BIO NEWS

No. 59 – 2023

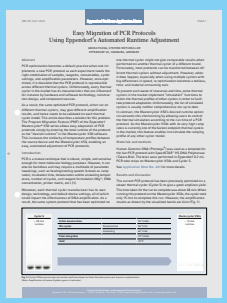
eppendorf

epMotion®: Gain Freedom to Do What Really Counts

> Pipette tips – sustainability is now a reality
> ISO 8655-6:2022: the high art of pipette calibration
> Improve bioprocess data quality, decrease effort

Application Notes

Easy migration of PCR protocols using automated runtime adjustment · Rapid separation of lipoprotein fractions from human serum by ultracentrifugation · etc.


Easy Migration of PCR Protocols
Using Eppendorf's Automated Runtime Adjustment

Welcome

to a new edition of Eppendorf BioNews.

In our leading article on pages 4–5, we present to you the epMotion®, one of the most precise systems for automated liquid handling available. Free up your time with an epMotion for what's most important: Your research!

For Eppendorf, sustainability in the laboratory has been a subject close to our heart for years now. On page 6, we explain how we cut down on plastic by implementing smart changes to the design of racks and packaging forms. But our raw materials are also under continuous development. Following the successful launch of Eppendorf Tubes® BioBased, we have now also changed the material of some premium pipette and filter tips to a biobased polypropylene, where crude oil is largely replaced by 2nd generation cooking oil – without compromising product performance and quality.

"I should have made more notes," an often-heard heartfelt sigh when there are problems with the documentation of information relevant to samples. Yet it could be so easy – with the SafeCode system from Eppendorf, available for a multitude of consumables (p. 10).

Watch out, bioprocess engineers! Using our new Bioprocess Autosampler can improve your bioprocess data efficiency and reduce workloads. Read more on page 11 and in Application Note 3–4.

Other topics in this issue: Pipette calibration in accordance with ISO 8655-6:2022, our new Service Portal, sustainable ULT freezers, PCR, tips on cell cultures, 8 pages of Application Notes, and much more.

And as always, there are attractive prizes for your laboratory in our prize competition on page 15!

Your Eppendorf BioNews team

PS: Would you like to share your thoughts with us about BioNews? Do you have ideas or requests? If so, please send us an e-mail to bionews@eppendorf.de. We look forward to your feedback!

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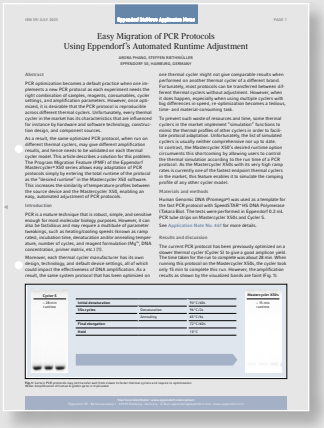
Eppendorf BioNews Application Notes


Easy Migration of PCR Protocols
Using Eppendorf's Automated Runtime Adjustment

BERRIT HOFF, EPPENDORF SE

epMotion®: Gain Freedom to Do What Really Counts

In our leading article, we invite you to get to know the epMotion, one of the most precise systems for automated liquid handling on the market. If you are striving for maximum reproducibility in your assays and the highest possible flexibility in adapting to changing experimental requirements, read our interview with Dr. Tim Schommartz, Global Marketing Manager. Tim is a molecular biologist himself (with a focus on virology), and he knows from his own experience about the potential that can be unleashed for actual research through the use of automated systems.

With our epMotion systems, you will gain time and mental freedom for your true passion – research

BioNews: Tim, February 2023 saw the worldwide debut of the new generation of epMotion at the SLAS conference in San Diego, CA, USA. Your conclusions?*

Tim Schommartz: The SLAS is basically "the place to be" for automated systems, and we were completely thrilled to be on site at this important event.

Our motto "Unleash Your Potential", too, hit the bullseye. When it comes down to it, it's about nothing else! With our epMotion systems, researchers gain freedom with respect to both time and creativity, and they can now realize their full potential for their true passion – research.

BN: By handing tedious tasks off to a "robot"?

TS: Exactly – it's about the switch from the manual to the automated workflow. We aim to show how easy and intuitive it is to implement our epMotion systems for routine tasks, in particular to those users who have not yet had a chance to familiarize themselves with laboratory automation. Even in smaller laboratories and with lower throughput, it can be done in a short period of time and without the need for extensive training!

BN: What is it that distinguishes the new generation of epMotion?

TS: The new instruments represent an advancement of the epMotion 5073 and epMotion 5075 series which have been established for nearly 20 years. These had been continually improved over time – with a focus primarily on technological

Drawer for more storage space and increased waste disposal capacity

improvements, that is to say, their "inner values" – while their original, blue-dominated design remained unchanged.

In contrast, the new generation now also features a new design (in addition to thoughtful improvements of details): white, clean, and clear – but also solid and robust!

BN: What exactly has been optimized?

TS: It was particularly important to us to further improve the user experience. For example, the waste system was re-engineered. It now has a higher capacity for liquid as well as solid waste, thus allowing for longer protocol runtimes and (even) fewer manual interventions throughout a run.

The superb liquid handling performance for which the epMotion systems are renowned remains unchanged in the new generation of instruments. epBlue, the user software, has likewise undergone only gentle changes as it was already designed with maximum ease of introduction for the novice in mind. The grouping of commands, for example, has been added as a comfort feature.

BN: What support will epMotion owners receive?

TS: All Eppendorf installation services and service products are also available for the new generation of epMotion. This includes our premium application support for on-site establishment of methods. We offer our users an enormous number of qualified protocols by leading manufacturers of molecular biology reagents. It's practically an all-round comfort package!

BN: Is it possible to combine the new generation of epMotion with existing systems?

TS: This is not a problem as basically all dispensing tools, consumables, and accessories of the new generation are compatible with those of the previous generation. In principle, nothing stands in the way of the expansion of an existing epMotion fleet through the addition of the new systems. Even protocols established on older epMotion systems can be transferred to the new generation with the help of our application support.

More information at:
www.eppendorf.com/automation

Dr. Tim Schommartz, Global Marketing Manager Automation, with the new epMotion at the SLAS conference in San Diego

*Society for Laboratory Automation and Screening

News

Document Your Pipetting Activities

The connected electronic pipette system *Eppendorf Pipette Manager* received a new major feature: *Pipetting Records*. The latest software update adds the ability to automatically record pipetting activities with the choice to export recordings as a PDF file via USB. The Pipette Manager now not only enables faster operation and guidance for the correct handling of challenging liquids but also digital documentation of every pipetting step with connected pipettes.

After the integration of Move It® pipettes in 2022, the Pipette Manager is now compatible with all Eppendorf Xplorer® (plus) pipettes. The system includes several other features that are designed to help you effectively manage your pipette fleet and enhance collaboration with ease. Overall, the Pipette Manager is an essential, easy-to-use tool for every lab that seeks to improve the efficiency and reproducibility of workflows with many intricate pipetting steps.

Learn more and discover
our digital demo tool at
www.eppendorf.com/pipette-manager

BRIGITTE KLOSE, EPPENDORF SE

Pipette Tips – Sustainability is Now a Reality

We at Eppendorf know about the key role that consumables made from plastic play in the laboratory. At the same time, we are aware that the balance between the demands of modern science and the concern for the environment represents a pivotal challenge in the management of a life science laboratory. For these reasons we adhere to the principle of "Reduce, Reuse, Recycle" when and wherever possible, and we place increasing emphasis on the use of biobased raw materials.

Sterile Reloads and optimized epT.I.P.S. Box 2.0

Reduce, Reuse, Recycle

With respect to the packaging options for our epT.I.P.S.® pipette tips, we have been counting on our reusable epT.I.P.S. Boxes exclusively since 2002 for non-pre-sterilized tips. The epT.I.P.S. Boxes can be re-filled with our pre-stacked Reloads again and again and, if needed, they can be autoclaved up to 100 times.

Only recently, the design of our epT.I.P.S. single-use Racks, which meet the highest demands of our customers, was streamlined to such a degree that up to 30 % of plastic could be saved, depending on rack size.

This year, we have taken a further step in this direction: especially for pre-sterilized pipette tips, we have developed a novel type of packaging which, compared to the single-use Racks mentioned above, now requires even less raw material – requiring up to 54 % less polypropylene, depending on size. These "Sterile Reloads", together with the newly designed epT.I.P.S. Box 2.0, comprise a sustainable plastic-saving system.

Biobased raw material

In parallel to the introduction of the new Sterile Reloads, we are also optimizing the sustainability of the pipette tips contained therein. Following the successful launch of the Eppendorf Tubes® BioBased made from biobased polypropylene (PP), the pipette tip variants of the new sterile Reloads are also manufactured from a biobased PP. In the case of biobased PP, crude oil is for the most part replaced with cooking oil of the second generation, i.e., cooking oil waste and leftover oil generated by the food industry. This PP, which is based on renewable raw materials, as well as all manufacturing steps, are certified through ISCC Plus – a reliable, globally leading certification system for the production of sustainable products.

