Nordic Alliance for Clinical Genomics

WORKSHOP REPORT

NACG 12th Workshop, 28-29 April 2022,
Reykjavik, Iceland

Thank you for contributing to the content of this workshop report:

- Eirikur Briem
- Dag Undlien
- Valtteri Wirta
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- Ebbe Norskov Bak
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EXECUTIVE SUMMARY

This report provides a summary of the 12th workshop of the Nordic Alliance for Clinical Genomics (NACG). The workshop took place at Reykjavik, Iceland, 28-29 April 2022, bringing together 100 participants from 27 organisations in 8 countries.

The workshop invitation including agenda is included in Appendix 1.

The theme for this workshop was ***Overcoming short-read insufficiencies using long-read sequencing***.

KEYNOTE

Session chair: Eirikur Briem (Landspitali)

Keynote speaker & affiliation	Title	Key topics
Patrick Sulem, MD, Head of Clinical Sequencing, deCODE	"From Research to Clinics - 25 years of deCODE genetics"	Patrick presented on the topic of Whole Genome Sequencing at deCODE genetics in Iceland. deCODE has 10 years of experience with clinical sequencing. Medically actionable genotypes in Iceland - 1 in 25 WGS Icelanders (4%) carry an actionable genotype. de novo sequence variants expertise. Routine re-analysis of cases every 6 months. Discovery of novel disease genes and updates in analytical methods Comparison of ONT, Illumina and PacBio for Population genetics and clinical sequencing. Whole genome sequencing by long read methods at deCODE: "By 2022, deCODE has sequenced 8 thousand individuals with long read methods".

NATIONAL UPDATES

Session chair: Dag Undlien (OUS)

Country	Presenter	Key updates
Norway	Dag Undlien	National strategy for personalized medicine is being revised in 2022, work ongoing Project for establishment of National Genome Center focusing on ICT infrastructure ongoing
Sweden	Valtteri Wirta	Various updates on Genomic Medicine Sweden initiative Increasing uptake on NGS diagnostics across all areas Mapping of legal constraints for data sharing/secondary usage Pilot project for digital consenting initiated Pilot projects in infectious disease (metagenomics), rare disease (long read + RNA seq) and cancer (WGS + WTS in solid tumors + hematology) initiated,
Denmark	Kasper Thorsen & Ole Lund	New disease groups are being included in DNC WGS program (pediatric and adolescent cancer, hereditary hematological disorders, endocrinological disorders, PID, hereditary cardiac disorders) New seq. QC system New/updated bioinformatic pipelines
Iceland	Eirikur Briem	Working on IVDR adaptation Implemented new LIMS (GLIMS) Electronic requisition forms and electronic reports directly to patients implemented
Finland	Janna Saarela	New law on secondary usage of health data

		Drug Development Center established Finngen: Approx 400.000 with both genome data and health data available for research iCan - initiative for profiling 15000 cancer samples across different cancer types will be profiled by 2026

TECHNOLOGY PRESENTATIONS

Session chair: Valtteri Wirta (SciLifeLab)

Provider	Presenter	Key technology updates
Oxford Nanopore Technologies	Tonya McSherry	Overview of portfolio, including methods in active development: adaptive sequencing (targeted sequencing), methylation analysis and short fragment sequencing mode Improvements in early access testing will improve speed of sequencing, accuracy of sequencing and improved variant calling. Overview of clinical applications, including ultra-rapid whole-genome sequencing (8 hours)
Pacific Biosciences	Neil Ward	Updates on comprehensive characterisation of the human genome, including detection of more variants (SVs and variants in difficult-to-map regions) compared to short-read technologies Targeted assays for hard to analyse genes (for example: Cyp2D6, SMN1/2, GBA, FMR1). 96 barcodes validated, 384 available, for low-cost sequencing Pharmacogenomics enrichment panel together with Twist Biosciences, capturing 43 PGx genes
Bionano Genomics / Triolab	Adrian Silberman	Update on technology and performance estimates and examples of clinical use cases

SITE-WISE BRIEFINGS ON LONG-READ/ OPTICAL MAPPING IMPLEMENTATION

Session chair: Janna Saarela (FIMM)

