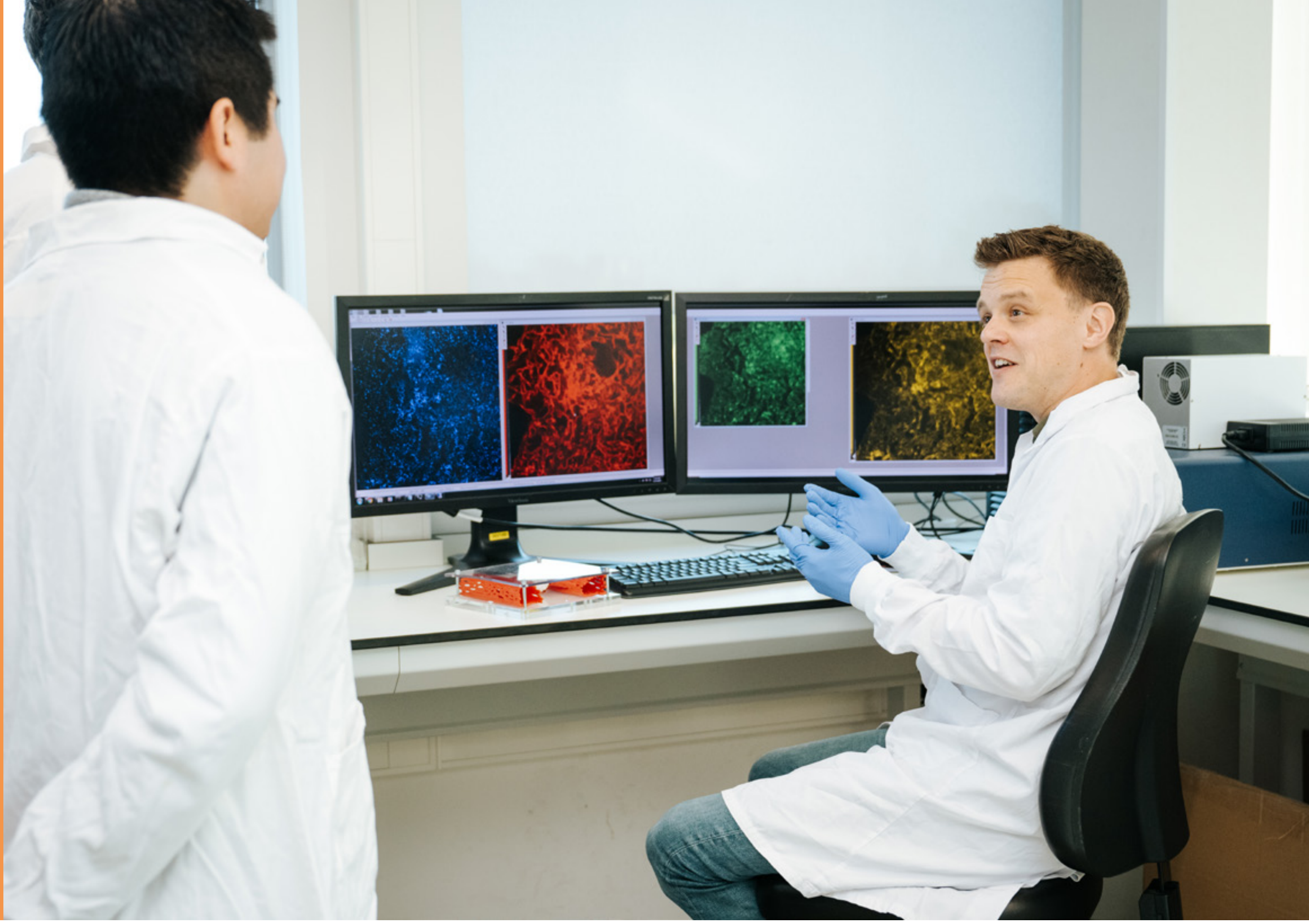


Deep Dive into Lab-on-Chip
Microfluidic Applications in Nanotechnology

Deep Tech Fonds, Invest-NL
November 2024

Deep Tech

INVESTNL

Introduction

This report offers a comprehensive deep dive into the evolving landscape of Lab-on-Chip (LoC) technologies, with a particular focus on the Dutch ecosystem. Lab-on-Chip, along with Organ-on-Chip (OoC) and biosensors, represents a significant intersection of microfluidics, nanotechnology, and biotechnology. These technologies have the potential to revolutionize sectors from healthcare to environmental monitoring.

Conducted by Invest-NL's Deep Tech Fonds, this study explores the dynamic opportunities and challenges within the Dutch scientific and entrepreneurial ecosystem. By mapping key institutions, start-ups, and stakeholders, the report aims to highlight the strengths and weaknesses in translating cutting-edge research into commercial applications.

The Netherlands has emerged as a global leader in this field, fostering innovation through its academic hubs and facilitating the commercialization of technology. Yet, hurdles such as funding gaps, regulatory challenges, and scaling infrastructure persist. Through a detailed analysis, this report provides a roadmap for bridging these gaps, ensuring the continued growth of the Lab-on-Chip sector.

We hope this report serves as a valuable resource for innovators, investors, and policymakers, helping to shape the future of Lab-on-Chip and its transformative impact on society.

Gert-Jan Vaessen
Invest-NL Deep Tech Fonds

Contents

Executive Summary

Advances in microfluidics have blossomed the possibilities in nanotechnology. Applied with electronic chips, the combination enables large-scale processes to be minituarised and multiplexed. The so-called, 'lab-on-chip' technology has grown rapidly in recent years as its applications are expanding to different industrial sectors.

This deep dive on Lab-on-chip, not only focuses on innovations within the Lab-on-chip but also the similar but distinct technologies in Organ-on-chip and Biosensor technologies. With the core of each technology enabling a complex harmony between different fields of microfluidics, electronics, engineering and biochemistry, the distinction can be found in its application and commercial use case. This report dives into how these technologies are being developed in the Netherlands and how its commercialisation is being is facilitated.

Interviews were conducted with the different stakeholders in the field (academics, start-ups, TTO/KTOs, national organisations, funders, commercial end-users). A thriving ecosystem can be found within the Netherlands, both of academic development and budding start-ups working to scale their innovation.

Highlighting some strengths:
Innovation hotspots dot the Netherlands with each area providing expertise in a core area of developing lab-on-chip technologies. This enables a melting pot of talent to come to the Netherlands and develop novel applications from ongoing research initiatives. Translating academic innovation to commercialisation is facilitated by local TTO/KTOs, providing support in the setting of start-ups and the commercialisation of the technology.
While a positive melting pot is seen in the early stages of development, several hurdles lie in the road towards scaling and commercialisation.

Defining the commercial use case provides a challenge. While initial ideas may seem straightforward, understanding how the innovation will fit in within the current processes of end-users remains a mismatch. This partly lies in the regulatory landscape which presents a challenge, specifically for organ-on-chip technologies.

While pre-seed and seed funding opportunities enable start-ups to start the process towards commercialisation, a funding gap can be seen.

To ensure that innovation is able to mature and reach commercial scale, it is important to address the weaknesses and provide support to budding start-ups to bridge the innovation gap.

Invest-NL's Deep Tech Fonds focuses on Deep Tech early stage start-ups in The Netherlands (NL)

"Deep Tech companies apply a **novel scientific and engineering breakthrough** for the first time in the form of a product. This means there is technological risk in getting the idea to actually work.

Deep Tech starts with an extended R&D phase and involves a higher share of technical staff compared to conventional ventures. Deep Tech also often involves the development of hardware and/or IP which are more **capital and time intensive**.