BioBased – no compromise

These pipette tips do not exhibit any differences from fossil-based epT.I.P.S. and ep Dualfilter T.I.P.S.® pipette tips with respect to quality and performance. All quality guarantees provided with our product and lot-specific certificates are equally valid for epT.I.P.S. and ep Dualfilter T.I.P.S. BioBased. The switch to these pipette tips made from biobased raw material does not pose a risk to your samples or experimental results.

More information:
www.eppendorf.com/eptips-news

CHRISTINE COWEN-ELSTNER, EPPENDORF SE

Vaccinations – A Success Story

The perpetual struggle between viruses and vaccines is one of the oldest stories in the field of medicine. 1500 BCE marked the beginning of the fight against smallpox in China as doctors ground pieces of the crust of smallpox lesions from infected people and administered the powder through the nose. In Asia and Europe, people transferred the contents of smallpox pustules to healthy people in order to immunize them.

Over the past few decades, a number of vaccine technologies have been developed which support us in our battle against viruses. Traditional inactivated vaccines boast a proven track record for many diseases. While these vaccines still require the cultivation of the pathogen, all the vaccines of the newer generation, e.g. recombinant protein and nucleic acid vaccines, need the genetic sequence of the pathogen. These groundbreaking platforms can considerably accelerate the processes involved in development and manufacture, as well as open up a new potential for a broad spectrum of indications at a speed never seen before.

Inactivated vaccines (e.g. against hepatitis A, rabies, polio) still contain the entire repertoire of immunogenic compounds of the original pathogen. Correct and thorough inactivation is imperative in order to prevent reactivation and replication of the virus inside the host.

Protein-subunit vaccines (e.g. influenza, hepatitis B and C) have been a tried-and-tested strategy, and to this day, they represent a core element of pandemic management.

mRNA technology

Nucleic acid-based vaccines consisting of mRNA or plasmid DNA contain the blueprint for viral antigen components, and following injection, they lead to the production of pathogen-specific antigens. The groundbreaking technology of mRNA vaccines experienced its breakthrough with SARS-CoV-2, and it shows potential in many novel clinical areas, including HIV, cancer, shingles, influenza, cardiovascular applications, and Zika.

Our battle against viruses will never be over, but thanks to modern vaccine technologies, we now have more tools at our disposal with which to combat them and protect the health of the global population.

More information

www.eppendorf.link/vaccine-research

News

Happy 60th, Eppi®!

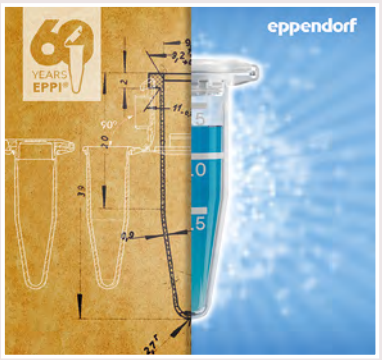
This year, the Eppendorf Tube is celebrating its birthday; it was 60 years ago that the first micro reaction vessel by Eppendorf was introduced to the world. Since that time, the tube, to which our customers lovingly refer as "Eppi", has made an international name for itself.

Only very few innovations go on to generate standards in the laboratory world and revolutionize application processes. This definitely applies to the Eppendorf Tube!

It all began in 1963

The Eppendorf Tube 3810 entered the market and rapidly gained popularity in medical and science laboratories all over Germany. Smaller sample volumes in the microliter range could now be aliquoted and stored in a practical fashion. As such, the Eppi became a major component of the microliter system developed by Eppendorf which had been launched two years earlier, with the first piston-stroke pipette laying the groundwork. Rotors, mixer blocks, tube racks, and much more was custom designed for the Eppendorf Tube in order to enable seamless laboratory workflows.

Throughout the past 60 years, Eppendorf has consistently added more chapters to the Eppi success story with its variety of new Eppendorf Tubes®*. And it is far from complete!



www.eppendorf.link/60YearsTubes

*Eppendorf Tubes are meanwhile also available in amber for effective light protection for sensitive samples. More on this topic in our video "Maximum Light Protection with Eppendorf Amber Tubes: How it works".

HANAË KÖNIG, EPPENDORF SE

Successful Transfer of PCR Protocols

Your PCR cycler has been running reliably for years, and all protocols have been saved and optimized. But now, a new model is being purchased. If the heating and cooling rates differ between instruments, PCR results may be impacted. Almost every cycler offers the option of adjusting the heating and cooling rates.

The results obtained from a PCR program which was carried out on two different thermocyclers can deviate from one another. One reason could be the different heating and cooling rates. Here, we consider a few options for solving this problem.

1. Manual setting of the heating and cooling rates

One method consists of setting the heating and cooling rates outlined in the technical data sheet of the thermocycler. Some competitors' instruments, however, only allow setting of the heating rate, but not of the cooling rate.

In addition, it may not be clear whether the heating rate is linear or non-linear. This is a rather uncertain method which bears a great risk that the PCR protocol will have to be re-optimized.

2. Selection of the instrument from a list saved in the new instrument

Some manufacturers' cyclers offer a list of competitors' instruments, the heating and cooling rates of which can be simulated. This is a practical function, as long as the former instrument can be found on the list. If this is not the case, the only option that remains – if at all possible – is programming the rates as described in section 1, with the disadvantages mentioned.

3. Programming the total run time of a PCR protocol

Programming the total run time of a PCR protocol directly in the software of the Mastercycler® X50 by Eppendorf is an easy method. The instrument determines the heating and cooling rates automatically, thus reproducing the same protocol. The PCR result is often comparable to the original, and further optimization is not necessary.

You will find detailed information on this function in Application Note 1–2 in this issue.

Tip

A Closer Look at Mastercycler® X50

The new Mastercycler X50 elegantly combines speed, flexibility, and ease of use. With its intuitive touch screen offering precise fingertip control, the Mastercycler X50 PCR thermocycler enables easy PCR optimization in advanced molecular biology research and dependable standardization in routine PCR applications. It is also perfectly fitted for NGS.

More information, also for download, can be found at the following links:

> Website **The Next Stage**: all about the Mastercycler X50 family

> Website **Sustainability for PCR Cyclers**

> Mastercycler X50 brochure: **The Next Stage** (PDF)

> Eppendorf PCR systems brochure: **Master of Class** (PDF)

> Mastercycler X50 Poster: **Reduce noise in your lab! Save time! Reduce your CO_2 footprint!** (PDF)

> Mastercycler X 50 Stay Informed Infographic: **Reproducibility and Speed in PCR** (PDF)

Last but not least, don't miss our short video on YouTube™: **Speed up and save time!**

Easy Migration of PCR Protocols Using Eppendorf's Automated Runtime Adjustment

ARORA PHANG, STEFFEN RIETHMÜLLER
EPPENDORF SE, HAMBURG, GERMANY

Abstract

PCR optimization becomes a default practice when one implements a new PCR protocol as each experiment needs the right combination of samples, reagents, consumables, cycler settings, and amplification parameters. However, once optimized, it is desirable that the PCR protocol is reproducible across different thermal cyclers. Unfortunately, every thermal cycler in the market has its characteristics that are influenced for instance by hardware and software technology, construction design, and component sources.

As a result, the same optimized PCR protocol, when run on different thermal cyclers, may give different amplification results, and hence needs to be validated on each thermal cycler model. This article describes a solution for this problem. The Program Migration Feature (PMF) of the Eppendorf Mastercycler® X50 series allows easy adaptation of PCR protocols simply by entering the total runtime of the protocol as the "desired runtime" in the Mastercycler X50 software. This increases the similarity of temperature profiles between the source device and the Mastercycler X50, enabling an easy, automated adjustment of PCR protocols.

Introduction

PCR is a mature technique that is robust, simple, and sensitive enough for most molecular biology purposes. However, it can also be fastidious and may require a multitude of parameter tweakings, such as heating/cooling speeds (known as ramp rates), incubation time, denaturation and/or annealing temperature, number of cycles, and reagent formulation (Mg^{2+}, DNA concentration, primer matrix, etc.) [1].

Moreover, each thermal cycler manufacturer has its own design, technology, and default device settings, all of which could impact the effectiveness of DNA amplification. As a result, the same system protocol that has been optimized on one thermal cycler might not give comparable results when performed on another thermal cycler of a different brand. Fortunately, most protocols can be transferred between different thermal cyclers without adjustment. However, when it does happen, especially when using multiple cyclers with big differences in speed, re-optimization becomes a tedious, time- and material-consuming task.

