoming evaporation and reducing costs

using protein crystallography to develop new flu drugs

membrane protein crystallisation – is it still a fine art?

when customer service makes all the difference!

welcome

Last year's international year of crystallography brought greater awareness of the benefits of crystal structure determination to our everyday lives. It also highlighted the global nature of research in this field. Our latest edition of labCrystal includes work from Kurt Krause's laboratory in Otago, New Zealand using protein crystallography to develop new flu drugs, as well as work in the UK and USA.

May 2015 saw the inaugural TTP Labtech users group meeting (UGM) at our headquarters in Melbourn, UK. I was extremely honoured to have such prestigious speakers at the meeting and proud to see many mosquito users that I have built up relationships with over the last 10 years – there was even a debate about who actually received the very first mosquito instrument in their own laboratories! It was good to know that all these instruments are still working efficiently and there is the same enthusiasm for them than there ever has been.

As a company, we value our close relationship with you, and continue to develop products and ideas in line with your needs – this is why we love hearing from you about your work and how we can help.

Joby Jenkins,
global head - liquid handling

I hope you enjoy reading this edition of labCrystal and please get in touch if you would like to present your own work in a future edition.

contents

finding solutions that really solve your problems

a report from our first mosquito user group meeting

Our inaugural UGM took place on 21st and 22nd April 2015 at TTP Labtech's head office, Melbourn Science Park, Hertfordshire, UK.

The aim of the event was for crystallographers to discuss their own work, exchange ideas and collaborate with other mosquito users from all over the world. There was also an opportunity to learn more about the capabilities of the instruments and to ask any questions about their usage, benefiting from on-site TTP Labtech expertise.

This international meeting consisted of 11 high profile speakers from both academic and commercial laboratories representing UK, mainland Europe, Scandinavia and Asia.

TTP Labtech was honoured to have the very first mosquito Crystal users present at the meeting. We are delighted that they are still using their original instruments, more than 10 years later.

top-class scientific talks

Many of the talks discussed the benefits of mosquito in crystallography for drug development commenting on its speed, accuracy and flexibility. New methods for screening membrane proteins were presented and the essential use of mosquito LCP for these experiments highlighted.

mosquito was proven to function well for many techniques including crystallisation in vapour diffusion, LCP, LCP-FRAP, constructing thermophore assays, crystal soaking and *in situ* crystallisation. It is also a visually attractive and technically impressive instrument in the crystallography laboratory - one institute explained that they use mosquito Crystal as its star instrument for important public engagement events!

lively roundtable discussion

As part of the event, TTP Labtech hosted a roundtable discussion to ascertain a 'wish list' for instrument enhancements or new ideas to improve the workflow. This led to a lively debate and consolidated several requests that were popular amongst the audience. The product development and engineering teams have taken these new ideas on board and have immediately started forming working groups to discuss how these developments could also be put into practice.

'behind the scenes' site tour & social event

The final activity of the event incorporated a well organised tour of the manufacturing and development facilities demonstrating the range of other products designed and produced by TTP Labtech in the cell imaging and sample management areas.

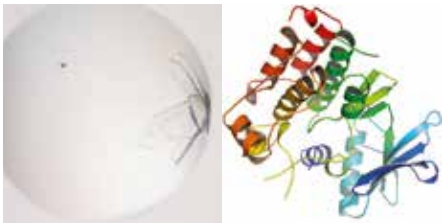
mosquito users learn about mosquito tip production

Due to the overwhelming success of this UGM, plans have already been made to run a similar event in the Americas in 2016. Please let us know if you would like to get involved in the future as a speaker or delegate and we would be happy to keep you informed as plans progress. **crystallography@ttplabtech.com**

"I enjoyed the mosquito UGM very much and it was a good opportunity to see how the mosquito can be used in different ways - we certainly picked up a few things we can try out!" **commented an attendee at the UGM.**

overcoming evaporation and **reducing costs**

Fig 1. TTP Labtech's mosquito Crystal plus active humidity chamber



a b

Fig 2. Human tyrosine kinase receptor. (a) optimised crystal in SBS sitting drop plate, 400 nL protein + 200 nL reservoir solution; X-ray diffraction limits typically 1.6 - 2.0 Å resolution, (b) cartoon ribbon representation of 1.65 Å resolution crystal structure of tyrosine kinase receptor kinase domain solved in complex with clinical candidate small molecule (not shown).