Once technological risk is overcome, there is additional risk in proving market demand for that product. If market demand is proven, Deep Tech startups have **stronger defensibility from competition thanks to technology barriers**, instead of having to rely on network effects and market lock-up. **What's Deep Tech today is not necessarily Deep Tech tomorrow**. Once the technology or product is no longer novel and as the company scales, what was once Deep Tech becomes regular tech. "

Invest-NL serves as the Dutch National Promotional Institution. As a leading impact investor, its core mission is to facilitate financing for ventures that may initially seem challenging to fund. By working in collaboration with diverse stakeholders, including financiers, investors, and development specialists from both the public and private sectors, Invest-NL actively tackles significant societal challenges. These encompass the transition towards a carbon-neutral and circular economy, promoting affordable and accessible healthcare and fostering advancements in deep tech. Established in 2020, Invest-NL operates as a privately-held entity, financed through public funds, with the Dutch Ministry of Finance as its sole shareholder.

Invest-NL's Deep Tech Fonds was established in 2022 by Invest-NL and the Dutch Ministry of Economic Affairs & Climate to bolster the fundability of the Deep Tech companies in the Netherlands.

Many Lab-on-chip Technology companies fit the mandate of Deep Tech Fonds because of their capital requirement and timeline to reach their intended market.
All companies are subject to the Deep Tech Fonds technical Due Diligence assessment process.

Main characteristics DTF

Fund	
Legal entity	Invest-NL Capital N.V.
Fund size	EUR 250 mln.
Limited partners	Ministry Economic Affairs (EZK) Invest-NL Capital
Duration	>15 years
Investment Strategy	
Co-investment	Pari passu with private (lead) investor
Instruments	Mainly equity
Company stage	Multi-stage (start-/scale-up), TRL 3-9
Scope	Disruptive key enabling technologies (R&D intensive, capital intensive and scientific base)
Ticket size	EUR 1 mln. – EUR 15 mln. per round Max. EUR 37,5 mln. per company
Portfolio	12 – 15 companies
Ownership	<50% (no majority)
Geography	The Netherlands
Impact	FTE, R&D and contribution to Dutch innovation ecosystem/economy

The DTF team / Investment team

Gert-Jan Vaessen
Fund Manager
Experience: Philips, Datelnet, Family office, Founder, BOM
Gert-jan.vaessen@invest-nl.nl

René Brama
Senior Investment Manager
Experience: NPM-Capital, InnovationQuarter, OostNL
rene.brama@invest-nl.nl

Liz Duijves
Investment Manager
Experience: Rabobank, Founder
Liz.duijves@invest-nl.nl

Bart van Campenhout
Investment Associate
Experience: Ardys, Founder
Bart.vancampenhout@invest-nl.nl

Stella Hak
Investment Analyst
Experience: Willis Towers Watson
Stella.hak@invest-nl.nl

Frits de Vries
Senior Investment Manager
Experience: Robeco, Fortis, Rabobank
Frits.devries@invest-nl.nl

Johan Stins
Senior Investment Manager
Experience: multiple investor and cfo roles
Johan.Stins@invest-nl.nl

Harold van den Brink
Investment Manager
Experience: Siemens, Manus VR
Harold.vandenbrink@invest-nl.nl

Yvonne Greeuw
Investment Manager
Experience: Delft Enterprises, Founder
Yvonne.greeuw@invest-nl.nl

Henri Schellen
Senior Investment Manager
Experience: Rabobank, NV BOM
Henri.Schellen@invest-nl.nl

Invest-NL’s Deep Tech Fonds focuses on Deep Tech early stage start-ups in The Netherlands (NL)

The DTF team / Investment Committee

Frits van Hout
IC Chairman
Current role: SB chair/member of several companies

Hans Büthker
IC Member
Current role: CEO Neways Electronics

Eline van Beest
IC member
Current role: CEO Hybridize and Venture Partner Thuja Capital

Aruna Subramanian
IC Member
Current role: Managing Director SABIC and IC member Energie Transitie Fonds

Steven Tan
IC Member
Current role: Founder/Director Nascent Ventures

Impact

€60 mln. Invested

>480 FTE

2.75x Investment Multiplier

>260 patents

Portfolio as of October 2024

LioniX International
Effect Photonics
Nearfield Instruments
Smart Photonics
Qblox
Innatera
Axelera AI
SCIL Nanoimprint solutions

54 organisations from the Dutch LoC, OoC and Biosensor ecosystem were interviewed for this report

AZAR Innovations
Bi/ond
Bionomic
Biotech Booster
Bondus
Brabantse Ontwikkelings Maatschappij (BOM)
Capricorn Partners
Cell4Pharma
Charles River Laboratories
chiron
COMDI EU
Curie Capital
Delft Enterprises
Delta Life Sciences
Demcon
Eindhoven University of Technology
Fetch Research
Gilde Healthcare
hDMT (Consortium)
Health~Holland
Helia Biomonitoring
Hello R&D
Holst Centre
HUB Organoids
iamfluidics
imec
Innovation Quarter
Insect Sense
Invest-NL
Lifesciences@work
LURIS
Mantispectra
MedTech Twente
Micronit
MIMETAS
Nanotech Ventures
Ncardia
NeuroGut Insights
Novel-T
NXTGEN Hightech
OccamDx
OnePlanet Research Center
Respiq
River Biomedics
Roche
Scope Bioscience
Surfix Diagnostics
Thuja Capital
TNO
TU Delft
UMC Utrecht
University of Twente
Utrecht Holdings
Wageningen University

we thank all the interviewees for taking the time to answer the questions to make this report

What you need to know about lab-on-chip

Microfluidics in lab-on-chip technologies


30 µL Pipette Tips
Tip Capacity: 30 µL
384 tips/tip box
REF B85745
Certified
FREE


Biomek
60µL

Definitions

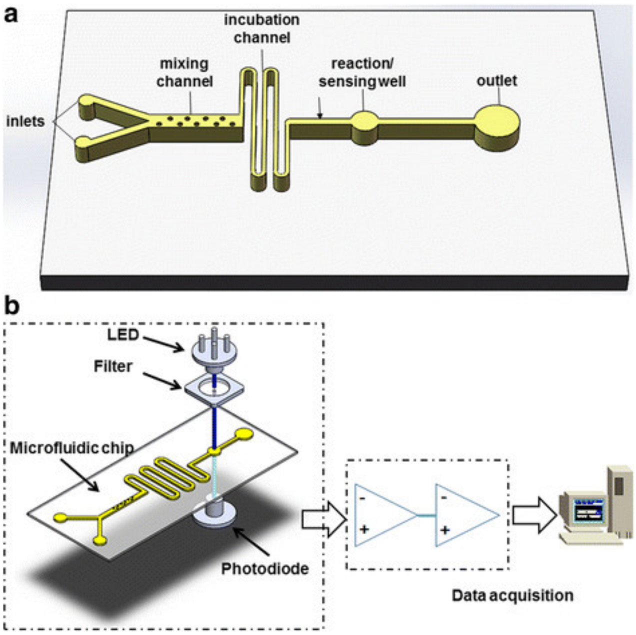
The role nanotechnology has on shaping the future of biotechnology is broad and applicable to many industries. Therefore, quantifying the impact of nanotechnology depends on how it is defined and measured. Focusing on the intertwining sub-domains of microfluidics and nanobiotechnology, this report dives into the prospects of how research innovation is translated into commercial value in the Netherlands.

Defining the role of microfluidics
Microfluidics plays an enabling role in the development of nanotechnology applications. Facilitating the miniaturisation of laboratory processes through the manipulation of fluids in submillimetre scales, microfluidics allows the precise control of fluids and rapid sample processing. Thereby, allowing processes that previously required a full-scale laboratory to be conducted in a microfluidic device.