To prevent such waste of resources and time, some thermal cyclers in the market implement "simulation" functions to mimic the thermal profiles of other cyclers in order to facilitate protocol adaptation. Unfortunately, the list of simulated cyclers is usually neither comprehensive nor up to date. In contrast, the Mastercycler X50's desired runtime option circumvents this shortcoming by allowing users to control the thermal simulation according to the run time of a PCR protocol. As the Mastercycler X50s with its very high ramp rates is currently one of the fastest endpoint thermal cyclers in the market, this feature enables it to simulate the ramping profile of any other cycler model.

Materials and methods

Human Genomic DNA (Promega®) was used as a template for the fast PCR protocol with SpeedSTAR™ HS DNA Polymerase (Takara Bio). The tests were performed in Eppendorf 0.2 mL PCR tube strips on Mastercycler X50s and Cycler S.

See Application Note No. 461 for more details.

Results and discussion

The current PCR protocol has been previously optimized on a slower thermal cycler (Cycler S) to give a good amplicon yield. The time taken for the run to complete was about 28 min. When running this protocol on the Mastercycler X50s, the cycler took only 15 min to complete this run. However, the amplification results as shown by the visualized bands are faint (Fig. 1).

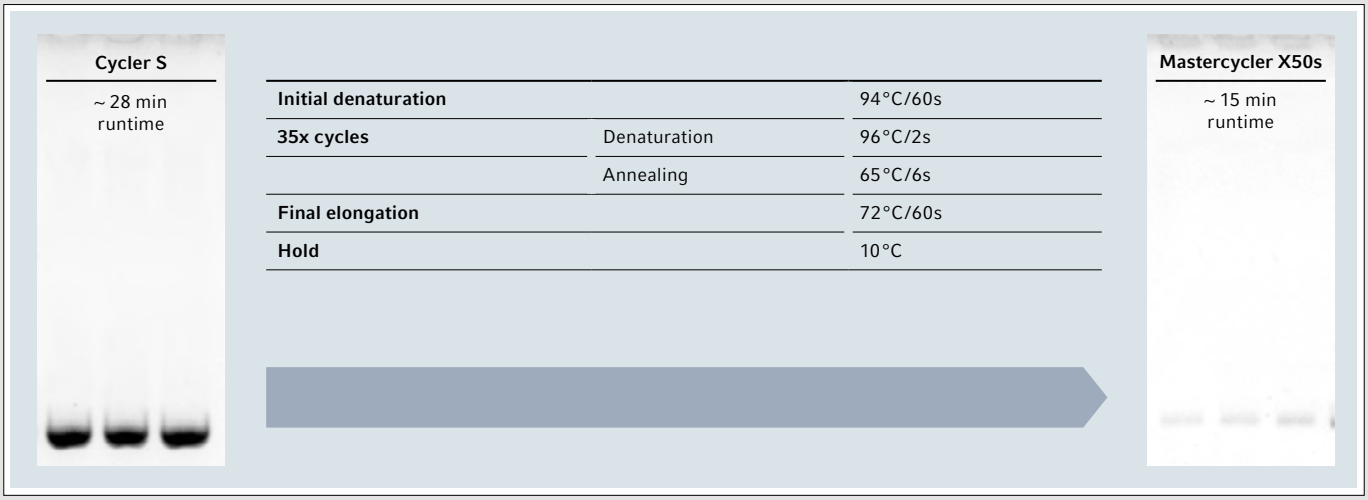


Fig. 1: Certain PCR protocols may not transfer well from slower to faster thermal cyclers and require re-optimization
(Note: Amplification of human ß-globin gene in triplicates)

Easy Migration of PCR Protocols Using Eppendorf's Automated Runtime Adjustment

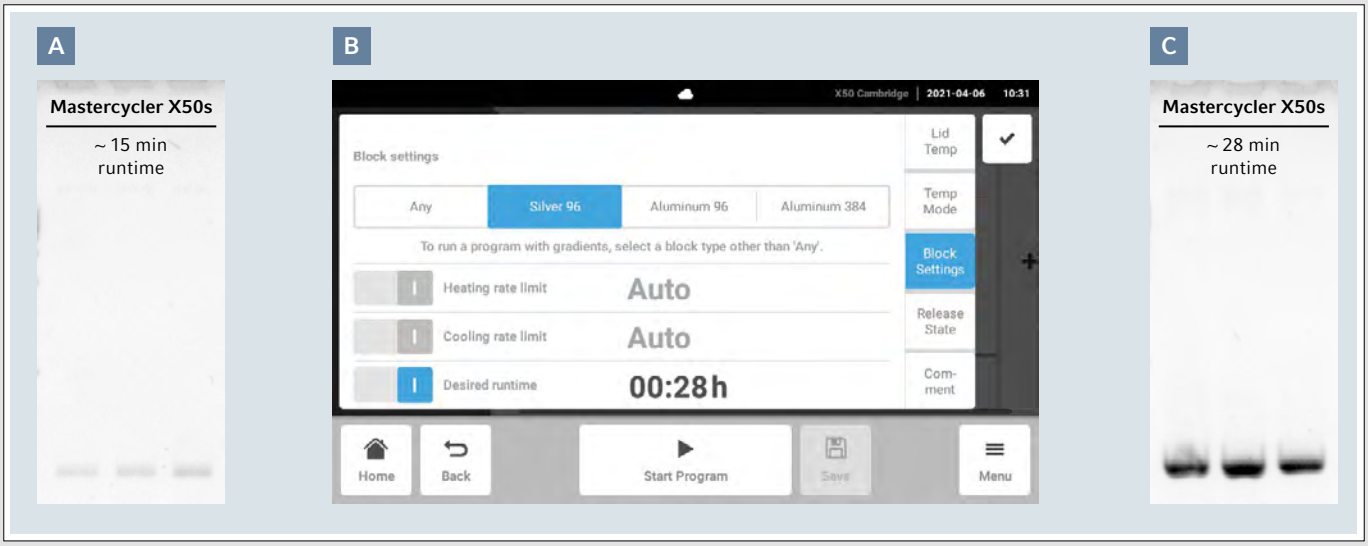


Fig. 2: PCR results before (A) and after (C) the Program Migration Feature (PMF) was activated using the "Desired runtime" option (B)

Usually, when facing such problem, the user can manually program the heating and cooling rate on the target cycler (e.g. Mastercycler X50s) according to the desired result on the original cycler (e.g. Cycler S). However, due to the multitude of hidden parameters that the user cannot directly access, a few runs might be needed to find the right corresponding ramp rates. By activating "Desired runtime" in the software of the Mastercycler X50, one can easily mimic the thermal profile of the cycler of interest, thereby saving time and reagents.

The desired runtime enables the adjustment of a PCR program from thermal cyclers with a lower ramping speed to a Mastercycler X50. The run time of the slower cycler was measured from after lid heating (at the beginning of block heating to 94 °C in the first denaturation step) to reaching 10 °C final block temperature in the hold step.

This way of run time measurement would negate the influence of lid heating time and minimizes contributing factors in measuring cycler speed. The time needed for the Cycler S to complete the PCR run measured this way was 28 min.

In the header settings of the Mastercycler X50, the function "Desired runtime" is displayed under "Block Settings". The Mastercycler X50 automatically calculates the appropriate ramping rates according to the desired runtime without the need for further interference by the user. This also solves the need for multiple trial and error to find the right ramp rates when transferring protocols to other thermal cyclers.

Fig. 2 shows improved amplification yield of Mastercycler X50s after adaptation of protocol speed using the desired runtime for this challenging PCR protocol.

In conclusion, PCR optimization can be fastidious and time-consuming, with each change requiring revalidation of the protocol. Hence, thermal cyclers which offer additional features that can simplify such processes can vastly boost user convenience and make life in the lab easier.

Conclusion

The Mastercycler X50 brings the advantages of fast ramping and shorter PCR run time. Additionally, if speed adjustments are necessary when transferring protocols from slower cyclers, the desired runtime option offers a simple and fast solution.

Download of full Application Note No. 461

Literature

[1] Eppendorf Mastercycler®: Meeting all your PCR needs with reliability and flexibility. Eppendorf SE, White Paper No. 32.

Automated Sampling Using the Bioprocess Autosampler for the Analysis of an *E. coli* Fermentation Process

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Abstract

Bioengineers analyze multiple process parameters at various time points during a bioprocess run to ensure optimal growth conditions and gain process understanding. While parameters such as pH, temperature, and DO (dissolved oxygen) can be easily followed online, others are often monitored using external analyzers, after taking samples from the bioreactor. Examples include nutrient, product and byproduct concentrations, biomass, and product quality attributes.

Analyzing many process conditions at multiple time points during the bioprocess run requires a substantial number of samples. The use of autosamplers can increase bioprocess development efficiency by reducing the drudgery of manual sampling while increasing data quality, since the desired sampling interval can be maintained outside normal work hours. We document in this Application Note how a DASbox® Mini Bioreactor System was equipped with the Bioprocess Autosampler from Eppendorf, which was used for sampling of eight parallel fermentation runs and for storing the samples in a cooling stack.