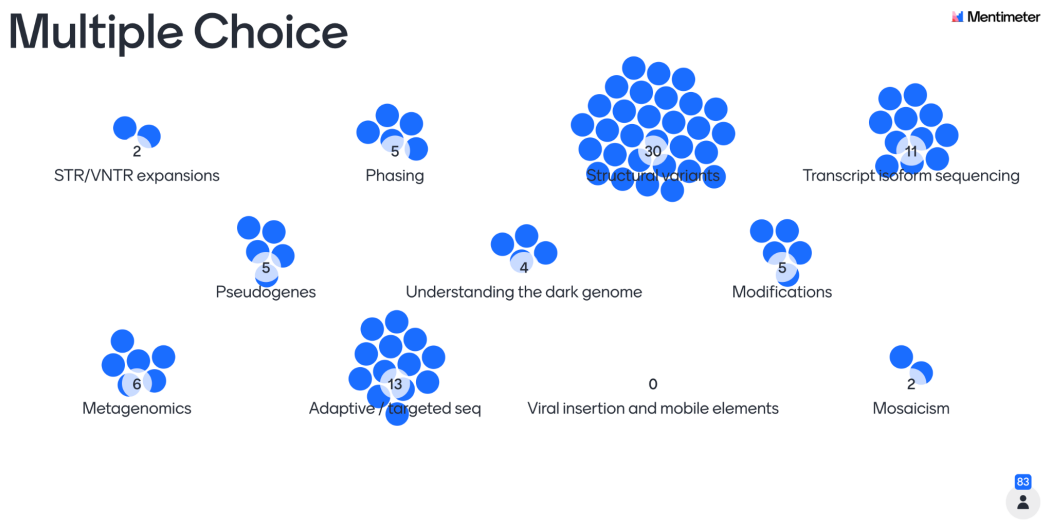
Site	Presenter	Key updates
MOMA (Department of Molecular Medicine) Aarhus University Hospital	Ebbe Norskov Bak and Ester Ellegaard Sørensen,	Implementation of Nanopore sequencing for unresolved cases at MOMA. ONT used for discovery and validation: RNA seq, WGS and pseudogene regions (CYP21A2/CYP21A2P), translocations (SRY), SV identification (colorectal cancer). Plus: good protocols & support; Minus: inconsistent output, failed runs, bioinformatics in development.
Department of Clinical Genetics, Odense University Hospital	Martin Larsen	Ongoing clinical long-read projects and status of the danish national long-read initiative. Applied to detection of repeat expansions HTT and FMR1 Tandem Repeat Expansions), mapping SV breakpoints (BRCA1), non-invasive prenatal testing, Covid-19 seq, methylation/imprinting diseases, and non-solved diagnostic cases. Targeted sequencing of 27 genes associated with triple repeat diseases.
Center for Genomic Medicine, Rigshospitalet	Tobias Overlund Stannius and Lusine Nazaryan-Petersen	Bioinformatic tools for alignment and structural variant calling in long reads. Best/functioning combinations of alignment and variant calling algorithms. Long-read sequencing applications for hard-to-sequence genomic regions. PacBio HiFi and ONT for SV detection and validation (inversion and truncation of F8 gene). Planned applications: developmental disorders and other likely genetic diseases with negative WGS+array, regions flanked by segmental duplications and other repeats (UNC13D), SNVs in homopolymer and pseudogene regions.
Department of Medical Genetics, Oslo University Hospital	Arvind Sundaram	Optical genome mapping (BioNano) and ONT (MinIon). Examples of challenging cases with SVs. In Hereditary cancer syndrome insertion detected in MSH2 with both technologies.

Institute of Biotechnology, University of Helsinki	Lars Paulin	DNA Sequencing and Genomics Laboratory. > 10y long read seq experience, PacBio and ONT, mostly de novo genomes of non-model organisms (wet lab and bioinfo pipelines), but also human genomes.
Karolinska Institute	Jesper Eisfeldt & Anna Lindstrand	Characterization of structural chromosomal variants by long read sequencing. Comparison of analysis of cases with complex SVs (translocation involving 6 chromosomes, ring chr21) by short read WGS, BioNano, PacBio and ONT: prize, seq depth, GC content, seq quality, seq yield, GC, result, and examples of previously unsolved cases. Ongoing LR projects: structural variants, expansions and homologous regions in patients with rare diseases.
Department of Clinical Genetics, Rigshospitalet	Ulf Birkedal	ONT in Functional Genetics. Full length transcript seq, optimization, automation example: SDHA - quantitation of del of ex4; BRCA1.
Institute for Molecular Medicine Finland, University of Helsinki	Johanna Lehtonen	Gaining long-read information synthetically using linked reads. Applied to WES & WGS of large muscle disease genes for phasing and haplotyping.
SciLifeLab, Uppsala University/Uppsala University Hospital	Malin Melin and Joakim Klar	Long-read sequencing at Uppsala. PacBio seq of BCR-ABL1 fusion in CML, SARS-CoV-2 Nanopore. Adaptive sampling for a targeted gene set (repeat expansions, segmental duplications, cancer panel, other regions of interest) applied to HEK cells and clinical samples.
University Medical Center Groningen, the Netherlands	Dorieke Dijkstra	Long-read sequencing in the UMCG genome diagnostics lab. ONT applied to pseudogenes, repeat expansions, exon deletions (SMN1, IKBKG). CRISPR-CAS targeting.

