A decade of challenges with automated storage systems at ultra-low temperatures – are we better off without them?

Bartłomiej Wilkowski, PhD, EMBA – **Danish National Biobank**, Statens Serum Institut, DK

Nordic Biobank Conference 2022

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Conflict of interest

None

Bartłomiej (Bart) Wilkowski

BAW@ssi.dk

Statens Serum Institut (2011-)

- 2020 - : **IT section leader** (Danish National Biobank & Testcenter Denmark)
- 2017 - : IT team leader (Danish National Biobank)
- 2011 - : IT system developer - Danish Biobank Register (biobanks.dk)

Technical University of Denmark (2007-2011)

- Research assistant & Ph.d. student - (Biomedical informatics, semantic text mining)

Technical University of Lodz, Poland (2002-2007)

- MSc engineer, International Faculty of Engineering, Telecommunications & Computer Science

Roadmap of my talk

- Danish National Biobank (DNB)
  - Introduction
  - COVID-19 effect on DNB
- Automated storage systems (ULT: -80 °C) – challenges and benefits
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- Summary

Danish National Biobank

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Automated storage

High throughput automation

Manual storage

Total storage capacity: >15M

High throughput analyses

Danish National Biobank

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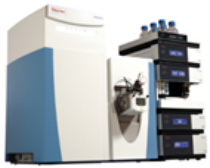
DNA extraction
1200 samples/day
One step conc./normalisation

Genetic analysis
- NGS-500 sequencing
- Array genotyping
- Targeted sequencing
- Mutation analysis
- Methylation
- mRNA microRNA profiling

Metabolomics and proteomics
- Explorative and focused using mass spec.
- LC-tandem mas spec. for small analytes
- MALDI-TOF mass spec.



Immunoassays
- Autoimmune disease diagnostics and development
- Biacore interaction analysis
- Antibody development
- Protein purification, characterization, conjugation
- MesoScale platform 10 analytes/run
- Luminex platform 30-50 analytes/run

DNB contains ~14 mio. biological samples

Sample type	Samples	Individuals
Serum	3,317,536	951,521
Dried blood spot samples	2,565,821	2,091,587
Plasma	1,488,350	442,752
Whole blood	830,524	320,872
DNA	678,237	451,455
Buffy coat	346,033	126,527
Urine	320,456	126,054
Saliva	90,407	42,554
Red blood cells	85,349	41,738
Amniotic fluid	66,407	56,505
Cord blood mononuclear cells	65,032	65,032
Proteins extracted from DBSS	39,168	38,979
Spinal fluid	28,596	16,498
Other (PBMS, feces, stem cells, biopsies, etc.)	83,430	49,040

COVID-19 samples (2020-):

Total samples		**COVID-19 (+)**
Throat swab	**4.300.000**	3.200.000
Blood samples	**33.000**	2.900

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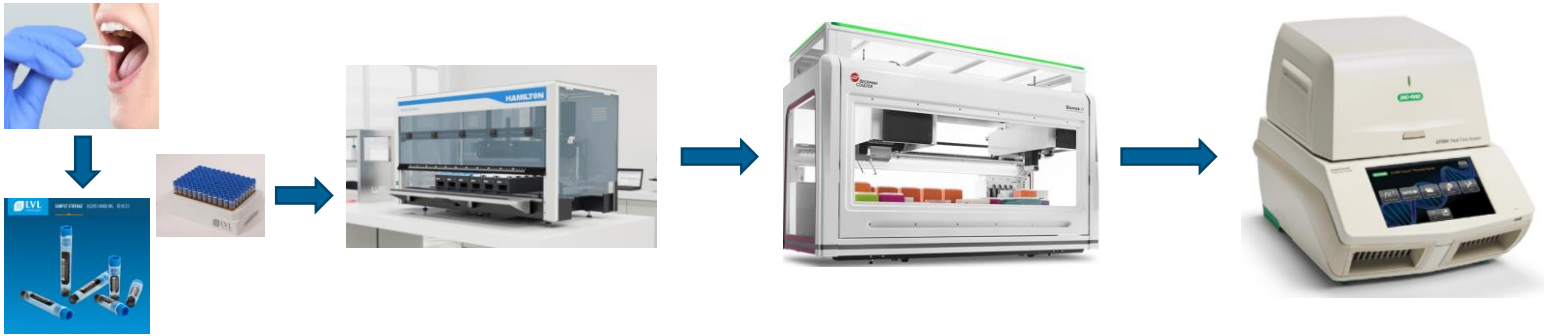
March 2020 - Testcenter Denmark