Low volume screening is very common in protein crystallography due to the limited availability of functional proteins, however this can lead to several issues including: 1) evaporation and 2) inaccuracy of dispensing. Both of these challenges can be overcome using TTP Labtech's mosquito® Crystal and its active humidity chamber.

Dr. Eric Johnson, Senior Scientist at Pfizer describes the use of the active humidity chamber in setting up initial crystallisation screens and how its use has led to a significant reduction in time and money.

multiple conditions with limited protein

The typical workflow in Dr. Johnson's laboratory involves crystallisation screening of new drug targets. This screening is usually performed at two temperatures against a minimal set of in-house proprietary screens, plus a number of commercially available screens as best suited to a particular target and protein availability (3-8 x 96 conditions). When using the mosquito Crystal (Fig 1), initial screening for *de novo* crystallisation conditions is done almost exclusively in sitting drop format with 100 nL protein to 100 nL crystallisation (reservoir) solution. With mosquito Crystal and a 200 nL total drop size, the crystallisation set-up is extremely clean and reproducible.

This workflow conserves protein and allows for greater exploration of crystallisation space. In comparison, other liquid handlers require greater than 400 nL total drop size to achieve equivalent results relative to other liquid handlers where 400 nL total drop size or greater is required to achieve equivalent results. Dr. Johnson comments, "The mosquito Crystal produces the cleanest results of any crystallisation robot we have used, and handles virtually all liquid types including protein detergent complexes, lipids (bicelle crystallisation) and relatively insoluble compounds."

Prior to addition of the active humidity chamber, each of these plates would be set up individually on the mosquito. With the active humidity chamber, drop evaporation is significantly reduced allowing much longer protocols so that plates can be set up in pairs. For example, 100 nL of protein is aliquoted across two plates. 200 nL of reservoir solution is aspirated and

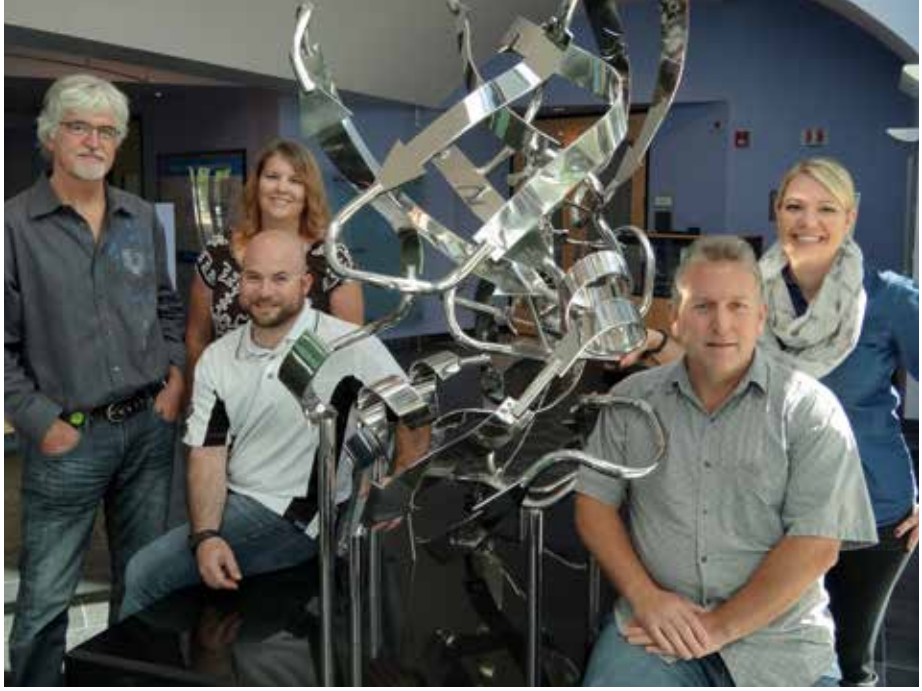
then using the multi-dispense function of mosquito Crystal, 100 nL is copied to the crystallisation drop of the first plate and 100 nL is copied to the second plate. There is no issue with cross-contamination because the two plates are duplicates of each other and contain the same protein and reservoir solutions in equivalent plate positions. This greatly speeds up the screening process, and can cut tip consumption in half.

your flexible friend

The great flexibility of the mosquito also allows for hanging drops to be routinely set up during the optimisation of hits obtained from initial screens in sitting drops.
"The mosquito Crystal can handle any type of crystallisation set-up I want to throw at it: sitting drops, hanging drops, microfluidic chips (i.e. Crystal Former), or microbatch crystallisation under oil," says Dr. Johnson.

