Cluster for Natural and Technical Science Arms Control Research

Fact Sheet December 2024

Biotechnology

DNA Sequencing, Synthesis, and Screening in Biosecurity

Dr. Kadri Reis (CNTR/PRIF)

DNA Sequencing

Biological agents, including **bacteria**, **viruses**, and **fungi** can be used for malicious purposes. They share one critical feature with all other living things: their genomes are made of nucleic acids (**DNA** or **RNA**).

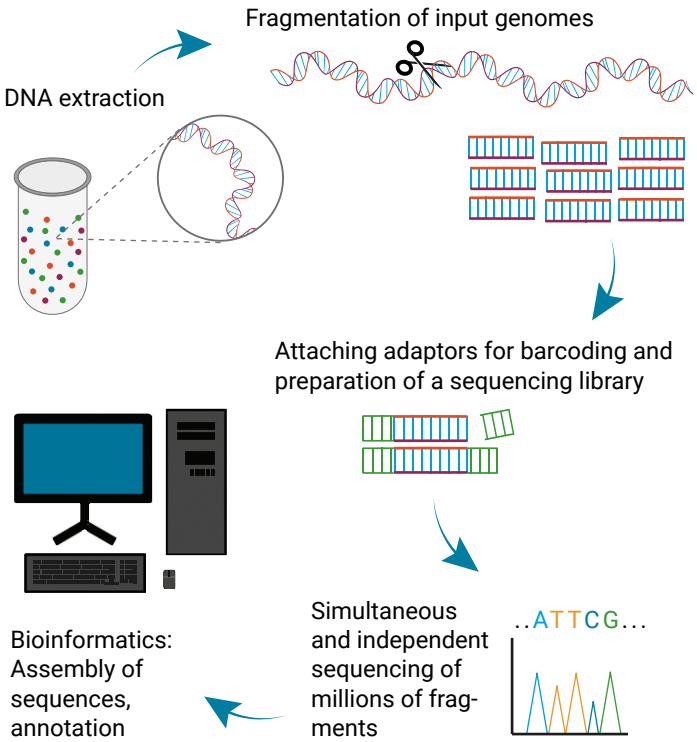
DNA can be isolated from any sample (live or dead, even ancient samples). This DNA can then be sequenced, i.e., "read". While being useful for ancestry studies and human heritable disease analysis, it also has usage in biodefense, and pandemic preparedness and response. The availability of **pathogen genome sequences** and **high-throughput sequencing** methods enable the detection of pathogenic microorganisms in complex environments.

For example, using **Next-Generation Sequencing (NGS)** to analyze the total DNA from a sample allows the identification of various microbial species and strains. **Metagenomic NGS methods,** such as Shotgun Metagenomic Sequencing enable comprehensive analysis of all genes from all organisms within a complex sample. This NGS method allows microbiologists to assess bacterial diversity and quantify the abundance of microbes across different environments.

Sequencing methodologies also play a crucial role in microbial forensics – helping to determine the likely source and/or perpetrator(s) of a deliberate release.

Genetic sequencing technology can be used to **track the spread of pathogens** or **identify bioengineered agents**. Such tools **could serve as part of a verification regime** by spotting unauthorized research activity or suspicious outbreaks.

Next-Generation Sequencing (NGS)