NACG IDEATION WORKSHOP

Session chairs: Valtteri Wirta (SciLifeLab) & Sharmini Alagaratnam (DNV)

Questions	Group input
Applications and challenges: Which cases are not solved by short-read sequencing?	As a joint effort, the following applications were identified: 1) Structural variant detection 2) Transcript isoform sequencing 3) Repeat expansions (short tandem repeat and variable number tandem repeat) 4) Phasing 5) Improved analysis of pseudogenes 6) DNA and RNA modifications, including methylations 7) Metagenomics 8) Understanding of the dark genome (ie genome not callable by short-read sequencing) 9) Adaptive / targeted sequencing 10) Viral and mobile element insertions
What are the potential solutions, and how can we get there together in the Nordics?	Survey of the interest of the Nordic community in various long-read applications summarized in Menti-survey image below. Key areas of interest include **SV detection** (30 of 83 respondents), **adaptive sequencing** (13) and **transcript isoform sequencing** (11). These, and other topics were discussed in smaller groups. Notes from these discussions are summarised in the tables below.



Detailed discussions on each topic

Structural variant detection (addressed by three groups)

Define the clinical application	Complex variations, find translocation breakpoints, balanced insertions, inversions, find clinically relevant genes, deletions within tandem repeats, define complex rearrangements	Solve unsolved RD cases. Replace other methods. Hematological malignancies.	Specific targets (i.e. nebulin, titin), gene with repetitive regions, pseudogenes Unsolved family cases Oddities: use long read to reveal details
What is the expected impact? What limitation with current technology does it solve?	Difficulties in mapping/align Array misses balanced events Karyotyping has not enough resolution Time/Cost in the future? (simplifies/fewer methods needed) Can detect structural variants in repeat sequences	Better/simpler workflow in the lab. Shorter TOT for patients. 2x the number of SVs detected compared to short read sequencing. (Also: Solve unsolved RD cases. Replace other methods. Hematological malignancies).	60% SV missing now, need to me discovered
What are the challenges? Consider lab, bioinfo, interpretation etc	Price Immature for diagnostics Learning how it works Interpretations Standardization Reference sequence (T to T available) Database (for polymorphism ect) Building up competence Long period of knowledge gain Error rate	Input DNA requirements. Challenging interpretation (lack of expertise and resources to scale). Lack of standardisation (e.g. bioinformatics best-practices). Follow the quick development of field. Everybody having data available for building experience.	Databases, references, software: non-existant or not optimised, lab-prep automation not ready, data and DNA storage and handling, FFPE samples, fragmentation, not possible to use old samples, compute power, short time until expiration date of kits Interpretation challenges: visualization software, filtering of the data Not mature, no best practice or knowledge from experience
What are the technical solutions?	Sharing interpretations? Implement both long reads and optical map	Many across the whole process... Examples of lacking tools: Better tool for integrating short/long-read calls.	Better software, wait until mature, use updated kits/methods, fresh samples, careful handling of DNA (sometimes shorter reads also help), automation
Are there any good ideas for Nordic collaborations ?	Share database Building up a golden standard NACG benchmarking Bioinformatics pipeline Share Genome in a bottle	Create an informal shared experience doc. Share data and pipelines.	Sharing knowledge, references, pipelines, interoperability External quality assessment, standardized validation and

	data Sharing of difficult variants		benchmarking Make systematic comparison of best practices and benchmarking
How could we follow-up this on subsequent NACG workshops?	Benchmarking Draw on past experience Sharing sessions	Have topic-focusing working groups suggesting ideas for topics and presenters for the organizers of NACG	ssion specific on current "hot" topics Replace or combine short reads When to use long-reads and when not necessary (cost, SNPs, routine to analyze only problematic genes or metabolic/pseudogenes)

Transcript isoform analysis

Define the clinical application	Effects of variants, Transcript fusion, Haploid Insufficiency, mRNA decay, parent of origin
What is the expected impact? What limitation with current technology does it solve?	Tissue specificity. A perfect transcriptome could replace DNAseq, cDNA bias
What are the challenges? Consider lab, bioinfo, interpretation etc	Reference Database requires large cohort (Tissue and Time specificity), Tissue specific Issues with sample Handling
What are the technical solutions?	5'Cap modification, RNA base modifications, Working in a clean environment, use of fresh tissue, standardization of methods to minimize method variations
Are there any good ideas for Nordic collaborations?	Share protocols that work, and do not work for sample specific handling
How could we follow-up this on subsequent NACG workshops?	RNA specific NACG Workshop