> "The mosquito Crystal produces the cleanest results of any crystallisation robot we have ever used"
>
> **Dr. Eric Johnson, Pfizer**

Variation of the ratio of protein to crystallant drop volume is also quite useful for initial screening and optimisation. Based on hits from initial screens at a 1:1 ratio, exploring different ratios has quickly produced optimised crystals of high diffraction quality (Fig 2). Structures were solved from human tyrosine kinase crystals and contained both the kinase domain (KD) and the juxtamembrane (JM) domain (Fig 2). A structure containing the juxtamembrane domain was unprecedented and the observed interactions of the KD and JM domains were found to be critical for binding of allosteric inhibitors. These results led to a robust structure-based drug design (SBDD) platform being developed and >100 co-crystal structures being delivered to the project.



Members of the PPPG at Pfizer's La Jolla campus from left to right, Ciaran Cronin, Michelle Kraus, Oleg Brodsky, Eric Johnson, and Nicole Grable

The multi-aspirate function of the mosquito Crystal can also be used for additive screening/seeding for example 100 nL protein + (90 nL precipitant with multi-aspirate of 10 nL additive/seed stock).

The mosquito Crystal has also been employed for other applications that require low volume liquid handling needs in an SBS plate format for example, thermal denaturing assays, dynamic light scattering and PCR.

Combining the advantages of mosquito Crystal, which consistently delivers small volume drops of any liquid, with the humidity chamber enables high throughput crystallisation screens to be achieved.

Dr. Eric Johnson is a senior scientist who provides expertise in protein purification and crystallisation for the Parallel Protein Production Group (PPPG) at Pfizer Global Research and Development, La Jolla, California, USA. Additional support is provided for high throughput protein crystallisation and various aspects of X-ray crystallography for the Structural Biology Group at Pfizer's La Jolla campus. The PPPG Group is responsible for protein expression, construct screening, and scale-up for both the Departments of Cancer Protein Sciences and of Biochemistry and Primary Screening. The Group also has responsibilities for gene-to-structure efforts on a number of in-house Structure Based Drug Design (SBDD) projects.

using protein crystallography **to develop new flu drugs**

Pandemic and world-wide emergence of Tamiflu-resistant seasonal human influenza has highlighted the need for the ongoing development of new anti-virals, efficient production of vaccine proteins and novel diagnostic tools. Analysis of drug-protein interactions using X-ray crystallography can be used to elucidate the key molecular contacts which lead to inhibition. These interactions can be optimised to establish strong anti-viral drugs. However this pioneering work requires large quantities of protein. Prof. Kurt Krause, Otago University, New Zealand and his group have been establishing a novel eukaryotic expression system for influenza neuraminidase (NA). Ashley Campbell, an MSc student has worked on expressing an NA protein in this system that is suitable for X-ray crystallographic studies.

miniaturising the crystallisation process

The influenza surface glycoprotein NA is essential for the efficient spread of the virus. When inhibited, viral spread between hosts is limited and symptoms of the disease decrease rapidly. Miniaturising the optimal expression system for an NA protein has proved to be challenging.

The initial stages required Ashley Campbell to set up small-scale crystal screens in order to find suitable conditions for crystallisation. Choosing these conditions can be a daunting experience when you need to conserve limited pure protein sample and set up very small and accurate drop sizes.

Using the mosquito® Crystal robot, crystallisation drop sizes were reduced to 150 nL, allowing more conditions to be screened. Ashley set up crystal drops using the hanging drop method on 96 well plates, containing various crystallisation conditions. The multi-aspirate function of mosquito Crystal allowed for the aspiration and mixing of 150 nL of protein sample with 150 nL of each crystallisation condition. Crystal hits occurred in 27 out of the 192 conditions (Fig 1a) allowing many opportunities to optimise the crystal (Fig 1b) from only a small protein sample.