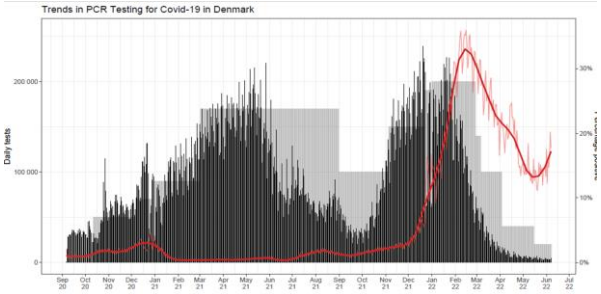


To do: Urgently build a high capacity laboratory (Testcenter Danmark) and an underlying automated laboratory data flow & IT system

Solution: Based on experiences from the automated solutions @ Danish National Biobank

Testcenter Danmark & biobank projects

- Capacity: 200.000 analyses/daily, RNA/DNA extraction
- Quality: ISO accredited flow,
  - Automated sample tracking
  - Semi-automated results release & validation
- Study design & project management
- Pipetting robots & PCR machines
  - 24 Hamilton Star & Vantage
  - 43 Biomek i7
  - 200 Bio-Rad thermal cyclers
- Automated storage system at +4 °C for picking of COVID19+ tubes
- Now: offers to take in diverse projects from biobanks



COVID19 effect on DNB

- Initially (March 2020): complete shut-down of the biobank – no projects
- In the meantime: days and nights spent contributing to establishment of Testcenter Danmark
- A few months later:
  - DNB opened again
  - Huge amount of new samples to be stored **daily**
  - Increase in number of research projects -> a lot of urgent PICKING! -> COVID-19 projects
    - On preexisting blood sample collection
    - On Testcenter's throat swab & serology samples

Perfect conditions and a job for
a **ULT automated storage system**

- But…
- the DNB's **automated storage solution** at -80 °C **out of order, no tube picking (which hardly ever worked), no robust plate picking**
  - Need to switch to 100% manual picking -> need for workarounds, alternatives, hire people, etc. …

Want to hear more about DNB's role during pandemic?

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THE DANISH NATIONAL BIOBANK

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Using the Danish National Biobank infrastructure as a platform to develop mass testing of COVID-19 in the population.

Karina Meden Sørensen

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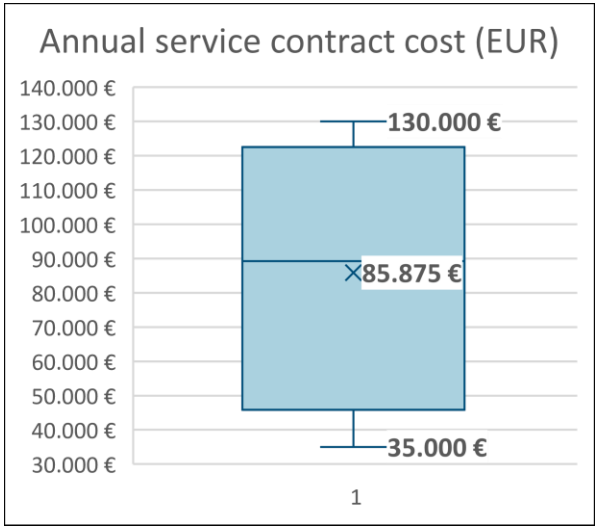
Survey across the Nordic biobanks

- Invited: 12 Nordic biobanks with a ULT automated storage system
- 6 responses

- The systems in operation for 4-8 years since the initial SAT
  - one of them has not yet passed a SAT:
    8 years since installation!