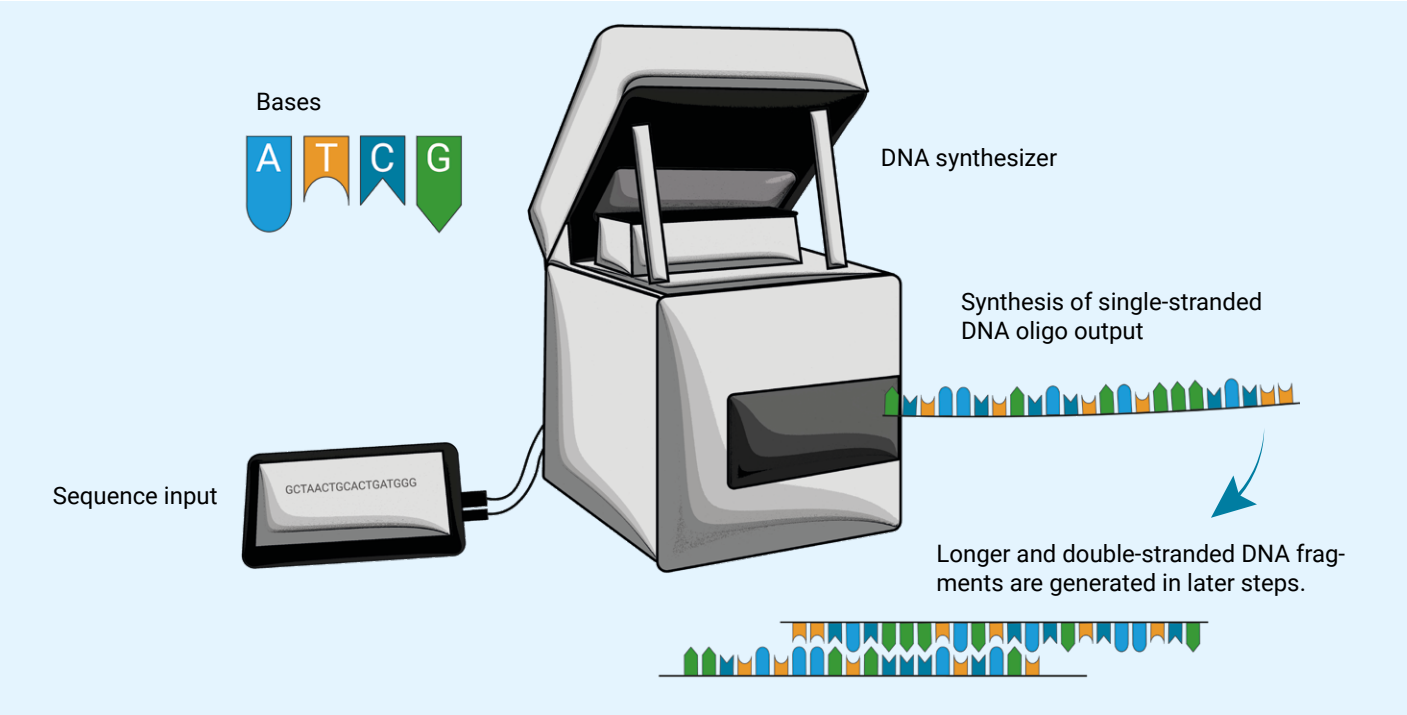


Comparing NGS and Metagenomic NGS

- While NGS often focuses on specific regions or individual genomes, **Metagenomic NGS targets entire genomes from all organisms in a complex sample** (e.g. microbiomes), providing a comprehensive view of the genetic diversity and functions present.
- NGS generates data for **predefined targets or single genomes**. Metagenomic NGS produces vast amounts of data, including both coding (genes) and non-coding regions, **across multiple organisms in the sample**.
- NGS is commonly used for diagnostics, gene expression studies, or sequencing specific organisms. Metagenomic NGS is used for analyzing microbial communities, studying interactions, and understanding ecosystem functions.
- **Metagenomic NGS is more computationally and financially intensive** due to the need to process mixed and highly diverse DNA from multiple organisms.

DNA Synthesis

Synthetic DNA is used globally in bioscience laboratories and is essential for many biotechnological advancements, including agricultural products, pharmaceuticals, advanced fuels, and other biomanufacturing applications. DNA synthesis technology “prints” DNA, allowing researchers to study and ultimately engineer biological systems to gain insights into their functions.



Many experts believe that the availability of next-generation benchtop DNA synthesis devices will make DNA synthesis more accessible to a wider range of users, including malicious actors. DNA synthesis screening is seen as a potential solution to mitigate this threat.

DNA (Synthesis) Screening

While screening nucleic acid synthesis orders is not mandated by any national government, DNA providers belonging to the International Gene Synthesis Consortium voluntarily screen both orders and customers to ensure that DNA containing potentially harmful sequences is not sold to individuals without a legitimate purpose. According to NTI (www.nti.org), however, these companies make up only an estimated 80% of the global market share. Starting at the end of 2024, and outlined in the Framework on Nucleic Acid Synthesis Screening, providers and manufacturers involved in U.S. federally funded research will need to screen purchase orders for sequences of concern (SOCs) and assess the legitimacy of their customers. This framework is based on the U.S. Executive Order on the Safe, Secure, and Trustworthy Development of Artificial Intelligence.

Depending on the results of the screening, orders may be rejected or further investigative proceedings may be initiated.

Steps in the Screening Process

Customer

Is the **customer legitimate**? (known researcher/lab in the scientific community)

Order

Are there **red flags in the order details**, e.g. shipping address, payment, device authorization?

Sequence

Does the ordered sequence **pose a biorisk**? Does the customer have a **legitimate use case** and **appropriate oversight**?

Appendix

Imprint

CNTR is a research alliance between the Peace Research Institute Frankfurt (PRIF), Justus Liebig University Giessen and the Technical University of Darmstadt. www.cntrarmscontrol.org · V.i.S.d.P.: Elisabeth Waczek (PRIF), Baseler Straße 27–31, Frankfurt a.M., Germany, Phone (069) 959104-0, info@prif.org, www.prif.org · Design: media | machine GmbH · Layout: CNTR

Gefördert durch:

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aufgrund eines Beschlusses des Deutschen Bundestages