Material and methods

For a full description of the material and methods used see Application Note 441.

Bioprocess system

DASbox Mini Bioreactor System equipped with Bioprocess Autosampler

Process control

The bioprocess as well as the Bioprocess Autosampler were controlled with DASware® control software.

Sampling strategy

The Bioprocess Autosampler was used to take samples from eight BioBLU® 0.3f Single-Use Bioreactors, which were run in parallel. During the bioprocess eight samples were taken: after taking an initial sample at the beginning of the run, seven samples were taken in equal time intervals in the course of the fermentation run time. These intervals were not disrupted overnight. The samples were transferred to sterile glass vials, which had been placed in sample racks inside the cooling stack.

First, a dead volume of 0.8 mL was drawn and discarded. Subsequently, a 4 mL sample was taken and evenly distributed to four glass vials; the aliquots were used for different analyses, including cell density measurements and product analysis. One aim of the study was to compare product storage at 4 °C and –20 °C. The samples for storage at –20 °C were transferred manually to a freezer.

Bioprocess

An *E. coli* fermentation process for plasmid production was carried out. The temperature was controlled at 37 °C, the pH at 7.0, and DO at 35 %. In a second use case, the autosampler was used to analyze a protein production process in *E. coli*. See Application Note 441 for more information on process parameters, control strategies, methods and results.

Fig. 1: DASbox Mini Bioreactor System equipped with the Bioprocess Autosampler. **A:** DASbox Mini Bioreactor System. **B:** Cooling stack. The cooling stack has three drawers. The temperature of the cooling stack can be regulated from 4 °C to 40 °C. **C:** Robotic arm equipped with liquid tools

Automated Sampling Using the Bioprocess Autosampler for the Analysis of an *E. coli* Fermentation Process

Results

Samples were analyzed to determine cell growth, compare product formation at different bioprocess conditions, and to evaluate different sample storage temperatures.

Fig. 2 illustrates the development of process parameters in a representative fermentation run. Temperature, DO, and pH were monitored online and controlled at setpoint during the fermentation run. The agitation speed (N) started at the initial setpoint of 300 rpm and increased up to 2,000 rpm approximately 14 h after inoculation, reflecting an increasing oxygen consumption of the growing culture. The OD_{600} and the product were analyzed offline. The OD_{600} reached a maximum of ca. 72 at the end of the fermentation run (EoF). Samples were stored either at 4 °C or –20 °C. The plasmid DNA (pDNA) concentration in samples stored at –20 °C was lower than in samples stored at 4 °C. In contrast, the proportion of covalently closed circular (ccc) plasmids was lower in samples stored at 4 °C. The lower proportion of ccc plasmids suggests that a higher percentage of plasmids exists in open circular and linear forms. These more open forms are caused by reversible strand nicks of the plasmid. Thus, storage at –20 °C is probably beneficial for the homogeneity of the plasmid sample.

Conclusion

In the study presented here, an 8-fold parallel DASbox Mini Bioreactor System was equipped with the Bioprocess Autosampler from Eppendorf. The sampler needed only little additional space, as it was mounted on the lab bench above the bioreactor system. Sampling was performed under aseptic conditions with local sterility, comparable to the conditions when sampling manually.

Typically, eight fermentation runs were carried out in parallel and eight samples per bioreactor were taken during each fermentation run. Thus, 64 sampling steps were performed by the Bioprocess Autosampler, which drastically reduced the routine manual workload.

Sampling was independent from normal working hours which ensured high consistency and avoided gaps in the collection during the night and at the weekend. For high flexibility, samples can be removed from the cooling stack at any time, for example to store them at lower temperatures as described in this study. The time needed for automatic sampling from eight bioreactors in the described setup was 2.5 h. While a 2.5 h sampling interval is suitable for many fermentation applications, shorter intervals may be desirable, especially to characterize a newly established process. To shorten the sampling intervals, splitting samples to multiple vials, as in the study described here, can be avoided. Additionally, a dual-head version of the Bioprocess Autosampler is available to further increase the sampling efficiency to up to more than one sample per hour per bioreactor.

The data presented here establish the convenience and versatility of the combined use of the DASbox Mini Bioreactor System and the Bioprocess Autosampler and their performance as an integrated unit. The control of the Bioprocess Autosampler is seamlessly integrated with DASware control 6 software, allowing flexible and customizable sampling schemes, like presetting samples prior to starting the experiment, scheduling additional samples outside the initial scheme in case of special events, and including manual samples in the storage pattern.

Download der vollständigen **Application Note 441**

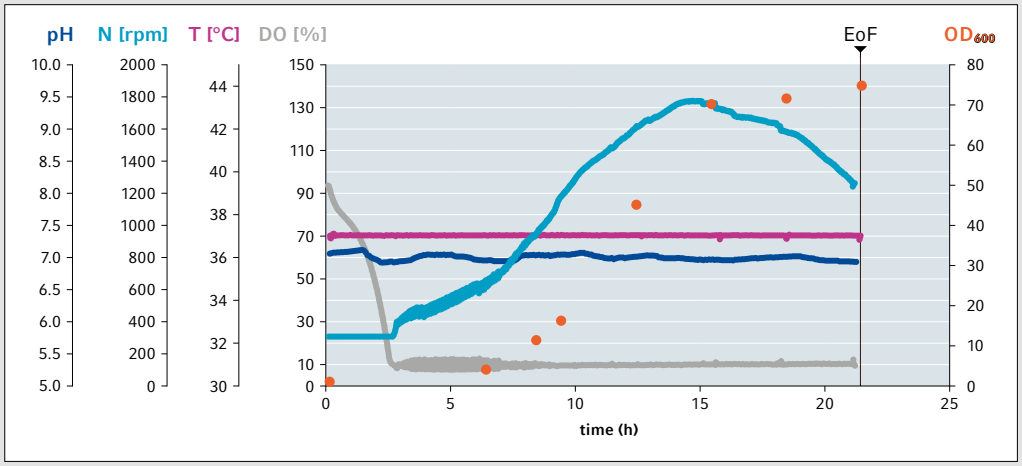

Fig. 2: Process parameters during a fermentation run for pDNA production. Temperature, agitation speed, DO, and pH were monitored online. The OD_{600} was analyzed in samples taken by the Bioprocess Autosampler with the exception of the sample at the end of fermentation, which was taken manually

Rapid Separation of Lipoprotein Fractions from Human Serum by Ultracentrifugation

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Introduction

Lipoproteins are complex particles with a central hydrophobic core consisting of non-polar lipids such as cholesterol, esters, and triglycerides. Lipoproteins can be divided into seven classes based on their size, lipid composition, and apolipoprotein composition (Table 1). The primary function of lipoprotein particles is to transport hydrophobic molecules within the extracellular water and plasma of the body.

Density is the underlying basis for the nomenclature of lipids, and density gradient ultracentrifugation is the reference method for measuring lipid density. Here, we demonstrate the use of the Centrifuge CS150NX or Centrifuge CS150FNX to isolate lipoprotein fractions from human serum in any laboratory workspace using a streamlined procedure and simplified consumables and reagents, while utilizing traditional power outlet requirements and minimal bench/lab space.

Materials and methods

Separation of serum lipoproteins by ultracentrifugation

The human serum was obtained after centrifugation of clotted blood at 2,000 x *g* for 10 min using Eppendorf Centrifuge 5810 R. Serum lipoproteins were separated by sequential ultracentrifugation using the compact Centrifuge CS150NX or Centrifuge CS150FNX with a fixed-angle Rotor S140AT.

Fractionations of serum lipoproteins

A total of three different density solutions were prepared to isolate the distinct fractions:

> Density solution A (ρ: 1.006 g/mL)
> Density solution B (ρ: 1.182 g/mL)
> Density solution C (ρ: 1.478 g/mL)

A volume of 600 µL of serum was transferred to a 1 mL 1PC Tube. For better visualization of the lipoprotein fractions after centrifugation, the serum was pre-stained using Sudan Fat 7B. For 600 µL of serum, 12 µL of the dye solution was added and mixed by inversion. The density solution A (300 µL) was added and mixed gently by inversion. After mixing, the tubes were loaded into the 10 x 2 mL fixed-angle Rotor S140AT in Centrifuge CS150NX and centrifuged (140,000 rpm, 16 °C, 50 min). After centrifugation, the top layer containing the CLM and the VLDL fraction was removed by pipetting (Fig. 1A).

To the remaining fraction containing IDL, LDL, HDL, 300 µL of the density solution B was added. The tubes were centrifuged (140,000 rpm, 16 °C, 80 min). Following centrifugation, the top layer containing the IDL and the LDL fraction was removed by pipetting (Fig. 1B).

For the last step of separation, 300 µL of the density solution C was added. The tubes were centrifuged (140,000 rpm, 16 °C, 140 min). The top layer containing only the HDL fraction was aspirated by pipetting (Fig. 1C). All fractions were stored at –20 °C.