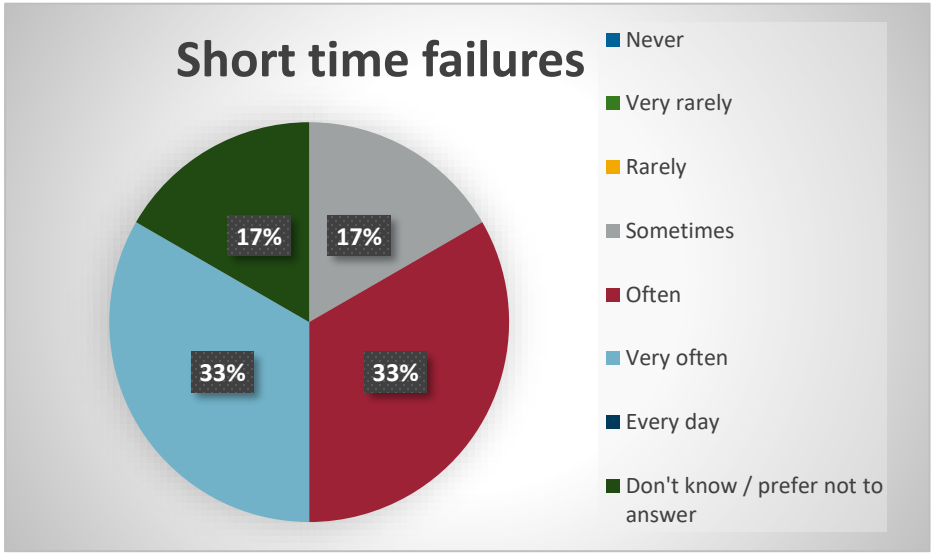
- Annual service contract price:



Survey across the Nordic biobanks

- Q: **Short-time failures** (fixed within a few hours) of your automated storage system: how often do you experience it?

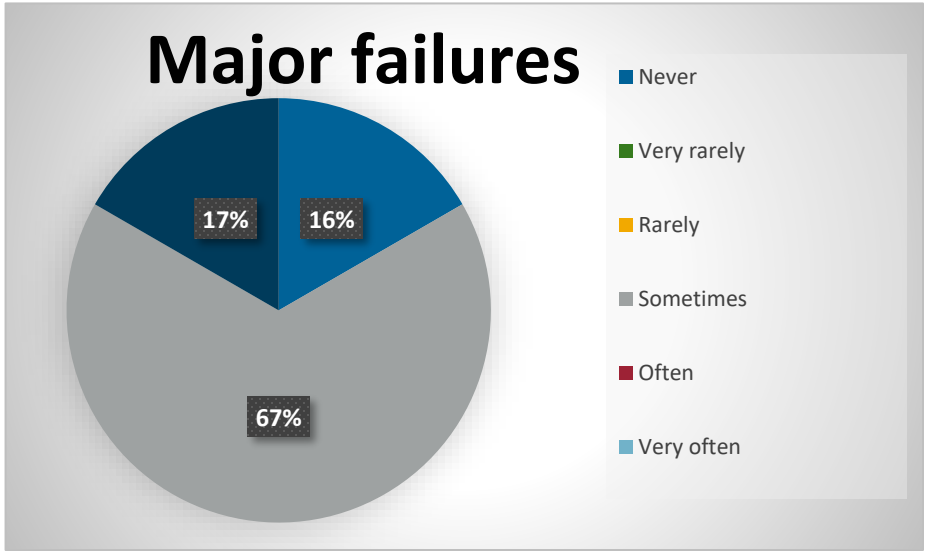
No one has answered: **Never, Very rarely or Rarely.**



Survey across the Nordic biobanks

- Q: **Major issues/failures** (days to weeks of downtime) of your automated storage system: how often do you experience it?