Improved analysis relating to pseudogenes

Define the clinical application	More easily analyse whether a mutation is present in the active gene or in the pseudogene
What is the expected impact? What limitation with current technology does it solve?	Gene-specific assays, labour intensive, only find what you are looking for
What are the challenges? Consider lab, bioinfo, interpretation etc	Which reference genome/mapping, are pseudogenes always pseudogenes, error rate, gene-defining mark should be in the same read as the mutation, DNA quality when long-read is used

	as a second test
What are the technical solutions?	Long-read reference data set, share between centra
Are there any good ideas for Nordic collaborations?	Reference data set
How could we follow-up this on subsequent NACG workshops?	Benchmarking exercise

Phasing

Define the clinical application	Tumor evolution, pharmacogenomics, transplantation monitoring, cascade testing/imputation for SV, compound heterozygosity, support when trio is missing
What is the expected impact? What limitation with current technology does it solve?	Decrease cost of wrong dosing, cheaper diagnosis, diagnosis when missing parents, donor-recipient matching
What are the challenges? Consider lab, bioinfo, interpretation etc	Legal, IVDR, hg38 bad - pan genome good, cost & accessibility of technology, input amounts, training, computing
What are the technical solutions?	Increase block-size, solve other sample types, better visualization, variant prioritization
Are there any good ideas for Nordic collaborations?	SOP sharing, what tools used, what did not work, clinical studies, resources available at sites, contact information,
How could we follow-up this on subsequent NACG workshops?	Regular meetings, topic-workshops

Adaptive / targeted sequencing (questions addressed by two groups)

Define the clinical application	Panels (genes, methylation, telomeres etc)	Targeted sequencing e.g. gene panels, gene fusions/rearrangements
What is the expected impact? What limitation with current technology does it solve?	Compared to LR WGS, cost efficiency, less input, higher coverage. Flexibility (Adaptive). Faster results	No wet lab optimizations, simple and flexible target design, fast turnaround time, decreases cost (both per run and sequencer investment)
What are the challenges? Consider lab, bioinfo, interpretation etc	Target validation for some enrichment, additional library preparation. Computer GPU, otherwise same as LR WGS.	Hardware (GPU required), DNA quality and integrity, analysis of challenging regions without a good reference

What are the technical solutions?	Adaptive (Nanopore), Cas9 enrichment (Nanopore), hybridisation capture (Pacbio/Twist).	GPU
Are there any good ideas for Nordic collaborations?	Samples, design, knowledge, bioinformatics	Sharing experiences, sharing fasta/bed files
How could we follow-up this on subsequent NACG workshops?	RESULTS, what works. Share samples, matchmaking (who does what and where). Common publication	A lot of labs are about to test adaptive sampling at the moment. Sharing our experiences would be very useful. Connecting through e.g. slack/email could be an alternative.

Metagenomics

Define the clinical application	Investigate if the patient has a microbial or viral infection Identify antibiotic resistance
What is the expected impact? What limitation with current technology does it solve?	Long reads allow rapid analysis
What are the challenges? Consider lab, bioinfo, interpretation etc	Robustness in the flowcell is a limitation Sample can clog the pore No good practices for classification
What are the technical solutions?	Even quality for the flowcells would solve problems Better sample prep would be helpful New classifiers needs to be developed
Are there any good ideas for Nordic collaborations?	Collaborate on reference databases, sample prep tricks
How could we follow-up this on subsequent NACG workshops?	Have metagenomics speaker(s)

Modifications

Define the clinical application	Detect imprinting defects in disease associated imprinted genes, UPD (uniparental disomi) Methylation associated with disease causing repeats expansions Epigenetic signatures - Cancer subtyping, i.e. brain-cancer subtyping - Epigenetic signature for rare disease syndromes - Liquid biopsy of circulating tumor DNA. Early cancer detection and cancer type

What is the expected impact? What limitation with current technology does it solve?	
What are the challenges? Consider lab, bioinfo, interpretation etc	Can be more complex due to tissue-heterogeneity Cell-type specific reference sample set GPU Hardware to rebasecall.
What are the technical solutions?	Native molecule sequencing (ONT, PacBio), Illumina (bisulfit-seq, enzymatic conversion)
Are there any good ideas for Nordic collaborations?	
How could we follow-up this on subsequent NACG workshops?	The methylation field is still evolving, a session enlightening possible clinical applications

LONG READ CHALLENGES AND SOLUTIONS – WET LAB

Session chair: Ebbe Norskov Bak, Lars Paulin, June Åsheim and Ida Höijer.