Table 1: Classification of lipoproteins

Family name	Density range (g/mL)	Particle diameter (nm)	Apolipoproteins		Major function
			Majors	Other	
Chylomicrons (CLM)	<0.93	>75	ApoB-48	ApoA-I, -IV ApoC-I, -II, -III ApoE	Transport of exogenous triglycerides
Chylomicron Remnants	0.93–1.006	30–80	ApoB-48	Apo E	Transport of triglycerides and cholesterol
Very low-density lipoproteins (VLDL)	0.93–1.006	30–80	ApoB-100	ApoA-I, -II, -V ApoC-I, -II, -III ApoE	Transport of endogenous triglycerides
Intermediate density lipoproteins (IDL)	1.006–1.019	25–35	ApoB-100	ApoC-I, -II, -III ApoE	Precursor of LDL
Low density lipoproteins (LDL)	1.019–1.063	18–25	ApoB-100	—	Transport of cholesterol and phospholipids to peripheral cells
High-density lipoproteins (HDL)	1.063–1.121	5–12	ApoA-I	ApoA-II, -IV, -V ApoC-III ApoE	Transport of cholesterol and other lipids from plasma to the tissues
Lipoprotein (a)	1.055–1.120	25	ApoB-100	Apo (a)	Transport of cholesterol

Rapid Separation of Lipoprotein Fractions from Human Serum by Ultracentrifugation

Results and conclusions

The present centrifugation procedure allows a rapid separation of serum lipoprotein fractions by density gradient using a micro ultracentrifuge at a single speed. While some of the fractions contain two classes of lipoproteins, more sophisticated density gradient ultracentrifugation methods can be employed with Centrifuge CS150NX or Centrifuge CS150FNX, to isolate single-class lipoproteins. Through using serial centrifugation steps with a maximum speed of 513,000 x *g*, single-class lipoproteins and further resolution of subcomponents can be achieved.

The easy-to-use separation approach described in this work highlights the isolation of lipoproteins into three fractions, notably achievable in less than 5 h. Centrifuge CS150NX and Centrifuge CS150FNX are compact and versatile micro-ultracentrifuges, which can reach up to 1,050,000 x *g* (140,000 rpm) – a speed required for the most efficient isolation of lipoproteins – in 90 s. Alternative protocols for the isolation of single-class lipoproteins can take up to 60 h of work.

There is a significant time advantage of targeting three fractions and using the maximum *g*-force rotor and centrifuge setup achieved with Centrifuge CS150NX or Centrifuge CS150FNX and Rotor S140AT.

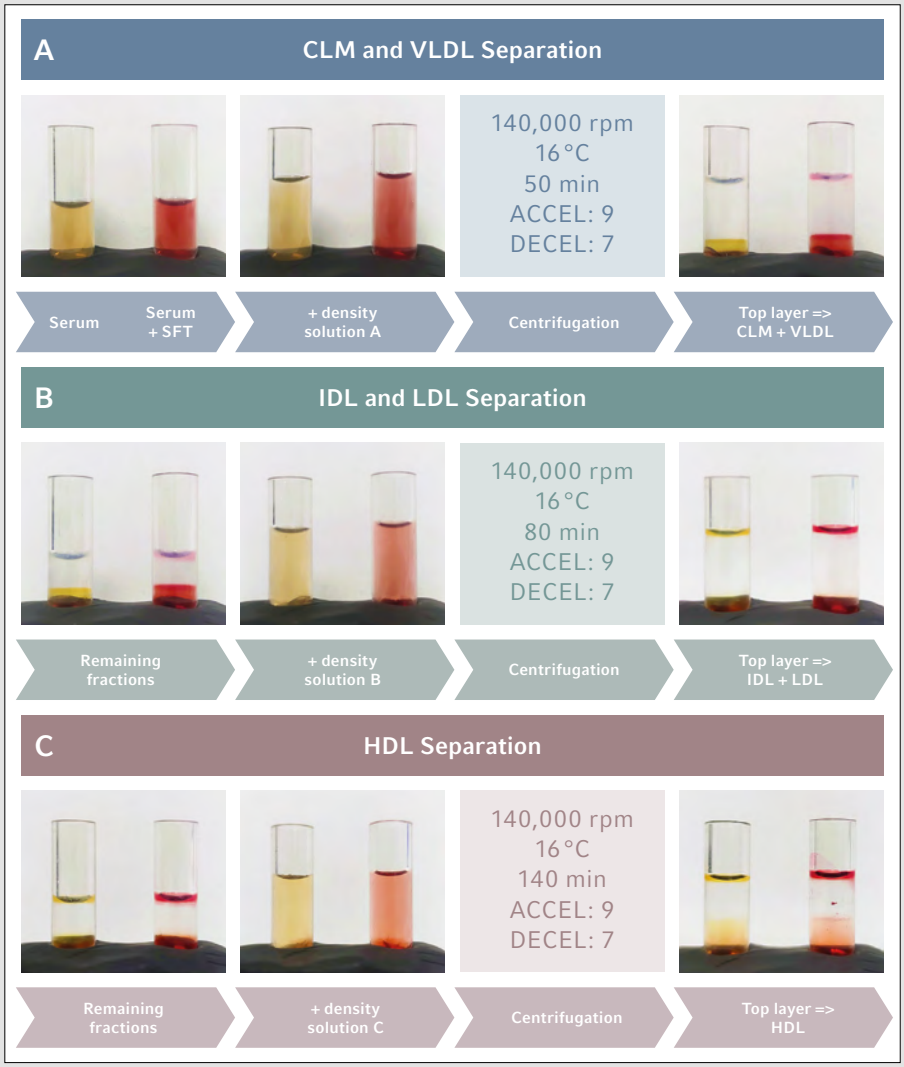

Fig. 1: Schematic representation of the separation of lipoproteins. **A:** CLM and the VLDL fractions. **B:** IDL and the LDL fractions. **C:** HDL fraction. SFT = Sudan Fat 7B

Summary

1. Lipoproteins are an important topic in biomarker research for coronary diseases.
2. Established methods can take up to 60 h to isolate single-class lipoproteins.
3. This Application Note shows how, in less than 5 h, lipoprotein fractions can be isolated using Centrifuge CS150NX or Centrifuge CS150FNX and Rotor S140AT.

In conclusion, the combination of the benchtop model Centrifuge CS150NX or the floor-standing Centrifuge CS150FNX coupled with Rotor S140AT allow for faster isolation of lipoprotein fractions in streamlined and simplified steps.

Download of full **Application Note 468**

Gentle for the Earth and Cells: Comparison of Cytotoxicity Parameters of Eppendorf Tubes® BioBased and Standard Eppendorf Tubes

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Abstract

With increasing environmental awareness and thus more stringent requirements imposed on life science laboratories, lab plastics present a growing challenge with respect to sustainability. One of the key approaches to improve sustainability of lab plastics is to use recycled and renewable feedstocks in their production. In this study, a potential material cytotoxicity of the Eppendorf Tubes® 50 mL made of an ISCC PLUS certified polypropylene biobased material was assessed in comparison to standard fossil-based Eppendorf Tubes 50 mL. The cytotoxicity effects of both material types were comprehensively evaluated by cell morphology and viability assays with compliance with the ISO 10993-5:2009 and ISO 10993-12:2012 standards. Neither fossil-based nor biobased material induced any major morphological changes or caused cell viability attenuation. This indicates that biobased material offers excellent properties regarding cell culture parameters, which are identical to fossil-based material.

Introduction

Conical tubes with screw cap belong to the most used laboratory vessel formats and are universally applied in a variety of laboratory procedures. With the recent increase in environmental awareness, also in the life science laboratory, lab plastics present a growing burden with respect to sustainability. One of the key approaches to improve sustainable properties of plastics in the lab is to use recycled and renewable feedstocks in their production.

For the first time, Eppendorf is able to offer a generation of tubes in 5.0 mL, 15 mL, 25 mL, and 50 mL formats that are made of an ISCC PLUS (International Sustainability & Carbon Certification) certified polypropylene based on renewable reused raw materials [1,2] applying the mass balance approach.

The objective of this study was to assess a potential material cytotoxicity of Eppendorf Tubes 50 mL made of biobased material in comparison to their standard fossil-based counterparts. The cytotoxicity effect was evaluated qualitatively (cell morphology evaluation) and quantitatively (MTT assay). The extraction conditions for the tube material (37 °C for 72 h and 50 °C for 24 h) and all test procedures were compliant with the ISO 10993-5:2009 ("Tests for in vitro cytotoxicity") and ISO 10993-12:2012 ("Sample preparation and reference materials") standards.