67% experience **sometimes** major issues/failures

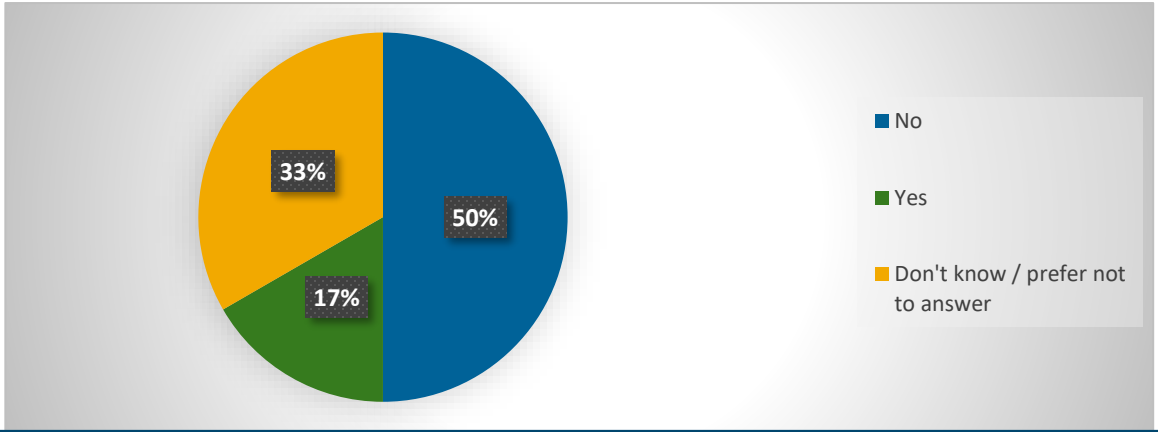


Survey across the Nordic biobanks

	1 2 3 4 5 6 7 8 9 10
How satisfied are you with the system?	4,17
How satisfied are you with the service from the provider during operation of the system?	5,17
How satisfied are you with the service and collaboration with the provider for minor issues that could be fixed through remote control?	6,17
How satisfied are you with the service and collaboration with the provider for major issues that requires on site attendance?	4,67

Survey across the Nordic biobanks

- Q: **Are we better off without the automated storage systems at ultra-low temperatures?**



Nobody really believes that we should drop the automation at ULT.
But the improvements are needed.

Survey across the Nordic biobanks

- Q: **How can you imagine your biobank to operate without such automated systems? Are there any substitute solutions you are aware of, have implemented or expect to implement in your biobank?**

- There is a consensus that **automated systems are needed**.
- Automated systems:
  - **increase the quality** of work,
  - **decreasing manual labor**,
  - while **increasing the speed of pick rates**.

Eliminating mundane and time consuming manual labor seems to be the primary motivation for having automated systems.

Survey across the Nordic biobanks

- **Final comments from survey's participants:**
- *"Our biobank has secured funding for an automated storage unit. However, hearing the experiences from other biobankers makes us **reluctant to go into this field**, yet, it is imperative with **more space-efficient sample storage** in our institution. We are **grateful for** the **strong national and Nordic network**, which gives the opportunity to learn from others!"*
- *" The **amount of work expected from** us as **users** is **very high** if you factor in the **service contract cost.** I'm all for performing service or trying to locate the part that is faulty my self, but then i would **expect the contract cost to be less**."*
- *"Our system is old, I **trust that newer systems would perform better** , but I **do not believe that -80 systems will run smoothly ever**!"*

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DNB workaround (tube picking) – when the automated storage system fails…