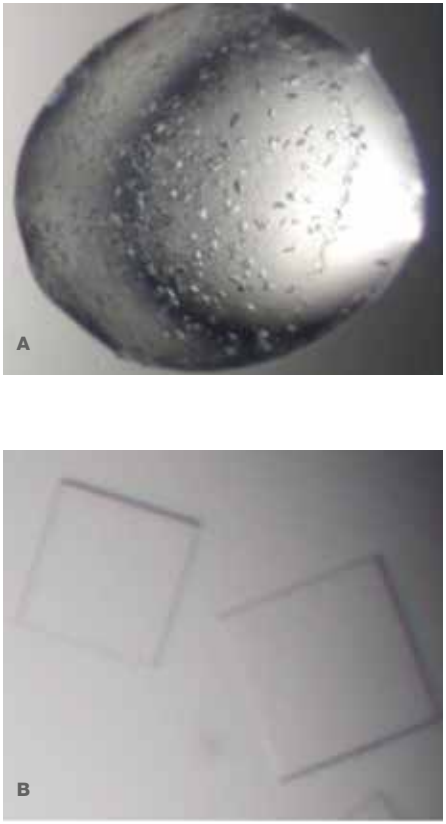


Fig 1: Crystals of influenza neuroaminidase. (a) A 300 nL drop, set up by mosquito Crystal in a crystal screen. The crystallisation condition containing 12% PEG-20,000, 0.1M MES, pH6.5 was further optimised to produce thin plate crystals (b).

"The mosquito Crystal has made it possible to work with more proteins that are only available in small amounts. This means that new projects can be started more readily and new vista are opened up for scientific inquiry."

Prof. Kurt Krause, Otago University

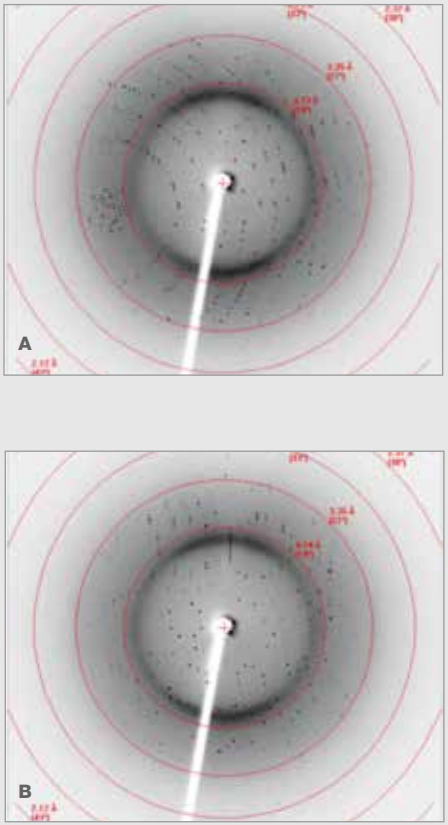


Fig 2: Good diffraction patterns of two optimised influenza neuraminidase crystals showing clean isotropic diffraction and well resolved spots into the high 2 Å ranges (in house data)

Further X-ray diffraction of these crystals produced crystals into high 2Å ranges (Fig 2).

accuracy and precision

Reducing dispensing volumes to nanolitre amounts requires accuracy and precision that is not possible using manual methods. Automating this process enables consistency in pipetting and minimise operator error. The volume range capabilities of liquid handling systems vary considerably and are dependent on on the type of dispensing technology. The accuracy of mosquito Crystal is unrivalled mainly due to its unique positive displacement pipetting. Prof. Krause commented, "The mosquito Crystal has made it possible to work with more proteins that are only available in small amounts. This means that new projects can be started more readily and new vista are opened up for scientific inquiry."

It also boasts a system of disposable micropipette tips that reduce the likelihood of cross contamination, remove the need for time-consuming wash steps or replacing costly, fixed-tip dispenser heads. The pipette tip design also allows the tip to reach the bottom of a well – leaving minimal (<0.3 µL) dead volume in the source well and no in-tip dead volume. This allows you to keep all the savings from an efficient set-up process.

From a student's point of view Ashely Campbell commented, "I have found mosquito Crystal very user-friendly which has meant that I can work independently and still produce high quality crystals."