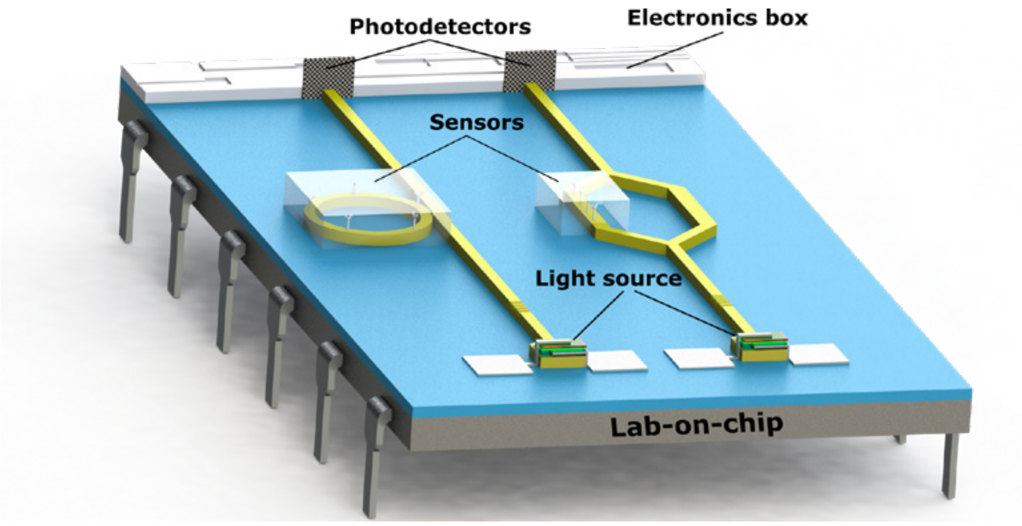
By integrating principles from various disciplines, including molecular biology, chemistry, electronics and engineering, microfluidics can be applied to develop systems that can perform complex processes with minimal fluid volumes for different commercial value propositions. This report dives into the Lab-on-Chip, Organ-on-Chip and Biosensors applications in the Dutch ecosystem that areas that demonstrate promise to lead the way.

Microfluidics

Technology that manipulates fluids and materials in channels smaller than 1 mm in at least one dimension



Microfluidic chip design. (a): Schematic diagram, (b) The picture of the microfluidic chip filled with a blue dye for visualization.



Design of a photonic lab-on-chip where multiple functions are integrated: light sourcing, waveguiding, analyte sensing, signal detection and processing. Image made by Benjamin Prat.

Definitions

What is lab-on-chip?

Lab-on-Chip (LoC) devices incorporate and automate microfluidics into a minituarised device to perform laboratory processes and analysis. The value of LoC devices is that they can handle microscopic fluid volumes that enables high-throughput screening and rapid testing applications. This enables for chemical reactions, biochemical analyses, and diagnostics to be conducted in in the LoCs.

Why is it better than current practice?
For diagnostic monitoring that requires large-scale laboratories to conduct testing, LoCs enable small capacity locations (i.e. GPs) to conduct the tests and provide results to patients without long waiting times.

Use case example
With healthcare shifting towards decentralized models involving patients, LoC can provide quick results away from laboratory and hospital settings. This is valuable in developing countries where traditional lab facilities may be lacking

What is organ-on-chip?

Organ-on-Chip (OoC) devices comprise of system that incorporates tissue cultures into a microfluidic chip to mimic human physiology. The recent roadmap towards standardization of OoCs by EUROoCS has defined in more details what comprises of an OoCs, which this report acknowledges as a more complete definition.

Why is it better than current practice?
The benefit of OoCs lies in being able to model organs in a 3D multicellular environment, whereas current cell-cultures are modelled in a 2D monolayer. The ability to study cellular interactions and the environment in OoCs enables improved modelling of human pathologies and treatment response.

Use case example
Streamlining the pre-clinical phase in drug development to optimize drug candidate screening. As specific disease states can be modelled in human organ tissues, disease mechanisms can be better studied that in animal models.

Lab-on-Chip

A miniature device incorporating microfluidics to conduct laboratory functions, such as biochemical analysis

Organ-on-Chip

A microfluidic chip aimed at simulates organ function and mimicking the microenvironment of human organs

What is a biosensor?

Biosensors measures biological or chemical reactions by generating signals proportional to the concentration of an analyte in the reaction. This can be applied broadly, therefore for the context of this report, the focus will be on biosensors that incorporate microfluidics for the detection and monitoring of biomaterials. Thus, biosensors present a similar technological scope to LoC. The main differentiation between the two technologies lie in their commercial applications. LoCs tend to focus on biomedical applications, while biosensors focus more broadly on agricultural, environmental and industrial applications. This can be simplified to the colour definitions of biotech: red, green and white.

Why is it better than current practice?
Some environments and materials do not allow for easy sample collection nor analysis. By providing ease-of-access monitoring, biosensors enable better detection of issues that may arise before the issue balloons.

Biosensor

A miniature device incorporating microfluidics to conduct biochemical analysis in environmental applications

Use case example
Biosensors can be used for real-time monitoring of pollutants or toxins in water sources or soil, aiding in environmental protection efforts. In industrial settings, biosensors facilitate the monitoring of glucose concentrations in fermentation vats.

Splitting of Biotech focus areas

Scope of biotech areas in this report

Commercial applications of the technologies can be clustered into four domains of applications: red biotechnology (healthcare), green biotechnology (agriculture), white biotechnology (industrial) and platform (applicable to all biotechnology applications).

Red biotechnology
The healthcare sector can be split into the pharmaceutical industry and medical profession. Most advances in the field are focused in this domain, which focus on improving patients' quality of life through the medical applications

Green biotechnology
Focuses on sustainable agriculture and food security, thus encompasses both agricultural monitoring and quality control management of food products. By ensuring the best product is picked and monitored throughout the supply-chain, the produce seen in groceries will be optimal for consumption

White biotechnology
Industrial microorganisms for manufacturing of chemicals and ingredients offer a sustainable solution to its production. Facilitating peak growth and production by the microbes in fermentation vats will help achieve sustainable chemical manufacturing faster.

Platform technology
Companies operating in this space focus on providing supplies to other companies that have a more industrial sector specific focus. Therefore, a general growth in the application of microfluidics in bionanotechnology increases the opportunity for platform technology companies to increase their operations

Added value of the technologies

The value of these technologies lie in the following applications:

Streamlining drug development
The current success rate for a novel drug to enter the market is roughly 10 – 20%. 90% of clinical failures of drug development are due to limited/lack of clinical efficacy, poor drug toxicity and poor drug-like properties. By improving the pre-clinical models used to select drug targets, drug development pipelines may improve the translation from research to clinical applications. Organ-on-chips could play a large role in increasing the rate of selecting the right drug candidate. As a holistic approach to pre-clinical research, OoCs reduce the need for animal models in the future.

Personalized medicine
With increasing access to medical and digital health technologies, individuals have greater opportunities to use innovations to improve their health outcome. Rather than requiring constant monitoring by healthcare professionals, patients with chronic diseases can manage their own symptoms. Point-of-care devices (e.g. lab-on-chip) may provide an alternative to time-consuming laboratory tests to support healthcare professionals with diagnostic and prognostic management. Furthermore, patient tissue may be used in OoCs for determining personalised dosage responses to treatment regimes.

Environmental assessments
Biosensors can facilitate the monitoring of environmental areas, where sampling and collecting pose challenges, to investigate environmental-related problems or water contamination analysis. By detecting hazardous chemicals or harmful microorganisms early, wide-spread issues can be detected early and the ballooning of impact can be mitigated.

Industrial manufacturing
With a push towards industrial production of sustainable ingredients, biosensors can monitor conditions in fermentation units to ensure maximum production is achieved. In addition, biosensors can be widely applied to address challenges in food production and its sustainability by improving quality control management.

Sustainability
An overarching benefit of these technologies is the reduction of samples and chemicals used to conduct the testing. The miniaturization of laboratory processes and facilitating multiple procedures into small devices allows for the reduction of energy and costs required to conduct the same experiments in a laboratory. Highlighting OoC, there is a strong push to reduce the number and eliminate the use of animals used in pre-clinical testing in drug development.

Driving of market growth from current market size

Expected market size for technologies

A sizable growth can be expected in the upcoming 10 years for the LoC, OoC and Biosensor sectors. The values presented were compiled from different market reports. Therefore, a range on the current and projected market size denotes the differences between the market reports.