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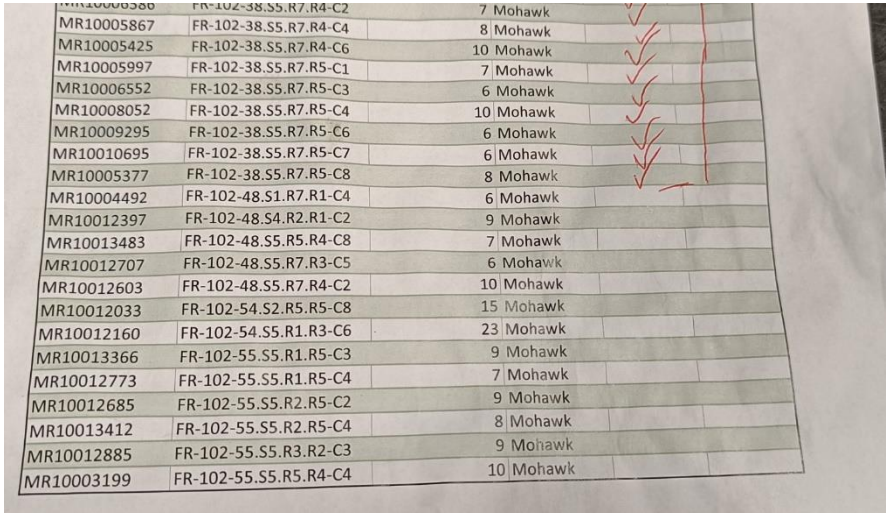
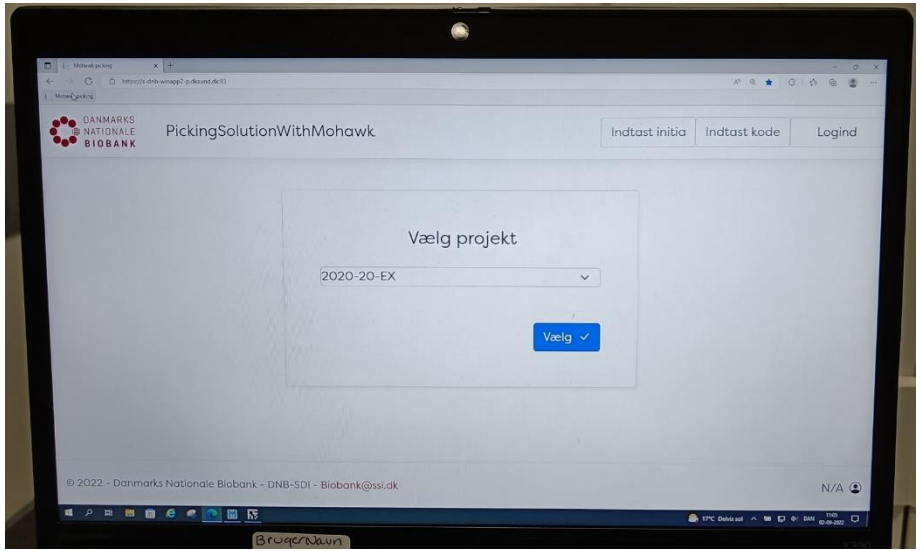
1. Generate a plate-level picklist (done by IT)



MR10005867	FR-102-38.S5.R7.R4-C4	8 Mohawk
MR10005425	FR-102-38.S5.R7.R4-C6	10 Mohawk
MR10005997	FR-102-38.S5.R7.R5-C1	7 Mohawk
MR10006552	FR-102-38.S5.R7.R5-C3	6 Mohawk
MR10008052	FR-102-38.S5.R7.R5-C4	10 Mohawk
MR10009295	FR-102-38.S5.R7.R5-C6	6 Mohawk
MR10010695	FR-102-38.S5.R7.R5-C7	6 Mohawk
MR10005377	FR-102-38.S5.R7.R5-C8	8 Mohawk
MR10004492	FR-102-48.S1.R7.R1-C4	6 Mohawk
MR10012397	FR-102-48.S4.R2.R1-C2	9 Mohawk
MR10013483	FR-102-48.S5.R5.R4-C8	7 Mohawk
MR10012707	FR-102-48.S5.R7.R3-C5	6 Mohawk
MR10012603	FR-102-48.S5.R7.R4-C2	10 Mohawk
MR10012033	FR-102-54.S2.R5.R5-C8	15 Mohawk
MR10012160	FR-102-54.S5.R1.R3-C6	23 Mohawk
MR10013366	FR-102-55.S5.R1.R5-C3	9 Mohawk
MR10012773	FR-102-55.S5.R1.R5-C4	7 Mohawk
MR10012685	FR-102-55.S5.R2.R5-C2	9 Mohawk
MR10013412	FR-102-55.S5.R2.R5-C4	8 Mohawk
MR10012885	FR-102-55.S5.R3.R2-C3	9 Mohawk
MR10003199	FR-102-55.S5.R5.R4-C4	10 Mohawk