Material and methods

For a full description of the material and methods used please see **Application Note 470**. The following polypropylene conical tubes 50 mL were evaluated:

> Eppendorf Tubes BioBased 50 mL, Sterile
> Eppendorf Tubes 50 mL, Sterile

Preparation of liquid extracts

Materials were cut in small pieces, placed into the extraction vessels with completed medium (MEM Glutamine 4 mM, Penicillin 100 UI/mL, Streptomycin 100 µg/mL, FBS 10 %). The extraction conditions were: 37 °C for 72 h and 50 °C for 24 h. The extracts were used immediately after the extraction incubation for cell culture. Each experiment was performed in triplicates.

Cell culture

L929 cells were cultured in the complete medium (ATCC®, 30-2003) (5 % CO_2), then digested by Trypsin/EDTA 25 % to get a single cell suspension. After inactivation of Trypsin-EDTA, cells were centrifuged and diluted in fresh culture medium to obtain a 1×10^5 cells/mL suspension.

Cell morphology evaluation

After cell cultivation for 48 h, the cell morphology was firstly examined: detachment, cell lysis, vacuolization. For each condition, the morphological status of cells was graded with compliance to ISO 10993-5:2009 standard. A grade greater than 2 is considered as a cytotoxic effect.

Cell viability – MTT assay

The MTT test with spectrophotometric evaluation of viable cell medium was performed according to the ISO 10993-12:2012 standard (details described in the full Application Note 470). A viability reduced below 70 % (compared to the control sample) was considered as a cytotoxic effect.

Results and discussion

Cell morphology evaluation

After 48 h of culture in presence of the tube material extracts, the L929 cell culture morphology was examined under microscope and the morphological status of cells was graded according to the Table 1 classification (see methods).

	72 h at 37 °C	
	Eppendorf fossil-based	Eppendorf biobased
Repl. 1	1	0
Repl. 2	0	0
Repl. 3	0	0

	24 h at 50 °C	
	Eppendorf fossil-based	Eppendorf biobased
Repl. 1	0	0
Repl. 2	0	0
Repl. 3	0	0

Fig. 1: Cell morphology grading of the L929 cell culture depending on the extraction condition applied and the extracted sample

Gentle for the Earth and Cells: Comparison of Cytotoxicity Parameters of Eppendorf Tubes® BioBased and Standard Eppendorf Tubes

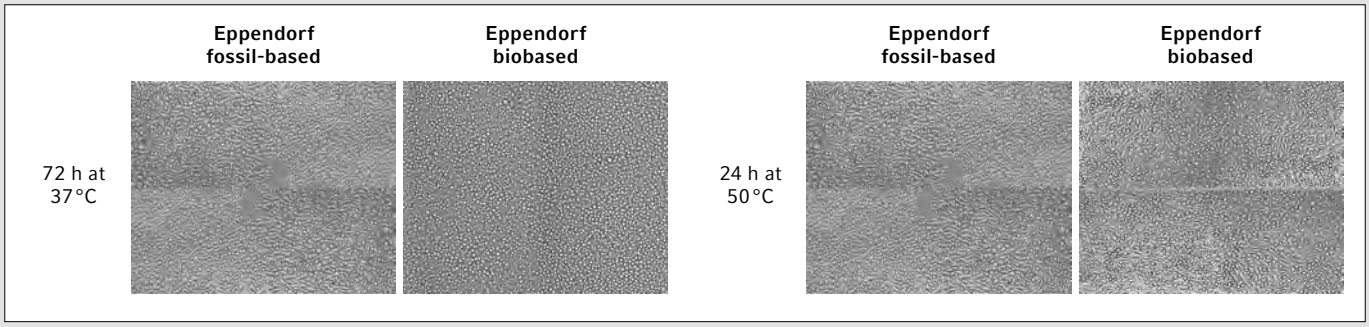


Fig. 2: Images of the L929 cell culture depending on the applied extraction condition and the extracted sample

As shown in Fig. 1 and Fig. 2, for all conditions, the cell morphology was not impacted, when cells were cultured in presence of material extracts. Neither fossil-based nor biobased material induced any major morphological changes under the extraction conditions tested: 72 h at 37 °C nor 24 h at 50 °C.

Cell viability – MTT assay

After the morphology assessment, the cell viability was quantified by a MTT assay which is indicative of living cell metabolism. The percentage of viable cells was assessed by comparison to the controls. According to the ISO 10993-5 standard, the cell viability below 70 % indicated a cytotoxic effect. The quantification evaluation unambiguously confirms cell morphology observations. Indeed, as shown in Fig. 3, the mean cell viability value is largely above 70 % regardless of the extraction condition applied or the tube material evaluated. The observed slight decrease of cell viability with long time extracts (72 h at 37 °C) may be indicative of unspecific degradation of cell medium (FBS).

Conclusion

In this Application Note, we assessed the material cytotoxicity of the Eppendorf Tubes 50 mL made of an ISCC PLUS certified polypropylene biobased material in comparison with standard, fossil-based Eppendorf Tubes 50 mL.

The cytotoxicity effects were evaluated with compliance to ISO 10993-5:2009 (“Test for in vitro cytotoxicity”) and ISO 10993-12:2012 (“Sample preparation and reference materials”) standards and included comprehensive cell morphology and cell viability evaluation.

Neither fossil-based nor biobased material induced any major morphological nor cell viability attenuation. This indicates that biobased material offers excellent properties regarding cell culture parameters, which are identical to fossil-based material. Biobased consumables therefore offer a major development in improving overall lab consumables sustainability while maintaining the same product quality and performance.

Download full **Application Note 470**.

Literature

[1] www.iscc-system.org

[2] Hermuth-Kleinschmidt K, Consumables Made of Bioplastics Enter the Lab, **Eppendorf White Paper No. 78**

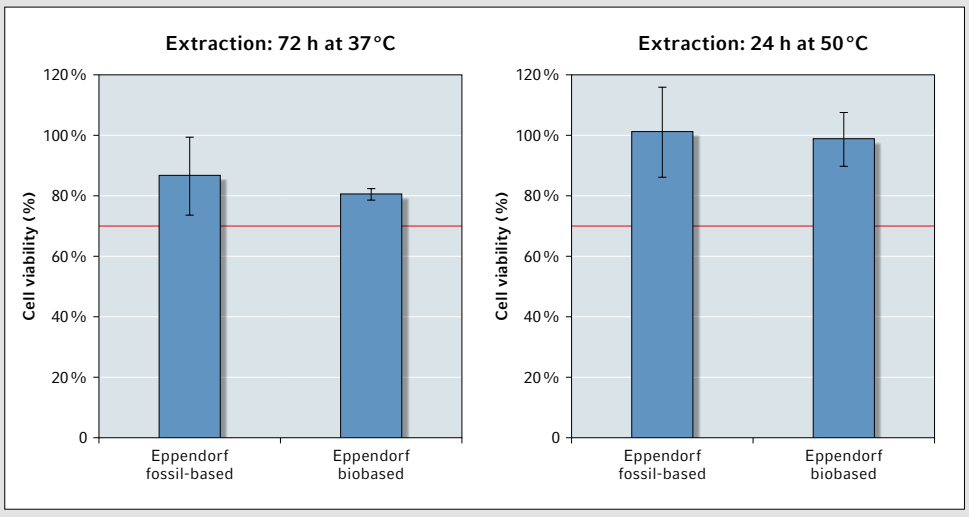


Fig. 3: Cell viability of L929 cells depending on the extraction condition and the extracted tube material

JESSICA WAGENER, EPPENDORF SE

Seeding Cells Right: Tips & Tricks

The seeding of cells is one of the standard techniques performed in every cell culture laboratory. Here, you will learn what is truly important when it comes to achieving reproducible results.

The time factor

During cell seeding, the transfer of the cells – for example, from a 15 mL tube into a multi-well plate – can vary not only between one user and another, but consistency is also dependent on the energy level of each user on any given day. The longer it takes to seed the cells, the more cells will sediment , and the fewer cells will be transferred with each individual pipetting step. While this process takes only a few minutes, it can lead to significant differences in the number of cells per well, and thus to a high variability between results (Fig. 1).

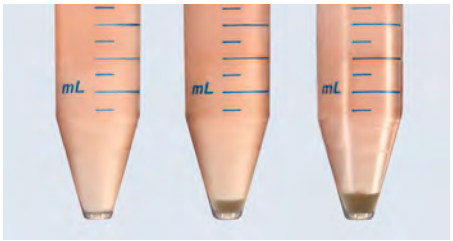


Fig. 1: The longer it takes to seed the cells, the more cells will sediment , and the fewer cells will be transferred with each individual pipetting step

Tip: Resuspend the sediment and mix the suspension gently once more. The subsequent seeding step should be carried out as quickly, and as gently, as possible.

Air bubble formation during cell seeding

Due to their high protein content, cell culture media tend to foam. Ensuing bubbles can potentially inhibit cell adhesion (Fig. 2), thus leading to well-to-well variability. This effect is particularly pronounced in small plate formats such as 96- and 384-well plates. In these small wells, an air bubble takes up more surface area in relation to total growth area and thus inhibits the adhesion of a relatively larger proportion of cells.