Ashley Campbell, MSc student, Otago University

Ashley Campbell is an MSc student in biochemistry, at the University of Otago. She works with Prof. Kurt Krause who is Director of Webster Centre for Infectious Diseases at the university. Ashley's research focuses on the expression and purification of the influenza neuraminidase protein in a eukaryotic cell line for the identification and characterisation of novel inhibitory drugs.

membrane protein crystallisation **is it still a fine art?**

Thirty percent of genes in the human genome encode for membrane proteins and 60% of drug targets are membrane proteins [1]. Mutations or improper folding of membrane proteins are associated with many known diseases such as heart disease, depression, cancer and many others. Dr. Isabel Moraes, Head of the Membrane Protein Laboratory (MPL) at Diamond Light Source (DLS), UK has recently reviewed the methods used for the successful crystallisation of membrane proteins [2,3]. This article will discuss the issues associated with crystal formation of membrane proteins and how modern approaches have helped to further this research.

bottlenecks

Membrane protein structure determination is challenging, complex, and subject to many bottlenecks. There are a wide variety of key parameters to monitor, steps in the process, and technical options that can be applied to each step – all of which need to be tracked and assessed against results. Consequently when membrane protein crystals are obtained, they are often extremely fragile. In addition, membrane proteins are very unstable and prone to aggregate, which often hampers the crystallisation process.

In the last decade significant efforts have been made to improve the production and crystallisation of membrane proteins. Many of the crystallisation strategies have benefited from developments in automation and miniaturisation.

"We really need a crystallisation machine that is easy to work with and reliable.....that's our mosquito!" **Dr. Isabel Moraes**

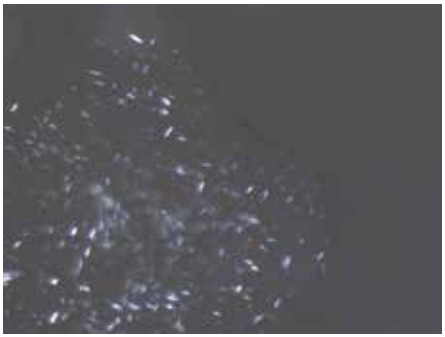


Fig 1: LCP crystals of the Human Histamine Receptor 1 in complex with anti-histamine drug. Crystals were set up with the mosquito LCP.

For example, the use of liquid handling robots such as TTP Labtech's mosquito® range has increased the number of potential crystallisation conditions that can be screened while at the same time reducing the amount of protein sample required.

lipidic cubic phase technology

In addition to the vapour diffusion method, membrane proteins are often crystallised in lipidic cubic phase (LCP). TTP Labtech's mosquito LCP provides

the combination of three important factors; 1) reduction of sample size down to nanolitre volumes, 2) speed (about 4 mins to complete a single 96-well LCP plate) and, 3) accuracy and repeatability. In the Membrane Protein Laboratory at DLS, mosquito LCP is a vital part of the crystallisation HTP platform. It helps the crystallisation of membrane proteins by setting up trays with small volume drops (25 nL upwards) in a short space of time. While drop evaporation of such small volumes has not been a significant issue, TTP Labtech's active humidity chamber provides excellent assurance of the integrity of even the most sensitive samples.

pursuing diffracting crystals

What is also notably true for membrane proteins is the difficulty in obtaining crystals of sufficient size (50-100 microns) and order (low mosaicity) to generate the high quality diffraction data required for structure determination. A major breakthrough in addressing these difficulties has been the arrival of dedicated microfocus beamlines. The MPL has a formal collaboration with I24 microfocus beamline at DLS, UK to develop new techniques for crystallisation and structural determination of membrane proteins [4].

There are still many challenges associated with the structure determination of membrane proteins but the combination of crystallisation automation and synchrotron instrumentation makes the future look bright.

Dr. Moraes, Head of the MPL at DLS remarked, "In our lab, 99% of the solved membrane protein structures are from crystals set up with our TTP Labtech mosquito LCP. At the moment, MPL has around 40 active projects- in all the projects the crystallisation process is being performed by TTP Labtech's mosquito LCP."

Recently, Dr Moraes's group, in collaboration with an industrial partner, have solved two holo H1R crystals structures bound to the highly selective second and third generation H1R antagonist (unpublished data). They will make a significant contribution to computational guided structure-based drug discovery of new antihistamine drugs targeting H2, H3 and H4 receptors where crystal structures are still absent (Fig 1).

Dr. Moraes continued, "Because we operate as a user facility and have many different external users making use of the lab, we really need a crystallisation machine that it is easy to work with and reliable....that's our mosquito! I have been using several generations of the mosquito for more than 8 years and it has never let me down!"

Dr. Isabel Moraes, head of MPL at DLS

Dr. Isabel Moraes is Head of The Membrane Protein Lab (MPL) at Diamond Light Source (DLS), Oxford, UK. MPL is a research and training facility for scientists interested in solving the 3D structures of membrane proteins by X-ray crystallography. The MPL is a joint venture between the Diamond Light Source in Oxfordshire and Imperial College London funded by the Wellcome Trust.