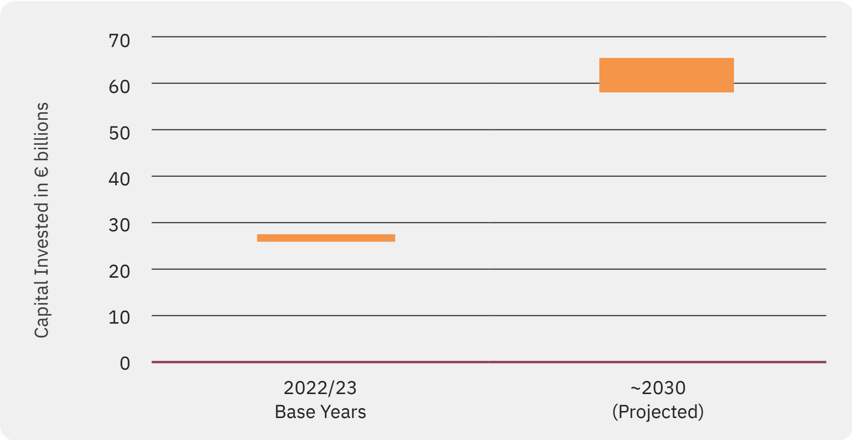
The main drivers of growth across the three areas, stem from the increased focus on personalised healthcare, which can range across from optimising drug development to point-of-care diagnostics. Note, it can be said the biosensor and lab-on-chip market reports that cited the figures include broader applications of the technologies within the market, which did not fall in within the evaluation of this report. Nevertheless, the figures demonstrate the added value towards the different market segments, from pharmaceutical and healthcare to consumer goods and products.

Whether this growth is achievable depends on multiple factors, including the technological innovations that increase sensitivity of readings, commercialisation of innovations, and overcoming regulatory hurdles for broader market application. The subsequent sections of this report will look to address these points from the perspective of the Dutch ecosystem.

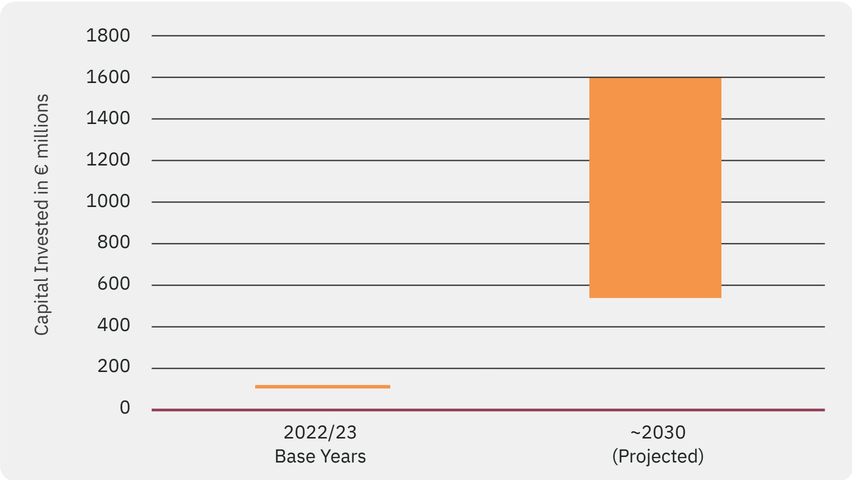
Technology focus	Baseline (2022/3)	Projected (~2030)
Biosensor	$26.6 – 28.5 billion	$58 – $65.2 billion
Lab-on-Chip	$6.2 – 7 billion	$10.7 – 13.9 billion
Organ-on-Chip	$103 – 117 million	$0.53 – $1.6 billion

References for values: Values taken from market reports from DataBridge, Markets and Markets and Allied Market Research

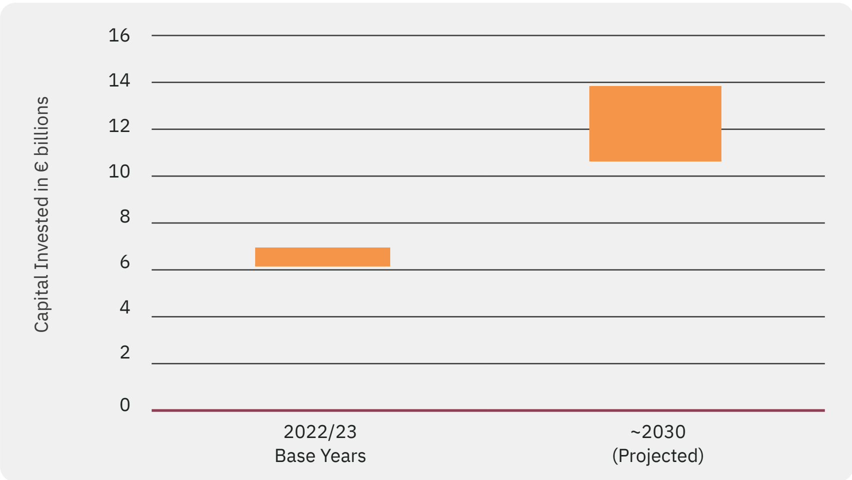
Biosensor Market Size Forecast



Organ-on-Chip Market Size Forecast (2022/23 - 2030)



Lab-on-Chip Market Forecast (2022/23 - 2030)

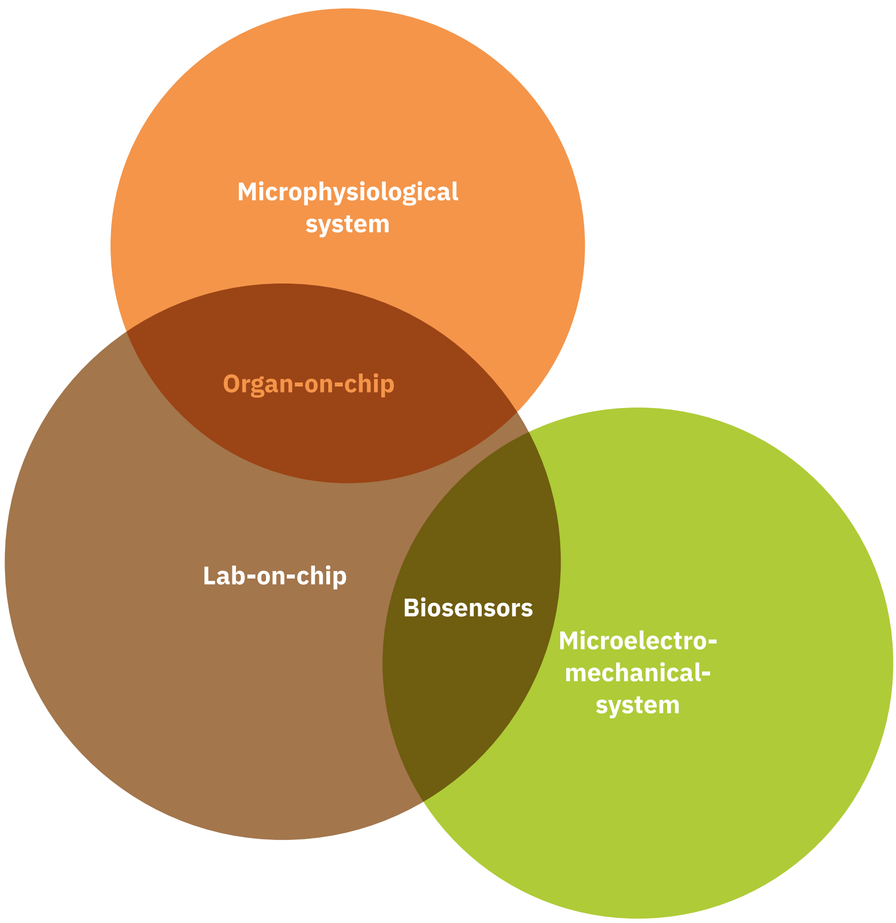


Data extracted from PitchBook by Invest-NL data team

Final considerations

Multiple definitions have been used across different academic and industrial fields, demonstrating an overlap on technological applications. There are other terms used in literature, such as microphysiological system and micro-electromechanical systems, but rather than complication an overlapping space, this report will be limited to lab-on-chip, organ-on-chip and biosensor technologies. This comes from the awareness to facilitate commercialisation requires having a defined use case where the value added is clearly represented. Therefore, this report will focus on LoC, OoC and biosensors and their commercial applications.