NACG Wetlab session summary

35-40 participants from more than 10 laboratories across the Nordic attended the wetlab-session. A briefing from each lab showed that more than half had experience with some long-read technologies with Nanopore being the mostly used platform. Several labs were planning to implement long read sequencing technologies. The participants discussed the following three topics in groups and finally in plenum.

DNA extraction and sample QC

Extraction of HMW DNA

Addition of extra EDTA to e.g. blood samples prior to extraction may help keeping HMW DNA intact. The following kits has been used successfully for blood samples: Circulomics (PacBio), Monach (NEB), Qiagen Genomic Tip and Wizard HMW (Promega). HMW DNA can be challenging to work with due to e.g. difficulties with dissolving the DNA. SPRI based cleanup (e.g. QIASymphony DSP DNA) gives N50 of 20-25 kb.

Storage of sample and HMW DNA extracts

Pure samples can be stored for weeks in the fridge without significant degradation (reported test of up to seven weeks). Freeze/thaw leads to shearing of HMW DNA.

Shearing, size selection

gTubes are recommended for easy shearing prior to library prep if higher sequencing yield is preferred to longer reads. Circulomics Short Read Eliminator Kit has successfully been used to enrich for longer fragments. More precise size selection for e.g. PacBio sequencing can be done with SageELF or BluePippin.

QC of fragment length and purity

Femto Pulse (Agilent) is recommended for size measurements. Tape station is not reliable for size determination of long fragments (e.g. with N50 >15 kb). OD measurements with e.g. Nanodrop and Dropsense are fast and gives some indication of purity. It requires knowledge of the precise buffer to make a prober blank, which can be challenging for samples send as DNA-extracts.

Targeting

Amplicons (PCR targeting)

Works well with e.g. the ONT ligation kits. Limits the read length. Participants reported good results using LA taq (TaKaRa). As PCR targeting usually has a very specific target it is possible to run ten's of samples multiplexed on a flongle and still get high coverage.

Adaptive sampling (ONT only)

Adaptive sampling is easy to setup and works well when the target represents >0.1% of the sequencing pool though the enrichment usually only is 2-4x. Currently only available on MinION but has been announced for PromethION. Adaptive sampling is interesting, as it does not require changes to the library preparation.

Cas9

Cas9 targeting works reasonably well. The enrichment is low, but usually enough. Participants have good experience with using a combination of chopchop and IDT for gRNA design.

Hybridization probes

Has been announced for PacBio in collaboration with Twist. There is a protocol for ONT, but no participants had hands-on experience with this. Traditional hybridization probes are less effective with long reads than with short reads targeting.

Implementation issues

The following challenges for implementation of long read sequencing technologies were identified:

- Validation – normal variation and interpretation, there is a need for reference samples
- Laboratory workflow
- Extra equipment
- Developing tech – new releases.
- Routines (compatibility)

No labs had fully implemented long read sequencing in a standardized clinical setting and thus fully covered the above challenges. However, e.g. ONT performs much better and reliable than a few

years ago and is relatively easy to set up and test with the MinION platform without the need for purchase of extra equipment.

Future collaboration

We established a slack group for future collaboration within long read sequencing. Please use the below link to join:

https://join.slack.com/t/nacg2022wetlab/shared_invite/zt-17ithyzqd-Xs7jIMYshT4CfK8TpuEAeA