DNB workaround (tube picking) – when the automated storage system fails…

1. Generate a plate-level picklist (done by IT)
2. Open **TubePicking** webapp in a browser (in-house solution)



DNB workaround (tube picking) – when the automated storage system fails…

1. Generate a plate-level picklist (done by IT)
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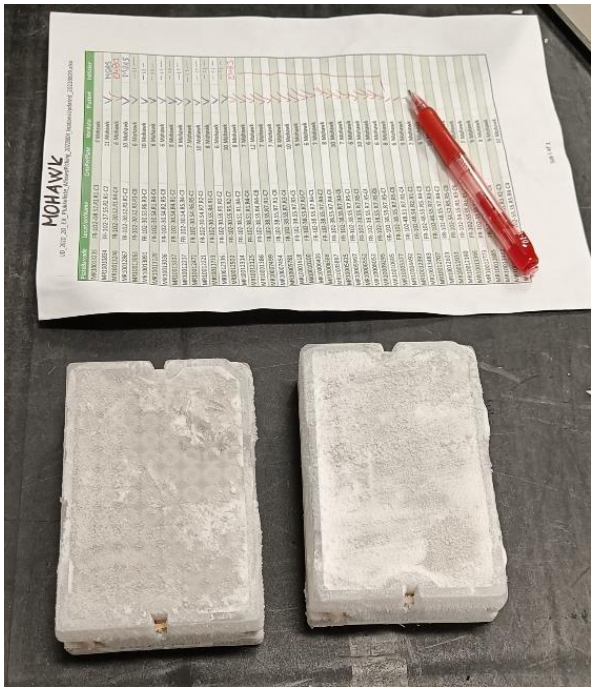
3. Pick 3-4 plates from manual -80 °C freezers



DNB workaround (tube picking) – when the automated storage system fails…

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4. Pick from a plate
   a) Remove ice using ethanol-soaked sponge rolls

DNB workaround (tube picking) – when the automated storage system fails…

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DNB workaround (tube picking) – when the automated storage system fails…

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   b) Place plate on a flatbed scanner, scan plate barcode and start tube scanning in the webapp
   c) Move plate to a Mohawk semi-automated tube picker and scan plate barcode in the webapp