Visual overlap of technology definitions



Breaking down the Dutch ecosystem and companies(list not exhaustive, from 2024)

Highlighting the active academic centres, enterprises and networks in the space of lab-on-chip, organ-on-chip and biosensors

Source: Interviews, TTOs, “Invest in Holland”

Mapping the Dutch ecosystem

The Netherlands has a diverse ecosystem of research and commercial activities spread across the country. Concentrating in five regions (Enschede, Leiden, Eindhoven, Wageningen and Utrecht) academic institutions facilitate innovative research development in technical areas and foster an environment to spin-out and develop new start-ups. Enterprises outside these areas remain closely tied to these regions, aligned to spinning out and establishing themselves in areas where facilities are suited towards their growth. On a national level, national organisations and foundations help prop up developments and work towards building bridges across the different regions.

The commercial focus areas of start-ups and scale-ups in the Dutch ecosystem mainly target the red biotechnology market (i.e. LoC and OoC). This does not mean that the commercial value for green and white biotech markets are limited in comparison. Rather, it highlights an opportunity for growth in the respective market segments for applying the technology as a disruptive force.

When looking at established companies (>100 FTE), their value is built as platform companies, catering to the different aspects of biotech (including red, green and white). For start-ups looking to achieve commercial maturity, this does not mean diversification of services is required. It is more indicative the current landscape is ripe for start-ups and scale-ups to grow into becoming a market leader in the field.

Translating academic innovation towards commercial propositions

The pipeline for new companies to start out in the Netherlands in an academic setting is well established, with research developments scouted by local TTO/KTOs to determine whether commercialising the innovation is feasible. For TTO/KTOs whether an academic idea is mature to commercialise, a TRL (technology readiness level) of 3 is generally expected, in addition to having a viable commercial use case. What has been highlighted is that defining the commercial use case at an early stage may differ on application how initial R&D develops towards scaling the technology. To help hone the defining of commercial use cases, incubator programmes provide budding entrepreneurs with the opportunity to flesh out academic research ideas towards building a commercial use case. Nationally, the Venture Challenge has been a cornerstone of facilitating start-ups in the field to learn how to develop their commercial value proposition.

With a push towards enabling innovative research on reducing the use of animals in research, some early ideas have been pushed to the forefront with the aim to address this issue. Since 2021, the foundation Proefdiervrij has worked in collaboration with Venture Challenge to facilitate the kick-starting of such ideas. This has led to an increase in the number of start-ups working in OoC technologies.

Public stakeholders driving innovation and it's commercialisation

While regional areas highlight the diversity and focus of innovation, public stakeholders also play an essential role in facilitating a national front towards leveraging technology breakthroughs.

- hDMT
The Institute for human organ and Disease Model Technologies (hDMT) is a consortium of Dutch universities, medical centres and knowledge institutes who work to share their expertise in developing Organ-on-Chip Models. The mission of hDMT is to develop and qualify cell culture models that mimic healthy and diseased human tissues based on Organ-on-Chip technology, and to facilitate their valorization and implementation. Acting as a 'laboratory without walls', hDMT partners work collaboratively on multidisciplinary projects, i.e. ORCHID, with commercial enterprises as part of the consortium. hDMT is also a leading member of the European Organ-on-Chip Society (EUROoCS)

- NXTGEN Hightech
Starting in March 2023, NXTGEN Hightech aims to stimulate the advancement of the Dutch Hightech clusters and contribute to solutions of major societal challenges. Within the Focus Area of Biomedical Production Technology, lab-on-chip and organ-on-chip are two project areas where transforming knowledge into groundbreaking products is focused on.

- Health~Holland
Under the guidance of Top Sector Life Sciences & Health (Health~Holland), public and private partners combine nationally their investments and activities to gain economic and societal impact for Health & Care. In 2019, Health~Holland facilitated early phase Organ-on-Chip technology development with 2.76 million euros in Public-Private Partnership Allowance, which enabled seven projects to be awarded. More recently, the ADOPT project aims to advance the deployment of organ-on-chip technologies to bring personalised medicine to the forefront.

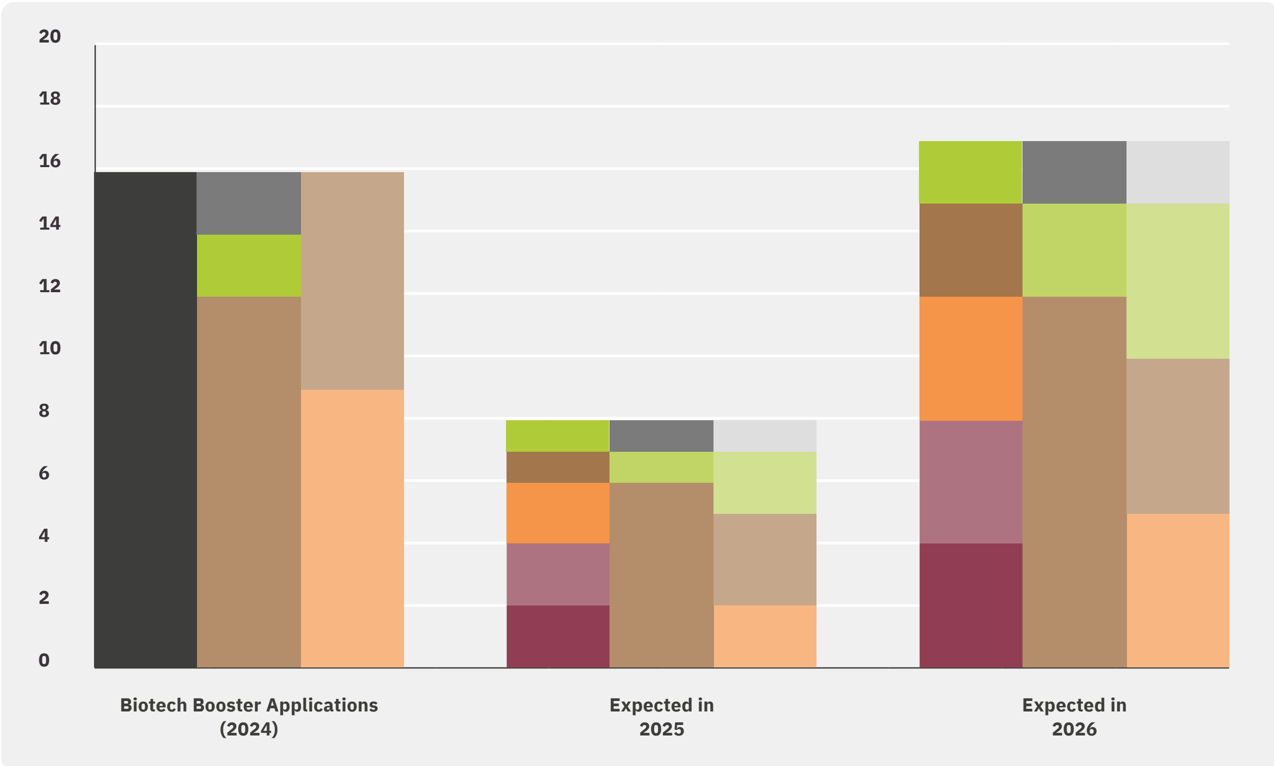
Projected start-ups in the coming year

Start-ups in the technology space have increased over the past decade. This partly lies with the technology maturing from initial innovative ideas towards commercial applications that have increase in users. With support from ROM's like InnovationQuarter, BOM and OostNL, multiple start-ups have spun out over the years, with some players maturing into the space. Looking to the future, the pipeline for new start-ups in the field of bionanotechnology is increasing within the Dutch ecosystem.

In 2024, Biotech Booster opened its first call for applications to be part of its program to obtain commercialization support. It was mentioned that out of the roughly 200 applications, just shy of 10% of applications (18) were focused on one the three technology areas. Majority of the applications focused on the red biotech domain which continues the trend of start-ups focusing on OoCs/LoCs for commercial development.