[1] Wallin, E. and von Heijne, G. (1998) Protein Sci. 7(4): 1029–1038.
[2] Moraes, I. and Archer, M. (2015) In: Raymond J. Owens (ed), Structural Proteomics: High-Throughput Methods, Methods in Molecular Biology, vol 1261
[3] Moraes, I. et al. (2014) Biochim Biophys Acta 1838(1 Pt A):78-87
[4] Axford, D. et al. (2012) Acta Cryststallogr D Biol Crystallogr 68(Pt5): 592-600

when customer service **makes all the difference!**

You buy a new instrument for your lab to optimise your workflow and everyone is happy……that is until something goes wrong! Whether the issue is due to instrument fault, user error or lack of maintenance, subsequent steps can make all the difference in getting you back up and running quickly. TTP Labtech's range of mosquito liquid handlers have earned a market-leading reputation for being very robust, simple to use and requiring virtually no maintenance. That is why the engineering teams at TTP Labtech take it very personally when a customer reports a problem with a machine. However you don't need to just take our word for it, Professor Rick Lewis, Institute for Cell and Molecular Biosciences, Newcastle University, UK describes his recent work and comments on his experience with TTP Labtech's customer service.

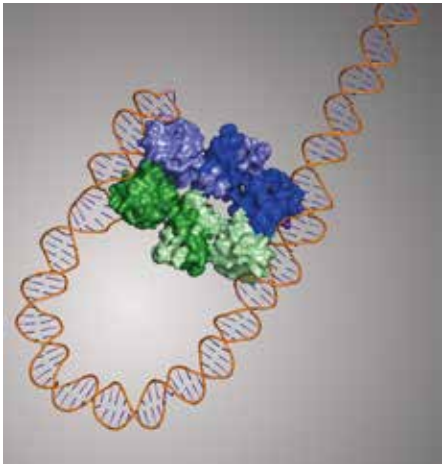


Fig 1. Structure of SinR bound to DNA. SinR inhibits the formation of the molecular glue that holds a biofilm together by binding to specific targets on the DNA. These targets are spaced so that the DNA forms a loop around the protein.

Newcastle Structural Biology Laboratory (NSBL) bought a mosquito® Crystal in 2006 as one of the first off the production line. Subsequently they went on to buy a mosquito LCP. Since then mosquito Crystal has become the leading crystallisation robot in the crystallography market. Prof. Lewis reported, "We chose TTP Labtech's liquid handler because the mosquito LCP came out top in our trials of the instruments from alternative manufacturers and the customer service has always been excellent." therefore purchasing an additional mosquito LCP was an easy decision to make.

supporting award winning research

The primary goal of Prof. Lewis' group is to solve structures of proteins and protein complexes from the Gram-positive model bacterium, *Bacillus subtilis,* using X-ray crystallography.

Published work from Prof. Lewis' lab won 'Paper of the year, 2013' in the Journal of Biological Chemistry, for its excellence and potential impact on the field [1]. This work examined the crystal structure of a molecular switch, SinR, which regulates biofilm formation. Bacterial biofilms are an increasing environmental and healthcare issue and therefore knowledge of the regulatory pathways underpinning its formation is essential to develop effective intervention strategies. The crystal structure of the SinR biofilm switch in complex with DNA was determined by setting up sitting drop vapour diffusion crystallisation trials of a SinR-DNA complex (in a 1: 1.2 ratio) at a concentration of 5 mg/mL using the mosquito® Crystal. The crystals diffracted to 3.0 Å and the resulting data

revealed that the most effective means of transcriptional control occurs by the looping of promoter DNA (Fig 1)[1].

producing crystals that were previously not possible

There are some crystallisation projects, however, that do not lend themselves to manual scaling-up and optimisation.

"If all our suppliers were like you then we'd be permanently happy. We really appreciate the fact that your company listen to what we say, and then act upon it accordingly!"