DNB workaround (tube picking) – when the automated storage system fails…

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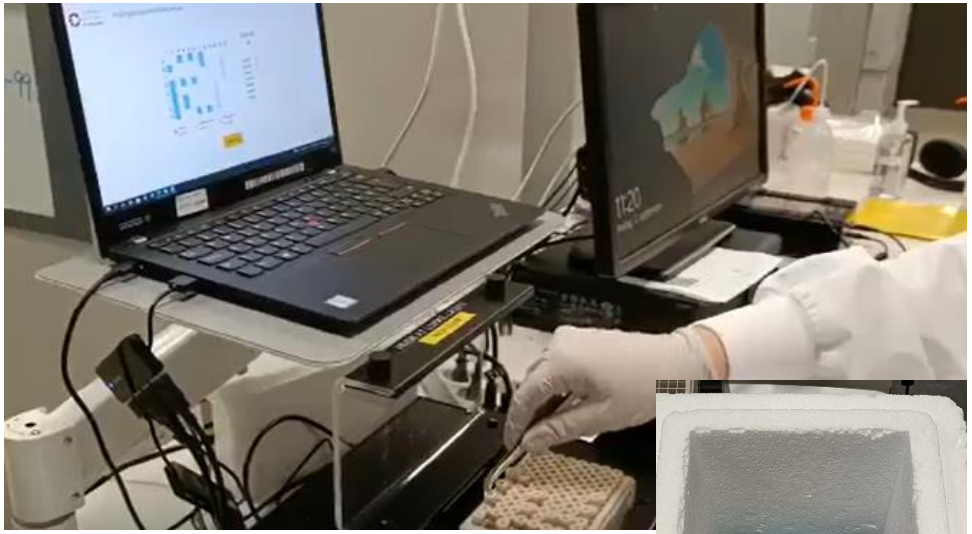
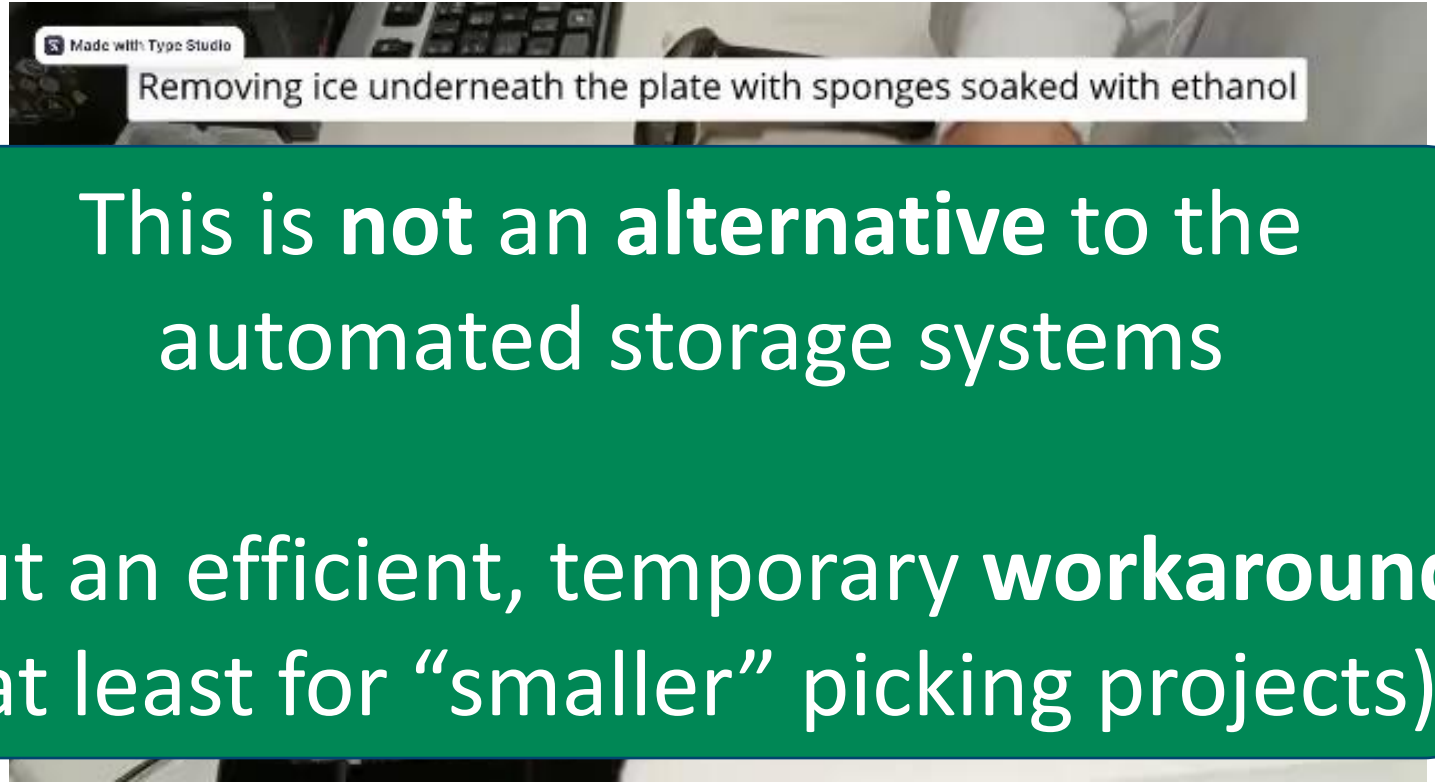
   a) Remove ice using ethanol-soaked sponge rolls
   b) Place plate on a flatbed scanner, scan plate barcode and start tube scanning in the webapp
   c) Move plate to a Mohawk semi-automated tube picker and scan plate barcode in the webapp
   d) Pick elevated tubes (w/ tweezers) and confirm (webapp)
   e) Loop back to step 3 as long as you pick all tubes.