In the coming two years, a steady pipeline of start-ups coming from the main regions will continue. The increase over the years includes the continued support provided by the Proefdiervrij Venture Challenge as well as the maturation of current research ideas towards commercialization. One facilitation of new start-ups will be the new BioMicroSystems Center in Twente, a joint innovation centre by TNO and UTwente that aims to facilitate start-ups to collaborate on commercial projects. Although majority of the focus of start-ups will remain on the red biotech domain, a growing interest in the technology application (i.e. biosensors) in green and white biotechnology demonstrates the additional growth opportunities in different markets.

Anticipated NL start-ups:
Location, Biotech Domain, Technology Focus

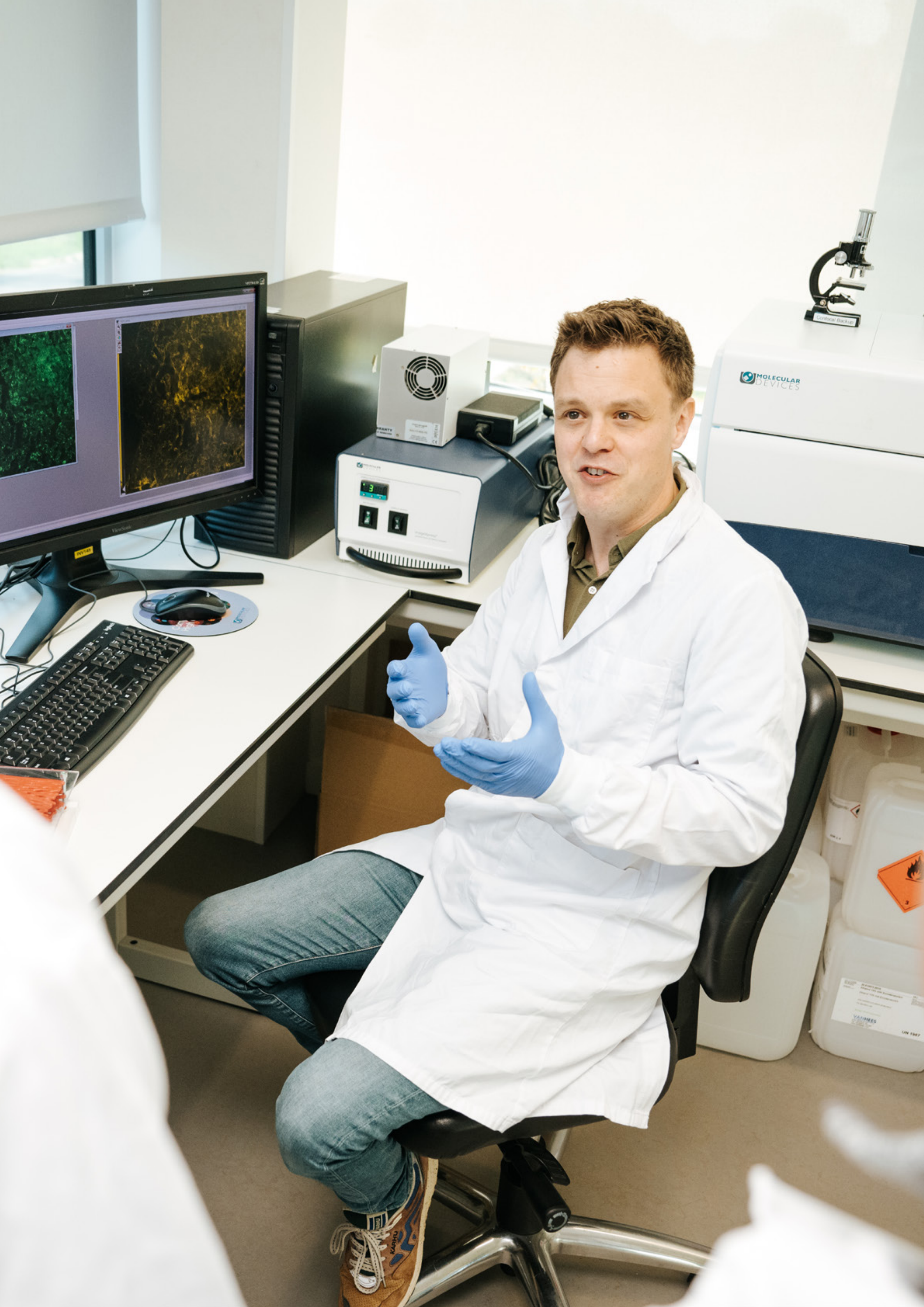


First column: Location
Second column: Red, Green, White, Platform
Tertiary Column: LoC, OoC, Biosensors

- Twente
- Leiden
- Eindhoven
- Utrecht
- Wageningen
- Biotechbooster
- Red
- Green
- White
- LoC
- OoC
- Biosensor
- Platform

Evaluating the Dutch Ecosystem

Strengths, bottlenecks and opportunities


MOLECULAR
DEVICES

Ecosystem strengths

Good knowledge capacity
The highlighted regions boast of internationally regarded academic output and budding start-ups that aim to commercialise innovative research. A direction the Dutch ecosystem has taken to improve the commercialisation of academic innovation is by increasing the opportunities for academics, especially early career researchers, to participate in entrepreneurship courses. While this development is still new, helping researchers understand how to develop a commercial proposition is a positive direction towards ensuring continued development of industrial and societal impact of one's research, outside of an academic setting. Start-ups can leverage this diverse talent pool to help with the development of their technologies, while fostering the next generation of researchers to apply their know-how in a different setting.

Knowledgeable talent acquisition
The nurturing of talent in the Netherlands is a core strength. Although for developing innovative multi-disciplinary products requires a diverse talent pool, the various research institutes across the Netherlands provide a melting pot for specialised skill-sets to acquire and apply their knowledge. The ability to travel across the country with relative ease allows talent to work across academic hotspots to translate their know-how into commercial applications. Thus, the knowledge transfer from local academic institutions to home-grown enterprises is able to flourish. As the function of management is not solely limited to understanding the technology but also understanding how the start-up/scale-up fits within the larger product development in multinational companies.

Support to start-up
TTO/KTOs provide an important bridge between research and practice to bring academic innovation towards commercial enterprises through technology transfer. As they are embedded in academic institutes, TTO/KTOs are positioned to best leverage local innovations to help develop the initial viable commercial use case. In addition, by providing the administrative support to setting up a company, the initial hurdles of establishing a start-up are supported and tech development can be focused on.

Exploring the bottlenecks

A challenge for any start-up lies in securing commercial traction of their product. Outside of securing commercial contracts, interviews with start-ups highlighted other areas that have presented challenges when developing their technology towards commercial use.

Regulatory hurdles
In the US, the FDA modernization act is a step in the right direction, with OoCs being able to provide support to applications to animal studies. Nevertheless, for current start-ups, 15 years is a lifetime away therefore, a push towards valorising their product is essential. This in turn requires, additional capital to run the required trials to validate their tests. Regulatory hurdles are also faced in start-ups focusing on other market areas, as market application data for agricultural testing requires multiple years before certification is obtained.