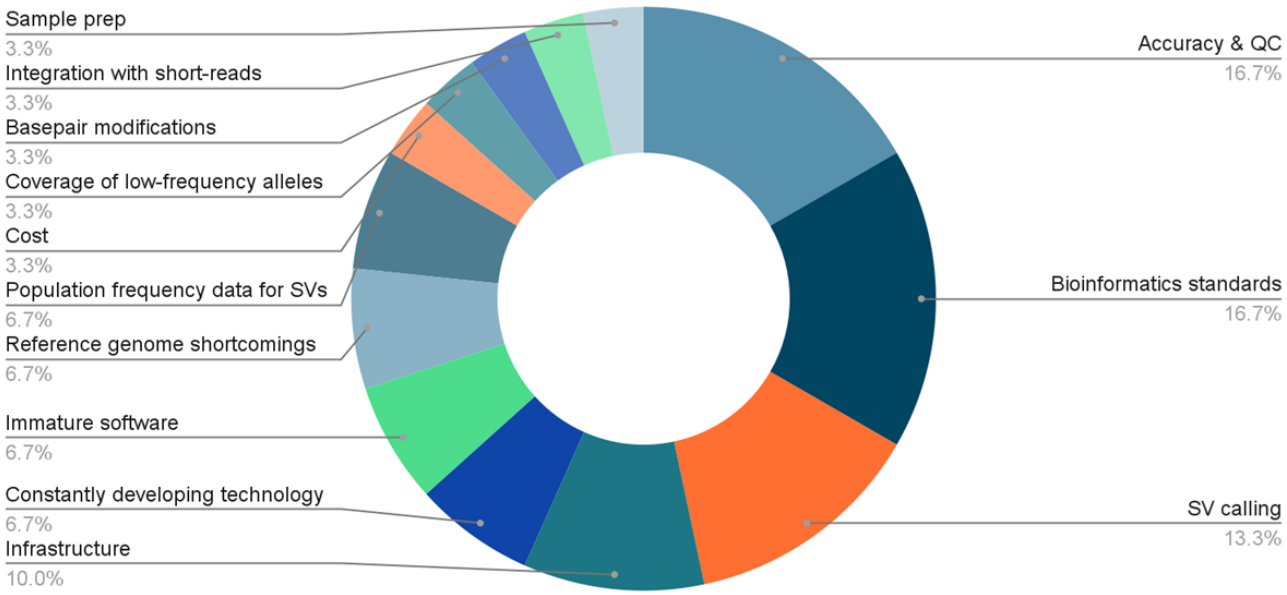
LONG READ CHALLENGES AND SOLUTIONS – BIOINFORMATICS

Session chairs: Anders Jemt (SciLife) & Ksenia Lavrichenko (OUS)

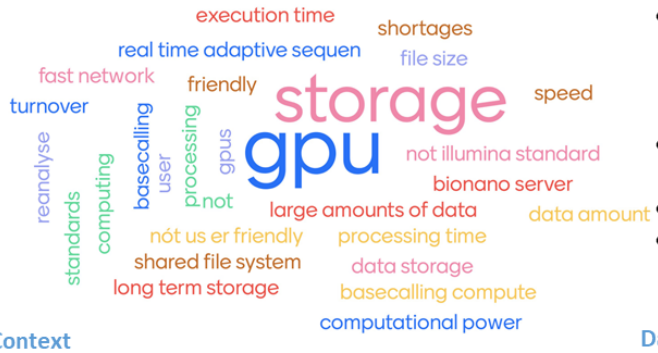
We already saw from the registration questionnaires that at least half of the participant institutions did not yet get to try any of the technologies. Among those who tried, ONT platforms were definite leaders with few who also worked with PacBio solutions and even fewer with Bionano. The group discussed the three most pressing challenges: infrastructure needed to incorporate long-read solutions, quality control specific to these technologies and calling of structural variants. We would like to thank the three volunteers who gave small talks in each of the discussed topics, sharing their approach and priming the discussions, thanks Martin, Simon and Ester!

The summaries of talks and discussions outcome can be found below.

Bioinformatics challenges with long reads



IT infrastructure



Context

- Basecalling converts raw fast5 files to fastq-files (ONT)
- Computationally expensive - requires access to GPU
- Raw data files (PacBio Movie file / ONT fast5) are large
- Detection of base-modifications (i.e. methylation) and repeat expansion requires fast5
- Proprietary and open software and hardware solutions

Challenges

- PromethION GPU
  - Undersized for "super accuracy" (SUP) Guppy basecalling
  - Live basecalling can only keep up with a single flowcell
  - Guppy updates are behind stand-alone version
- PacBio: Sequel IIE: Has compute - consensus generation occurs on the machine
- Amazon AWS / Cloud: Big data to transfer. Legal issues
- Bionano software: No docker image or installer, many dependencies. Bionano compute cluster is easy to use

Data storage

- Want to revisit basecalling with improved algorithms BUT: the gains of re-running basecalling have not been benchmarked, i.e. how much is accuracy improved?
- Is it feasible to re-analyse samples, whenever software is updated - and does it make sense in a diagnostic setting as soon as the report is written?

IT infrastructure: case solutions

By Martin J. Larsen

Dept. of Clinical Genetics, Odense Universitetshospital, DK
Clinical Genome Center (SDU/OUH), DK

#1 GPU computing

Local solutions

- PromethION compute unit (medico network restrictions)
- NVIDIA DGX STATION A100
- Custom build "gamer" PC

Centralized solutions

- University (SDU/DEIC) (requires datatransfer, sensitive data?)
- Danish National Genome Center (GPU nodes, costs?)
- Hospital (OUH AI/GPU cluster with T4 Tesla nodes)

#2 Storage

Single PromethION flowcell == 100 Gbases (~30x human genome)

Raw data (fast5): ~700 Gb

Basecalled (fastq.gz): ~70 Gb

Hospital central storage (NetApp incl. backup): 2500 DKK per TB (330 Euro) - **250 Euro per genome**

Alternatives ?