Target plate
Flamingo box

Semi-automated tube picking example…(video)



This is **not** an **alternative** to the automated storage systems

but an efficient, temporary **workaround** (at least for “smaller” picking projects)

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Lesson learned (survey)

- **Tender process**
  - Performance requirements – to be able to send system back if not passed.
  - Keep an eye on the point of no return
  - Refrigerants of better performance & environmentally friendly
  - Demand that systems that have ice build up on the outside have drip trays supplied or that the supplier ads more insulation to remedy the issue.
  - Demand a detailed energy consumption fact sheet
  - Demand a requirement list regarding the ambient environment (e.g. humidity, temperature, etc.)
  - Require a full SAT document already at this stage
  - Service contract cost

Lesson learned (survey)

- **Buying (decision)**
  - Make sure to understand suppliers specifications for compressed air and cooling water
  - Make sure that the system uses valves and solenoids that can handle -80 ^{o}C
  - Make sure to have a fire protection system (smoke detection & extinguishing system) – suppliers should demand that!
  - Make sure to handle humidity/temperature in the room
  - Expect to need some qualified staff members permanently (IT/engineering) – integration, error handling, communication wiht the supplier
  - Be prepared that your system will have issues

Lesson learned (survey)

- **Site Acceptance Test**
  - Thorough stress test (samples in & out)
  - Ensure Factory Acceptance Test (FAT) is complete
  - Accept the SAT only when all the performance criteria are fulfilled (in one go)

- **Operation & service contract**
  - Make sure that computer hardware is included in service contract ie. hard drives, UPS battery replacements.

Discussion about the future

- **Research & dissemination**
  - Sustainable materials
  - -80 or -70? etc. etc.
  - New technologies vs. standard technologies

- **Transparent relationship (suppliers & biobanks)**
  - Access to testing schemes & reports on the ULT automated storage systems
  - Reports on use & performance of the ULT automated storage systems (existing installations)

Discussion about the future

- **Partnerships (suppliers & public biobanks)**
  - Understand the challenges with ULT automated storage systems
  - High throughput, live testing of new ULT solutions at partnering biobanks
  - Extended collection & analysis of performance data / sensor data

- **National, Nordic & EU user networks**

- **Nordic Advisory Board for Automated Storage Systems ?**
  - Procedures for smoother acquisition of automated storage systems

Acknowledgements

- Kristian Hveem & Vegard Marschhäuser, NTNU, NO
- James Thompson, KI, SE
- Cathrine Hansen, Erik Sattler, Karina M. Sørensen, DNB, DK
- All participants of the survey
- Tam Nguyen, DNB, DK
- Whole DNB team

Stockholm Syndrome

noun Psychiatry.
an emotional attachment to an autofreezer formed by a laboratory head as a result of continuous stress, dependence, and a need to cooperate for survival.

James Thompson, KI, SE
@ Nordic Meeting on autofreezers
April 2022

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Thank you!

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