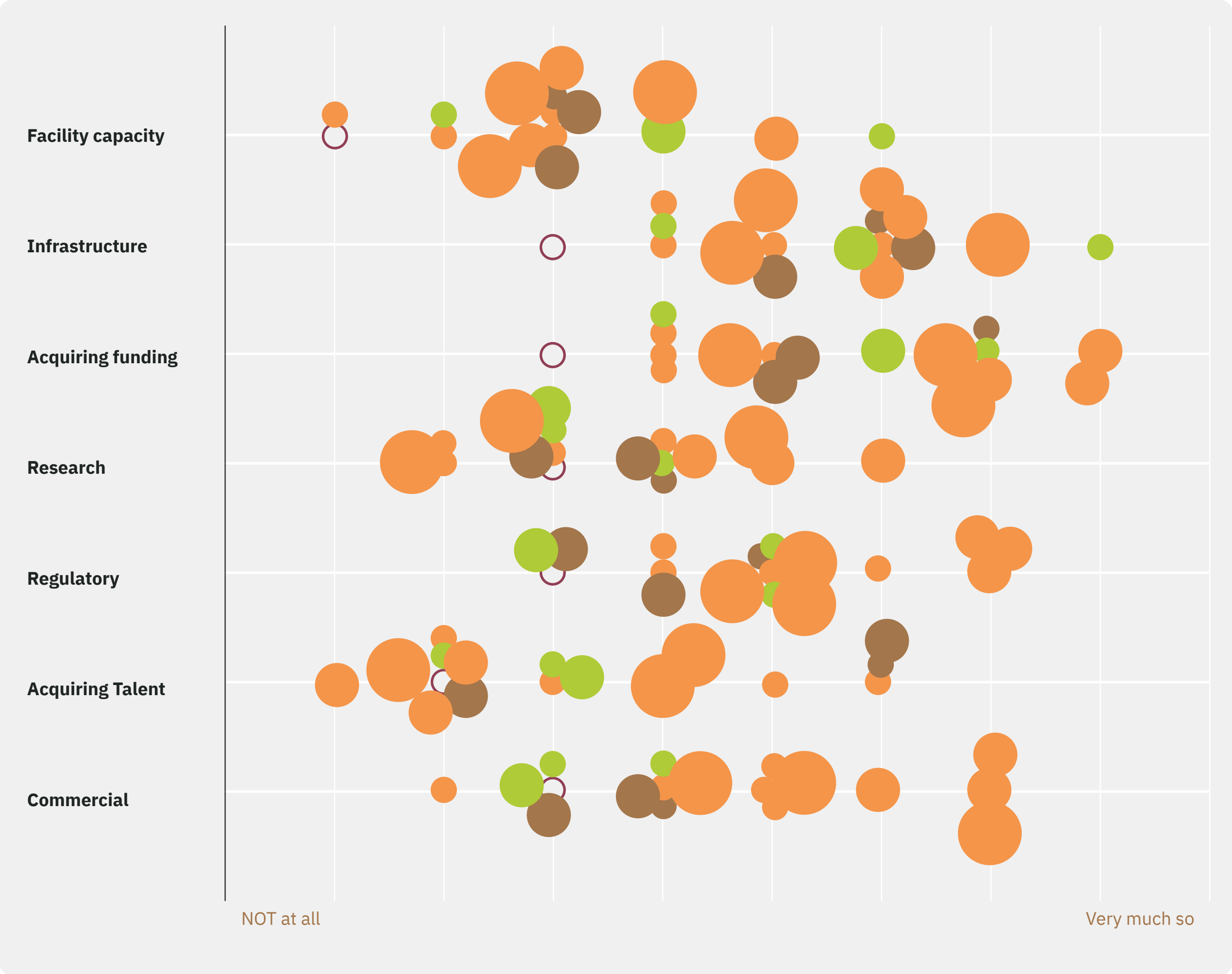
Infrastructure capacity
A pain point identified across start-ups looking to grow is the lack of space provided for scaling. While starting facilities are adequate for the initial development, as prototypes are optimised and a commercial product is developed, additional space is required to facilitate the scaling of the development. A concern to use funding raised to have a dedicated location proves too costly in the initial stages, therefore some capacity towards a shared scaling facility would support the jump from pure development towards commercial production and scaling.

Scouting for experienced talent
Although academic institutions develop many technologically savvy researchers and technicians, the talent pool for experienced talent has been raised as a bottleneck as start-ups grow and mature into scale-ups. While courses on entrepreneurship have increased to help new founders, understanding how a product fits in development pipelines of larger enterprises presents a bottleneck in building a successful use case. Having employees in start-ups with product development experience in larger enterprises provides an opportunity to address pain points faced and define how the start-up will remedy them.

Funding pain points
Funding for early start-ups come from funding instruments geared towards translating academic innovation to a commercial product. With multiple opportunities available to founders, from grants, loads and pre-seed/seed funding, it is a race against time before developing a commercially viable product or funding runs out. Once the stage is set for securing series A/B funding, start-ups are hard pressed to convince VCs to invest into their products commercialisation. While the technological innovation is attractive, whether the commercial use case is viable and whether the technology will scale to meet demands, remain hurdles that start-ups face when presenting to VCs.

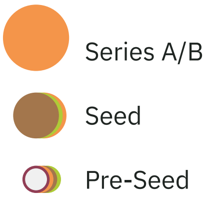
It has been highlighted that due to the technologies encompassing both biomedical development and electronics, regulatory uncertainty and limited precedence present a hurdle. Although MedTech funding provides an opportunity for start-ups, dedicated MedTech funding is limited and competes with other MedTech innovations, such as robotics. For start-ups that are not focused on red biotech, another challenge is faced as VCs in the other spaces, i.e. agriculture, focus more on more established developments in the field.

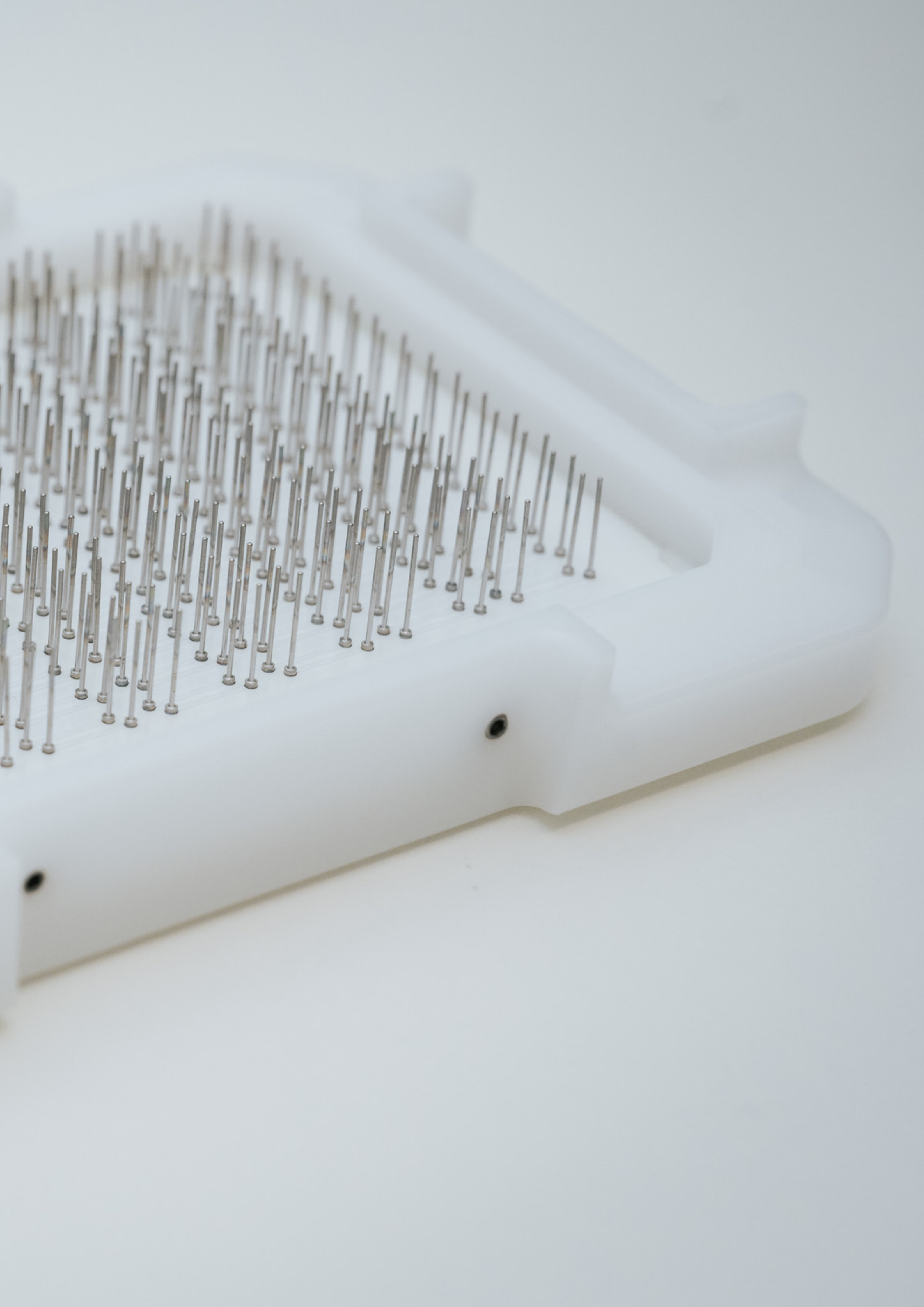
How did interviewed start-ups assess the bottleneck risks?