Tip: By mixing cell suspensions carefully, but not too vigorously or too frequently, you will prevent stress on the cells caused by strong shear forces.

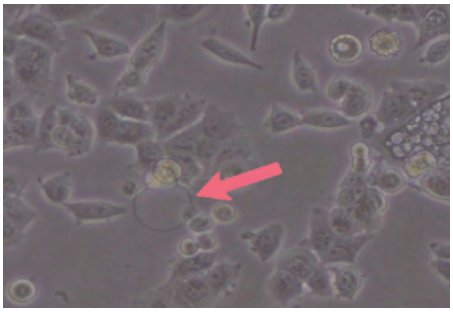


Fig. 2: The cell above the arrow is hindered from adhesion by an air bubble (arrow)

"Eight" or "cross" technique?

In addition to ensuring a consistent number of cells per culture vessel or well, the distribution of the cells on the surface will also influence the reproducibility of the subsequent experiments. Different techniques are common, usually passed from more experienced scientists in a lab to their trainees (Fig. 3).

Fig. 3: The correct seeding technique is one of the factors determining the homogeneous distribution of cells on the surface of the cell culture vessel

But which seeding technique is the best, and what role does the correct cell density play during seeding? Learn more in our online article in the Eppendorf Lab Academy.

More tips & tricks for cell culture needed?

Subscribe to our monthly publication *Inside Cell Culture Newsletter* for cell culture experts at www.eppendorf.com/icc

JAN-HENDRIK BEBERMEIER, EPPENDORF SE

“I Should Have Made More Notes”

The documentation of processes and samples is taking more and more time. However, this extra effort is rewarded later on when samples can be easily identified and accompanying data is available. With the SafeCode system, documentation is easier and more comprehensive than ever before, providing a real solution to the problem.

The fact that data is missing is usually only realized at a later stage. “I should have made more notes” is probably one of the most frequently uttered phrases in science. Particularly in the case of consumables, all relevant information about the lot/batch, type of product, or purity grade is printed on the outer box. This box, together with all the important information about the product, is usually the first thing to be disposed of, while the tubes with the corresponding samples are stored for years.

The SafeCode system solves these problems. The pre-coded consumables are pre-labeled with a DataMatrix code and a clear code that encodes a type of serial number for each individual consumable. This identifier provides far more reliable sample identification than self-made labels and allows access to the specific vessel information mentioned above as well as certificates. These data records can be downloaded from the Eppendorf website.

As sample management becomes relevant in many projects, the SafeCode data concept is optimized for the eLabNext software solution, but it can also be used as an open system. The SafeCode feature is available for various consumables such as CryoStorage vials, conical tubes, and different plate formats.

More information

> Discover SafeCode
> Get your free 30-day trial of eLabNext

News

Open to Collaboration

Digitalization helps make laboratory work more efficient while protecting samples and allowing you to get the best possible information from your data. For the purpose of user-friendliness, it is essential that different applications work hand-in-hand. VisioNize® Lab Suite (VNLS), the laboratory management system by Eppendorf, is compatible with systems by other manufacturers.

VNLS is an integral component of many Eppendorf products, including the “VisioNize touch enabled devices” – for example, the ULT-Freezer CryoCube® F740hi and the cell incubator CellXpert® C170i. It enables monitoring of devices, receiving of alarms, instrument management, and more. VNLS is an open platform, which means that older instruments, by Eppendorf as well as by other manufacturers, too, can be connected.

Clustermarket: Partner in the VisioNize ecosystem

Not many laboratories use instruments and software products by one manufacturer alone. For this reason, Eppendorf collaborates with selected partners in the integration of VNLS into the digital products by third-party vendors in order to offer customers a single-source technology digital solution.

Clustermarket is the newest partner of VNLS. With the help of the Clustermarket dashboard, users can plan and monitor the use and maintenance of laboratory instruments as well as view the status of all shared laboratory equipment. Clustermarket has more than 100,000 active users.

More information

ULRIKE RASCHE, EPPENDORF SE, BIOPROCESS CENTER, JUELICH, GERMANY

Improve Bioprocess Data Quality, Decrease Effort

Taking samples from your bioprocess is required in order to monitor how your culture is growing, how your desired product is produced, and to what extent nutrients are consumed. Such information is indispensable for process optimization. Delegating the sampling task to an autosampler facilitates sampling 24/7 at short and regular intervals, thus enabling the compilation of complete datasets.

Have you ever invested a lot of time and effort in sampling your bioprocess, only to discover that an important data point is missing? A data point that should have been taken in the middle of the night when you were not in the lab? Situations such as these can be avoided by delegating sampling to an autosampler.

Bioprocess Autosampler takes manual work off your hands

Let's take a look at an example of how autosampling can simplify the work of a bioprocess engineer. One of our customers has tested the new Bioprocess Autosampler in an *E.coli* fermentation process. This user planned a parallel process involving eight bioreactors in order to compare different bioprocess conditions.

Throughout the total process run time of 35 h, samples were to be drawn at eight time points at regular intervals. How could this have been accomplished with manual sampling?

First of all, this approach would have required a shift system to cover the process run time, during which the scientists would have spent a significant portion of their work time on sampling.

This user has been using a DASbox® Mini Bioreactor System from Eppendorf for some time, and now it has been upgraded with the Bioprocess Autosampler. In our example, BioBLU® Single-Use Bioreactors were used, but the system is equally compatible with glass bioreactors.

Furthermore, it can also be used with the DASGIP® parallel bioreactor system, if larger working volumes are required.

Autosampling at a glance

Per sampling step, the Bioprocess Autosampler drew one sample from a bioreactor and transferred it to a predefined sample vial, which was stored in a temperature-controlled environment. The sampling device was cleaned automatically, so that the Bioprocess Autosampler would be ready for the next sampling step. In this way, the Bioprocess Autosampler enabled regular sampling 24/7.

The storage position of each sample was predefined in the Eppendorf bioprocess control software DASware® control and the samples were positioned automatically. This automated method of sample storage eliminated the risk of human error.

To learn more about this specific application example read our Application Note 3–4.

More information

If you would like to find out more about the Bioprocess Autosampler and how it can help you obtain better bioprocess data, please visit **www.eppendorf.com/bp-autosampler**

JAN-HENDRIK BEBERMEIER, EPPENDORF SE

Your Personal –80 °C within Reach?

ULT freezers, with a temperature of –80 °C, are commonly used in many laboratories on a daily basis. Critical samples are stored in these chunky and energy-guzzling devices over the long term. Are there any options for safe sample storage as close as possible to your work bench?

Multiple research teams, and even different groups, share one ULT freezer. Quite often, the freezer is located in the hallway or even farther away in the basement. Both locations present challenges: a number of people have access to your valuable samples, and it can take several minutes before your critical samples will be stored at –80 °C.

The CryoCube® F101h addresses both challenges. This under-the-bench freezer provides "personal" –80 °C cold storage of your samples within reach. For high sample safety, we have further improved the device by shortening the pull-down time to –80 °C (120 min) and the quick door opening recovery (DOR; 60 s opening) to 21 min for a fast return to the set temperature of –80 °C.

Sustainability included

Eppendorf ULT freezers are assembled in our factory using 100 % renewable energy. The CryoCube F101h requires only 3.2 kWh/day (–70 °C; 230 V) or 4.7 kWh/day (–80 °C; 230 V), respectively. These values are based on external test runs.

In addition, you will benefit from the very low global warming potential (GWP) of the green hydrocarbon cooling liquids (R170/ R290). Since 2008, we have been continually expanding its use to include more and more of our freezer models.

Learn more at
www.eppendorf.com/freezers

Tip

"Welcome, It's Pipette Service Time!"

This is how we would like to welcome you to our new Online Service Portal* in the future!

> Here you will stay on top of all service needs for your pipettes
> Here you can order your pipette services hassle-free and intuitively

The new Service Portal

> Free cloud-based backup of your pipette inventory service data
> Individual calibration intervals with reminders for upcoming services
> Fast and intuitive online booking of pipette services
> Direct access to your service orders and documents
> Overview of the status and history of your services

Navigating the Service Portal

In the Service Portal, you can easily and quickly register your pipettes, define required calibration intervals, and book your pipette services from our extensive portfolio.

> Log into the Services Portal with your myEppendorf account
> Register or import your pipette data – upload of Microsoft® Excel® template is possible
> Order the services you need – upload of your documents is possible
> Print your order documents and pack your pipettes
> Ship your pipettes to the Service Center

Register here:
serviceportal.eppendorf.com

More information
www.eppendorf.com/pipette-service

*Not yet available in all countries

BARBRO PATTERSON, EPPENDORF SE

ISO 8655-6:2022: The High Art of Pipette Calibration

Regular maintenance and calibration ensure the pipette is performing optimally in accordance with specifications. Worn-out seals and O-rings are often not readily apparent. If a pipette fails a calibration "as found", the resulting effort can be huge – checking all analysis results since the last calibration, and repeating tests. The ISO 8655 builds the operational and regulatory guidance for calibration and testing procedures of piston-operated volumetric apparatus. In April 2022, the revised ISO 8655:2022 was published.