- Local NAS
- USB HDD (as low as 30 euro/TB)
- Not storing raw data, i.e. only basecalled

QC for long read sequencing

Considerations

- QC of input material - should we run it?
- Biological control samples: not part of routine yet.
- ONT: Have amplicon as spike-in control - not used by many
- Longer reads: less data, less pores available

What metrics?

- What metrics are important for long reads?
  - Q-score, Phred score, coverage (distribution)
  - Read length, N50, fragment length distribution
  - Alignment trimming: minimap2 soft trimming
- For adaptive sampling: looking at the coverage
- What is more important? Read length or quality of the read?
- Does mapping quality reflect read quality or reference genome quality?

What tools?

- PacBio: FastQC, MultiQC; ONT: proprietary tools
- NanoQC, NanoStat, nanofit, NanoPlot: fastq / fasta / bam: Can check actual error rate, with bam input
- PacBio-specific: ZMW occupancy, # passes
- MultiQC can parse various inputs, including PacBio and ONT, good for comparison of trends
- QC report is not reliable when the run crashes and some QC tools rely on it

QC for long read sequencing: case solutions

By Simon O. Drue

MOMA, Denmark

Other experts

- Steffen Møller Larsen (OUH) using Nanopore tools.
- Pia Laine (University of Helsinki) using fastqc for PacBio.

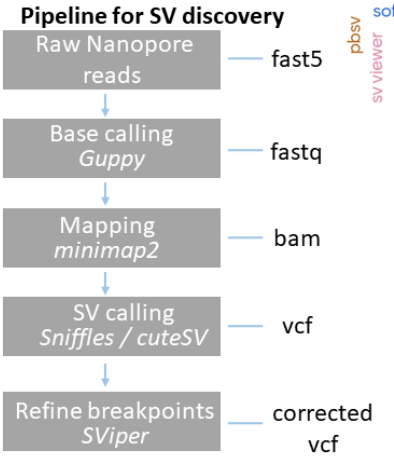
	NanoStat	pycoQC	MinIONQC	Falco	fastp
Input	SS	SS	SS	Fastq files	Fastq files
Output	Stats overview	HTML report	Plots (.png)	HTML report	HTML report
Parsed by MultiQC	Summary stats Reads by quality	Summary stats Read vs. base count Read length Quality score	Summary stats Read length	Sequence counts Sequence quality hist Per sequence quality scores Per base sequence content Per sequence QC content Per base N content Sequence length distribution Status check	Filtered reads Per base sequence quality Per base QC content Per base N content

SS = Sequencing_summary_[...].txt from ONT

Calling structural variants: case and reflections

By Ester Ellegaard Sørensen

MOMA, Denmark



Example correction

Start position

METHOD	SVTYPE.x	POS.x (Before)	POS.y (After)
sniffles	DEL	18273446	18273448
cuteSV	DEL	18273447	18273448
sniffles	INS	18281124	18281123
cuteSV	INS	18281129	18281123

Considerations

- Reference genome
  - HG19/HG38
  - T2T
  - Graph genome
- Assembly
- Variant Caller
- Consensus
- Genotyping
- Hybrid / correction by short-reads
- Biases in variant calling
- Benchmarking
- Databases

Appendix 1: Agenda

Day 1: 28th April 2022 (Room F and G)

8:15 Coffee (Room E)
8:30 Opening and Welcome **Dag E. Undlien**, OUS Department of Medical Genetics, NO, NACG chair **Eiríkur Briem**, Department of Genetics and Molecular Medicine, Landspitali - The National University Hospital of Iceland
08:40 Keynote lecture by Patrick Sulem, MD, Head of Clinical Sequencing, deCODE: "From Research to Clinics - 25 years of deCODE genetics" (Chair: Eiríkur Briem)
09:30 National updates related to clinical genomics from Nordic representatives (Chair: Dag Undlien) - 5 min presentation + 4 min Q&A Representatives from: Norway (Dan Undlien), Finland (Janna Saarela), Denmark (Kasper Thorsen & Ole Lund), Sweden (Valtteri Wirta), and Iceland (Eirikur Briem)
10:15 Coffee (Room E)
10:30 Technologies presentation (Chair: Valtteri Wirta) - 15 min presentation + 5 min Q&A Key technology providers in the long-read sequencing and optical mapping space including **Oxford Nanopore Technologies, BioNano Genomics and Pacific Biosciences** will provide introductions to their clinical applications, as well as recent technology updates.
11:30 Site-wise briefing on long-read/optical mapping implementation Part 1/2 (Chair: Janna Saarela) • Ebbe Norskov Bak and Ester Ellegaard Sørensen, MOMA (Department of Molecular Medicine) Aarhus University Hospital, Denmark (15 min) • Martin Larsen, Department of Clinical Genetics, Odense University Hospital, Denmark (15 min) • Tobias Overlund Stannius and Lusine Nazaryan-Petersen, Center for Genomic Medicine, Rigshospitalet, Denmark (15 min) • Arvind Sundaram, Department of Medical Genetics, Oslo University Hospital, Norway (15 min)
12:30 Lunch
13:30 Site-wise briefing on long-read/optical mapping implementation Part 2/2 (Chair Janna Saarela) • Lars Paulin, Institute of Biotechnology, University of Helsinki, Finland (10 min) • Jesper Eisfeldt & Anna Lindstrand, Karolinska Institute, Sweden (15 min) • Ulf Birkedal, Department of Clinical Genetics, Rigshospitalet, Denmark (15 min) • Johanna Lehtonen, Institute for Molecular Medicine Finland (15 min)