One example is the recent structure of the LdcB carboxypeptidase in complex with a product mimic. LdcB matures freshly-synthesised peptidoglycan in the bacterial cell wall, but the study of these enzyme types is hindered by the challenge of obtaining their substrates on a large enough scale to support crystallography. The scarcity of the ligand means that the only crystallisation trials that can be done are with small volume drops. Prof. Lewis' group set up hanging drops containing as little as 100 nL of protein: ligand complex. This was accurately dispensed by TTP Labtech's mosquito Crystal, producing crystals that diffracted to 2.8 Å [2].

technology and support you can rely on

Prof. Lewis stated, "There is little to go wrong with TTP Labtech's instruments, inveterate "fiddlers" can do little damage! However on the occasions where we have had to contact TTP Labtech with regard to any faults or breakdowns, the after-sales care has been excellent and could not be faulted."

Prof. Lewis continued, "Overall, TTP Labtech is a great company to do business with, and their mosquito products are truly excellent, best-in-class products."

Prof. Rick Lewis, head of NSBL, Newcastle University

[1] Newman, J.A. et al (2013) J. Biol. Chem. 288: 10766-78
[2] Hoyland, C.N. et al (2014) Structure 22: 949- 60

Prof. Rick Lewis heads up the Newcastle Structural Biology Laboratory (NSBL) within the Institute for Cell and Molecular Biosciences (ICaMB) of Newcastle University, UK. The group utilises a multi-disciplinary approach to determine the X-ray crystal structures of proteins and their interactions with small and large ligands. Working collaboratively with research groups in areas such as electron microscopy, biochemistry and cell biology the work provides functional context to defined structural data. Current work in Prof. Lewis' group includes solving structures of proteins and protein complexes that are involved in the formation of the cell wall of some bacteria, and how bacterial biofilms are formed and dispersed.

crystallographers' **favourite** crystallisation robots

TTP Labtech's liquid handling portfolio provides you with accurate and repeatable nanolitre to microlitre pipetting, every time, irrespective of liquid viscosity or environmental conditions. Each of TTP Labtech's disposable micropipette tips has its own individual piston – not an air gap or system liquid – offering true positive-displacement pipetting with no risk of clogging or cross-contamination.

mosquito® Crystal (25 – 1,200 nL)

miniaturising your crystallisation screening

mosquito Crystal is the market leading crystallisation robot. It brings together speed and accuracy with high precision pipetting of nanolitre volumes with zero cross-contamination from a disposable tip.

- **flexible automation** – rapid automated plate set-up
- **unrivalled reproducibility** down to 25 nL
- **cost savings** – assay miniaturisation reduces costs of reagents
- **no configuration changes** needed for different experiments
- **multiple-aspirate functionality** with a single dispense
- **precision drop** pipetting
- **ideal for multi-user labs**

mosquito® LCP (25 – 1,200 nL)

membrane protein crystallisation made easy

mosquito LCP is the ultimate tool for membrane protein crystallisation, screening, optimisation and scale-up. mosquito LCP allows you to dispense lipidic cubic phase (LCP) volumes as low as 25 nL, while automated calibration of syringe and pipette positioning ensures precise drop-on-drop placement to facilitate automated imaging.

- **versatility** - ability to set up LCP and traditional protein crystallisation experiments
- **sample flexibility** - pipetting a wide range of liquid viscosities with no format change required
- **speed** – rapid tip changing and no washing
- **negligible evaporation** due to rapid dispensing

dragonfly® (0.5 µL – 4 mL)

mosquito's ideal optimisation partner

dragonfly enhances protein crystal screen optimisation. dragonfly is the ideal system to complement TTP Labtech's mosquito in the protein crystallisation workflow. Once the initial crystal 'hits' are identified, dragonfly can create a set of optimised conditions to grow better diffracting crystals.

- **simple** - easy to use screen design software and no liquid classification required
- **accurate** - dispense any volume, into any well with no cross-contamination
- **fast** – rapid completion of plate (4-8 mins) irrespective of viscosity
- **negligible evaporation** of the dispensed reagents due to minimal set-up time
- **stock integrity** - positive displacement technology preserves stock integrity, even for volatiles

accessories

LCP mixer

The LCP mixer has been designed to automatically mix protein and monooelin, or other lipids, into a lipidic cubic phase from two coupled syringes. It accepts any combination of 100 µL and 50 µL Hamilton Gastight syringes and any starting sample volume (high or low) in either syringe. The simple and robust design, offers easy loading and on-the-fly adjustments of mix cycles without the need for a full calibration process.

active humidity chamber

mosquito's active humidity chamber reduces experimental inconsistencies caused by variation in the humidity in the environment, by allowing users to accurately control the relative humidity of each experiment. The humidity chamber enables up to a 90% reduction in drop evaporation.