The ISO 8655 is an international standard for calibration and testing procedures of piston-operated volumetric apparatus (POVA) like pipettes, burettes, dilutors, and dispensers. The ISO 8655 defines the criteria and the maximum permissible error limits for each volume tested: the number of measurements and volumes, controls for room environment, and the permissible quality of the test chain.

Pipette calibration intervals

> The compliance with the error limits according to the ISO 8655 must be checked at least once a year as part of your test equipment monitoring or analytical quality assurance.

> Shorter intervals and your own acceptable error limits can be specified depending on the application and accuracy requirements.

Changes in the ISO 8655-6:2022 with impact

The ISO 8655 Part 6 describes the gravimetric method for the determination of measurement error for POVA with the following major changes:

> *Number of measurements to determine the measurement error:* 10 measurements or more for each volume to be tested shall be performed.

> *Tip exchange during replicate measurement:* Tip exchange must be performed at least once to detect possible damaged or faulty tips and assess the variability of the tips.

> *Reporting of results:* The test report includes all information necessary for the interpretation of the calibration results, but without the extended uncertainty of measurement.

New chapter ISO 8655-7:2022

The ISO 8655 Part 7 describes alternative measurement procedures for the determination of volume for POVA with the following major changes:

Number of measurements

> For routine tests, 10 measurements are recommended. Fewer replicate measurements may be made, if the expanded uncertainty of measurement is fit for the intended purpose, but not less than 4.

> After repair or adjustment, a minimum of 10 measurements shall be performed.

Calibration in an ISO 17025 accredited lab

Do you require uninterrupted traceability of results for inter-laboratory comparisons and/or compliance with regulations? Our premium quality calibration services in our ISO 17025 accredited facilities include calibration certificates with all raw data and the extended measurement uncertainties. We are very happy to support you.

More information
in our **Online-Artikel**

CORDULA RICHTER, EPPENDORF SE

Dr. Maurice Michel Receives Eppendorf Award 2023

The independent jury chaired by Prof. Reinhard Jahn selected Dr. Maurice Michel from Karolinska Institutet, Stockholm, Sweden, as the 28th winner of the *Eppendorf Award for Young European Investigators*.

Maurice Michel, born in 1986, receives the € 20,000 award for his work on artificial functions of DNA repair enzymes. The Jury: "Dr. Michel showed that binding of a small molecule to the active site of a DNA repair enzyme not only increases its activity but also prompts it to carry out a reaction not found in the free protein, leading to enhanced DNA repair after oxidative damage. These ground-breaking discoveries may have far-reaching applications in the treatment of cancer or age-related degeneration."

Maurice Michel: "It is an immense honor to be awarded with the 2023 Eppendorf Award. This would not have been possible without the contribution and spirit of many scientists, be it colleagues or collaborators, as well as mentors and an incredible family I call mine.

Using small molecule organocatalysts, we installed new biochemical reactions within an enzyme and have thus succeeded in rewriting the base excision repair pathway. Our research now focuses on a broadening of this technology base by investigating other enzymes and understand biochemical reaction pathways and their biological consequences."

The award ceremony took place on June 22, 2023, at the Advanced Training Center of the European Molecular Biology Laboratory (EMBL) in Heidelberg, Germany.

Further information on application modalities, selection criteria, and previous winners can be found at

www.eppendorf.com/award

Eppendorf & Science Prize for Neurobiology 2023

The winner had not yet been determined at the time of publication.

More information at
www.eppendorf.com/prize

eppendorf & Science PRIZE FOR NEURO BIOLOGY

Win a Set of 3 Pipettes

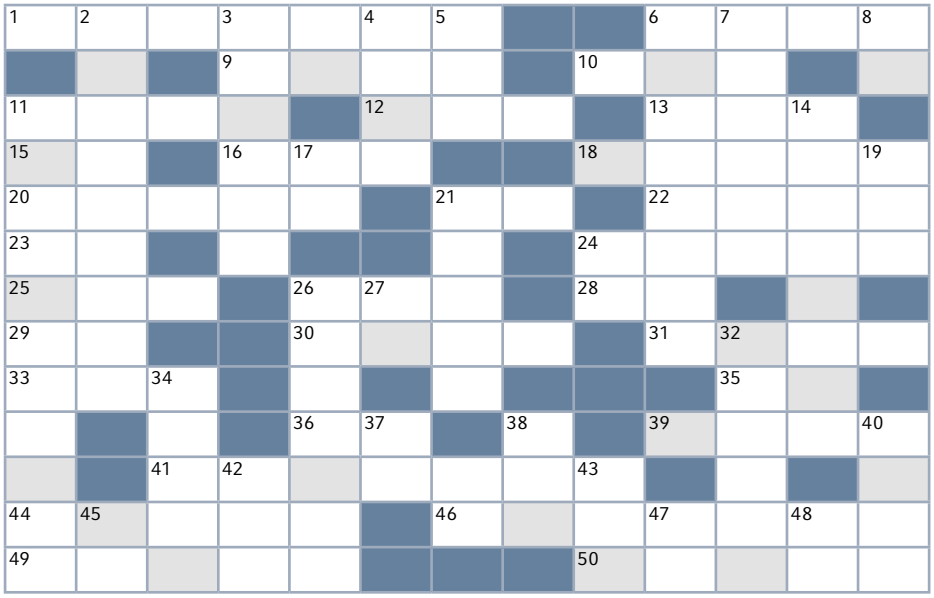
The solution of the prize competition of BioNews No. 57 was "EPPENDORF LAB CHANNEL". The main prize, an Eppendorf Xplorer® plus 8-channel pipette, went to Johanna S., Germany.

Good luck in our new competition!

Simply arrange all letters in the light gray boxes of the crossword in the correct order. Send us the solution until **November 30, 2023**.

Participate online at **www.eppendorf.com/bn-service** or e-mail the solution to **bionews@eppendorf.de**.

All correct answers will be considered for a prize for use in your lab. Winners will be notified in writing. Cash payment of the prize is not possible. No recourse to legal action. The judges' decision is final. Eppendorf employees and their families may not participate. The winner of the first prize will be published in BioNews No. 61.



1st Prize:

1 Eppendorf Research® plus 3-pack of your choice

2nd to 5th Prize:

1 Amazon® Voucher worth 50.00 EUR

6th to 10th Prize:

500 bonus epPoints® each

(epPoints registration required)

ACROSS

1 Usually permitted in designated areas only
6 Bag made of strong material
9 Cain's brother
10 Used in lamps and digital displays
11 Cellestial body
12 Resort providing therapeutic baths
13 Famous stock market index (short form)
15 Transportation system of a cell (abbrev.)
16 Sustainability label
18 Available as blanc, noir, gris
20 Direction
21 Small kingdom in Northern Europe (ISO country code)
22 Painter born in Barcelona
23 Nashville is the capital (abbrev.)
24 Troublesome, annoying
25 Has an electrical charge
26 Laboratory method discovered by Mullis
28 Not out
29 10^{-3} m (abbrev.)
30 Motor vehicle or car (short form)
31 Speak, communicate
33 Snakelike fish
35 Venice river
36 Element with atomic number 81 (chemical symbol)
39 Opposite of up
41 Handles, controls, directs
44 One of the best-selling female music artists
46 Device to modify air flow on cars
49 Generates a coherent beam of light
50 Pale hair color

DOWN

2 Clicking pendulum marking rhythm
3 Martial art
4 Place of rest, retreat, lodging
5 Quality assurance system in the laboratory (abbrev.)
6 Settles to the bottom of a liquid
7 Ancient Greek mythological figure
8 One thousand of it make one MB (abbrev.)
11 Governed by feeling
14 Sequence of steps in moving on in a labor process
17 Famous for cheese, chocolate, watches, and more (ISO country code)
19 Something for a child to play with
21 Precision sport using small pointed missiles
24 Mathematical constant
26 Companion, comrade
27 Between nickel and zinc (abbrev.)
32 Fly me to the moon …
34 Frontier of the Roman empire
37 Home of the Lakers (abbrev.)
38 Sales person
40 Enthusiastic about specialist or niche subjects
42 Type of beer
43 Male first name
45 Atomic mass unit named after John D. (abbrev.)
47 ISO country code for Israel
48 European Standards (abbrev.)

Solution hint for prize competition of BioNews No. 59:

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Send us the solution until **November 30, 2023**. Participate online at **www.eppendorf.com/bn-service** or e-mail the solution to **bionews@eppendorf.de**.
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