• Malin Melin and Joakim Klar, SciLifeLab, Uppsala University/Uppsala University Hospital, Sweden (15 min) • Dorieke Dijkstra, University Medical Center Groningen, the Netherlands (15 min)
15:00 30-minute booth and networking session (Room E)
15:30 NACG ideation workshop Applications and challenges: Which cases are not solved by short-read sequencing? What are the potential solutions, and how can we get there together in the Nordics? Facilitators: **Valtteri Wirta**, SciLifeLab, Sweden and **Sharmini Alagaratnam**, DNV, Norway
17:30 Conclusion of day 1, **practical information** (Chair: Eiríkur Briem)
19:00 Workshop dinner

Day 2: 29th April 2022 (Room F or G)

8.15 Coffee (Room E)	
08.30 Parallel Session 1 (Room F) **Wet lab - long read challenges and solutions** led by Ebbe Norskov Bak (MOMA)	**08.30 Parallel Session 2 (Room G)** **Bioinformatics – long read challenges and solutions** led by Anders Jemt (SciLife) & Ksenia Lavrichenko (OUS)
10.30 Coffee (Room E)	
10:45 Report back to plenary (Chair: Dag Undlien) **(Room F and G)**	
11:30 Conclusion and depart	

About NACG

The Nordic Alliance for Clinical Genomics (NACG) is an independent, non-governmental, not-for-profit Nordic association. NACG partners collaborate to identify and address emerging challenges to the implementation of clinical genomics and precision medicine.

Mission

NACG partners work together and learn from each other to lift performance standards. We aim at responsible sharing of trustworthy data for improved diagnosis and treatment, and as a resource for research.

Goals and activities

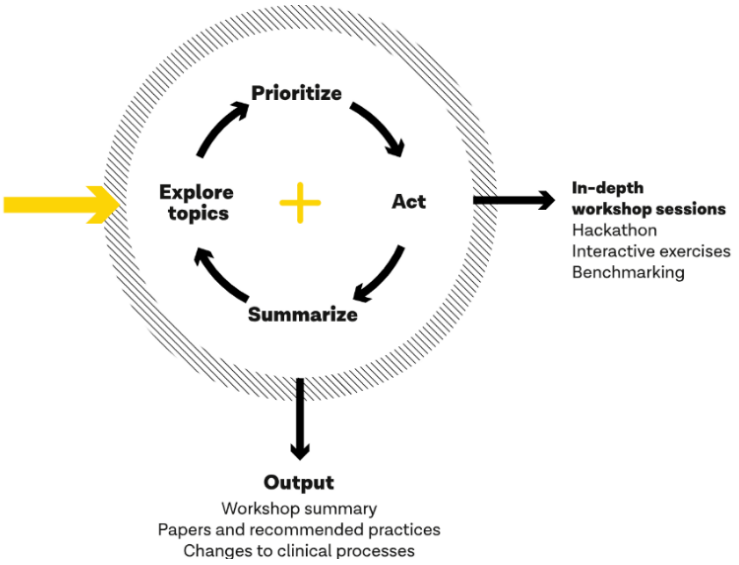
Facilitate the responsible sharing of genomic data, bioinformatics tools, sequencing methods and best practices for interpretation of genomic data.

Enhance quality of genomic data and processes and explore methodologies to provide assurance.

Understand legal barriers to the implementation of personalized medicine and to engage with key stakeholders that influence these barriers

Develop demonstration projects that challenge perceived legal barriers that limit responsible and ethical sharing of genomic and health data.

Build bridges between research and clinical communities, technologies and practices to foster innovation



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