MXone – in-well mixer

The MXone keeps the plate stationary, allowing for extremely fast mixing of even the most viscous solutions with no risk of spillage using high-speed oscillation of a disposable pin array.

mosquito® Crystal

mosquito® LCP

dragonfly®

specifications	mosquito® Crystal	mosquito® LCP	dragonfly®
pipetting range	25 – 1,200 nL	25 nL – 1,200 nL	0.5 µL – 4 mL
applications	protein crystallography set-ups e.g. additive screening, microseeding, microbatch, bicelles	lipidic cubic phase (LCP) screening plus all the functionality of mosquito Crystal	protein crystal optimisation and assay development without contamination or liquid classification
primary SBS plate format	48, 96, 384	48, 96, 384	15, 24, 48, 96, 384
reservoir capacity	n/a	n/a	10 mL
optional extras	activity humidity chamber	activity humidity chamber, LCP mixer	MXone automated in-well mixer
throughput	< 2 mins/ 96-well plate. 4 mins/ 288 drops	2 mins/ 96 drop plate for vapour diffusion 5 min/ 96 drop LCP plate	4-6 ingredient, 96-well plate in 4-8 mins, irrespective of viscosity

consumables

essentials for innovative technology

TTP Labtech is the sole supplier of the full range of consumables and accessories for our mosquito® liquid handlers and our new dragonfly® screen optimiser. They are developed and manufactured to the same high standard of design and engineering as our instruments – quality we also demand from our suppliers. The combination of cutting-edge innovation and precision manufacturing ensures accurate results in the lab, every time.

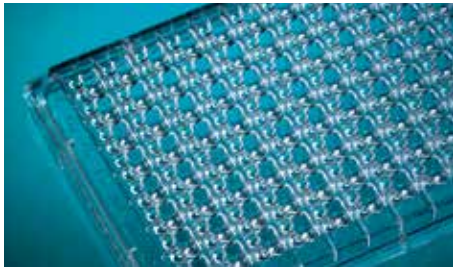
Our new online TTP Labtech Store combines speed and ease-of-purchase with a supply of the highest quality products. This covers all liquid handling essentials including LCP accessories, pipette spools, plate seals, plates and reservoirs, all of which are listed by consumable product or by instrument.

The store is also updated with regular "Tips and Tricks" videos to help you in your day-to-day laboratory work plus special offers.

Visit **www.ttplabtechstore.com** to view the full range of TTP Labtech consumables range.

new arrivals!

Check out our new and extensive range of Swissci plates for optimal sitting drop crystallisation experiments.



service excellence

Our consumables are covered by the same unparalleled technical and application support as the TTP Labtech instruments. We pride ourselves on the personal relationships that our dedicated team of experts build with our customers every day.

service and support

Stress-free ownership - we have got it covered anytime, anywhere!

why do I need a service contract?

Service contracts are much more than just a way to 'protect your investment' after purchase. Our contracts are designed to suit all budgets and requirements, whilst our engineers offer the very best in technical knowledge and live support. Other benefits include:

1. peace of mind
When critical equipment fails, knowing expert assistance is only a phone call or email away allows your team to get the project back on track quickly.

2. extended equipment lifetime
With regular and continued annual service, TTP Labtech instruments typically have a life cycle in excess of 10 years.

3. priority status
All our contract customers receive priority over those without contracts.

4. application support
All our contracts include exclusive access to our dedicated team of application scientists, who can offer help and advice to support all their application needs.

5. cost management
With a full service contract, service costs are fixed. Therefore total spend will always match the budget.

"The quickest customer service I've ever experienced. Outstanding!!!"

Tom Noonan, Automation Specialist, EMD Serono

For further information on service contracts, please contact +44 (0)1763 266708 or email us on LTsupport@ttplabtech.com.

Want to know how we can help you improve your crystallisation experiments? Want to see how our instruments work? For many more valuable resources for crystallographers, check out our website **http://ttplabtech.com/resources**

application notes

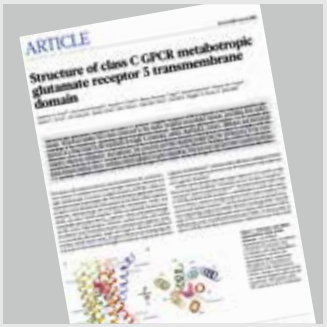
posters

webinars

videos

news, blogs and events

bibliography



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