Recap

From budding start-ups securing initial pre-seed funding to more established scale-ups, a diverse range of challenges are faced. Some are pervasive across the different stages of start-up, such as regulatory bottlenecks, whereas others are more specific towards start-ups looking to make the jump to scale-up. It may seem that start-ups in the green and white biotech space have less challenges to face when developing their commercial proposition, it should be noted that the small sample size of start-ups in these spaces may skew the findings in these sectors.





Ecosystem opportunities

From the strengths of the ecosystem, an opportunity is presented to galvanise the strengths and ensure continued growth in the technology sectors. These opportunities rely on having an established ecosystem where different stakeholders can support each others' developments while adding value towards one's propositions. If these opportunities are catalysed, the bottlenecks highlighted may not be so challenging to address in the future.

Fostering collaborations
One resounding point across different stakeholders was the call for greater opportunities to collaborate with local partners across different knowledge areas. With hDMT, a network of academic institutions to share their complementary expertise, facilities and ideas is facilitated. The translation of OoC expertise is not limited to academics as hDMT works in conjunction with consortiums and governmental organisations to shape how OoCs will play a role in the future of healthcare. For facilitating the roll-out of OoCs, the ADOPT project by Top Sector Life Science and Health aims to produce a roadmap of the Dutch ecosystem. Thus, the opportunity for collaborations in OoCs is a strong opportunity to leverage.

The National Growth Fund has provided NXTGEN Hightech €450 million to bring the Netherlands back to the forefront of technological innovation and to contribute to solutions of major societal challenges. Within the Biomed domain, both LoC and OoC play an important role as project focus points and foster an environment, where the multidisciplinary partners can align and collaborate with each other.

Strengthening use cases
As majority of start-ups focus on the red biotech domain, an opportunity to leverage developments into different biotech domains promise to increase the market opportunities of the technology. Rather than forcing commercial use cases, addressing areas where the need for increased monitoring, i.e. food quality control, has been highlighted provides the first step in entering new markets. Further applications would address gaps in current methods of monitoring where applying biosensors increases detection rate of issues at an early time period. One caveat raised was the commercial use case may not be as attractive as red biotech in the other domains. On the other hand, as costs increase in agriculture and biochemical production, ensuring quality products are delivered drives a strong call for implementing of biosensors.

Funding
Funding to facilitate the jump from start-up to scale-up would provide opportunities to leading start-ups that present a clear roadmap towards commercialisation but face long lead times, i.e. valorisation studies, regulatory timelines. As sector specific funding have preferred target areas, i.e. therapeutics for healthcare VCs, the technologies presented face a challenge to present enough evidence of the commercial use case. A dedicated fund for these technologies, which could be categorised as part of MedTech, may improve the progression of these innovations towards commercialisation.


INTEGRA
GILSON SERVICE
INV457
Picus
1200
1200

Clusters of Innovation

Comparison to Abroad

Paving the future forward with Organ-on-Chip

The Netherlands is one of the global leaders in the development and research of OoC technologies. Building from a diverse academic ecosystem, supported by the hDMT network, the translation for the academic innovation to commercial translation is growing.

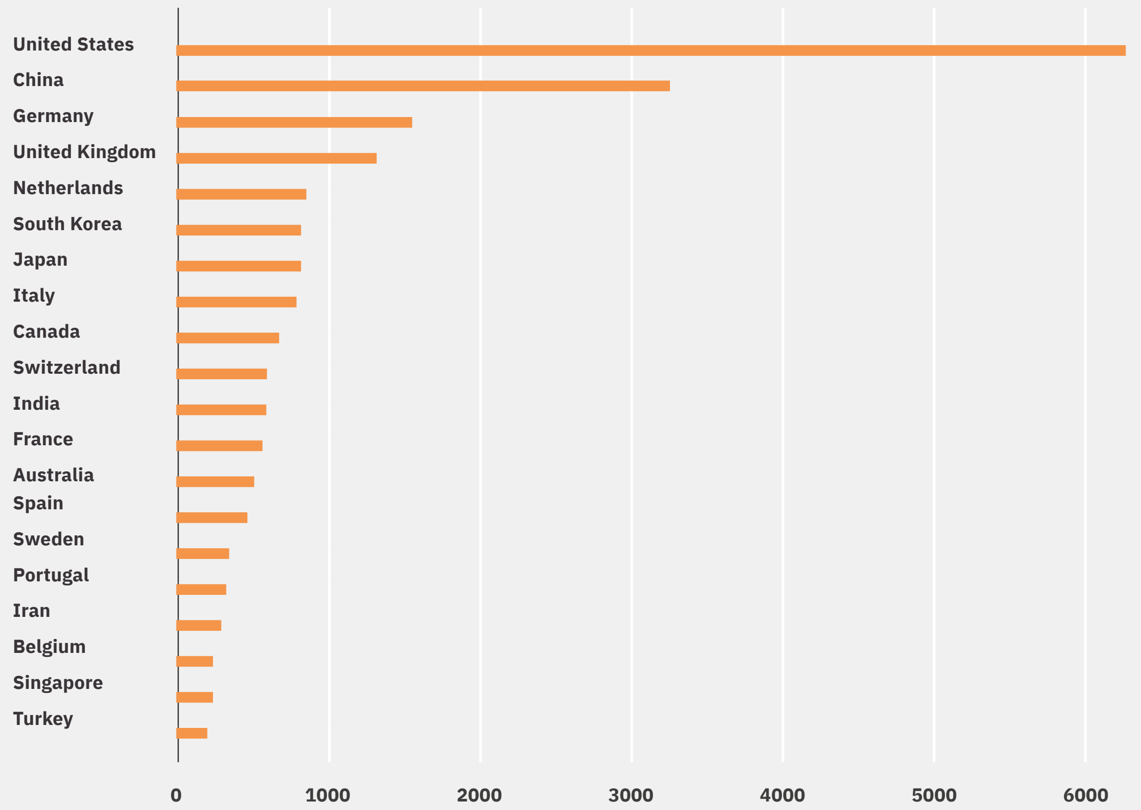
In academic research, University of Twente (Utwente) leads in OoC publications in Europe. The main driver for publications is led by the Applied Stem Cell Technologies group, which boasts many leading PIs that not only lead innovative research but also work towards translating research into commercially viable applications. This is further supplemented by the Organ-on-Chip Centre Twente, which is supported by the MESA+ Institute and TechMed Centre of the university.

Following closely behind UTwente, Utrecht University (UU) publishes the second highest number of publications on OoC. This number does not include publications by UMCU (University Medical Center Utrecht), which also publishes a fair number of publications in the field. With the Hubrecht Institute closely linked to the universities,

Outside of Enschede and Utrecht, Dutch universities in Leiden, Maastricht, Eindhoven and Groningen also have been prolific in publishing papers in the field. When compared to other larger countries, the investment in academia in this field has translated to a large skilled workforce in OoC. Within each regional hub, the translation of academic innovation to spinning out to establish start-ups have been greatly facilitated by the local Technology Transfer/Knowledge Transfer Offices.

Country	Research organization	n. publications	Citations (total)
Netherlands	University of Twente	132	4949
	Utrecht University	121	5158
	Leiden University Medical Center (LUMC)	107	4034
	University Medical Center Utrecht (UMC)	81	3849
	Maastricht University (UM)	78	2962

Number of publications by research organization (Top-50, selected Countries), 2003–2022, taken from: da Silva (2022), Organ Chip Research in Europe: Players, Initiatives and Policies

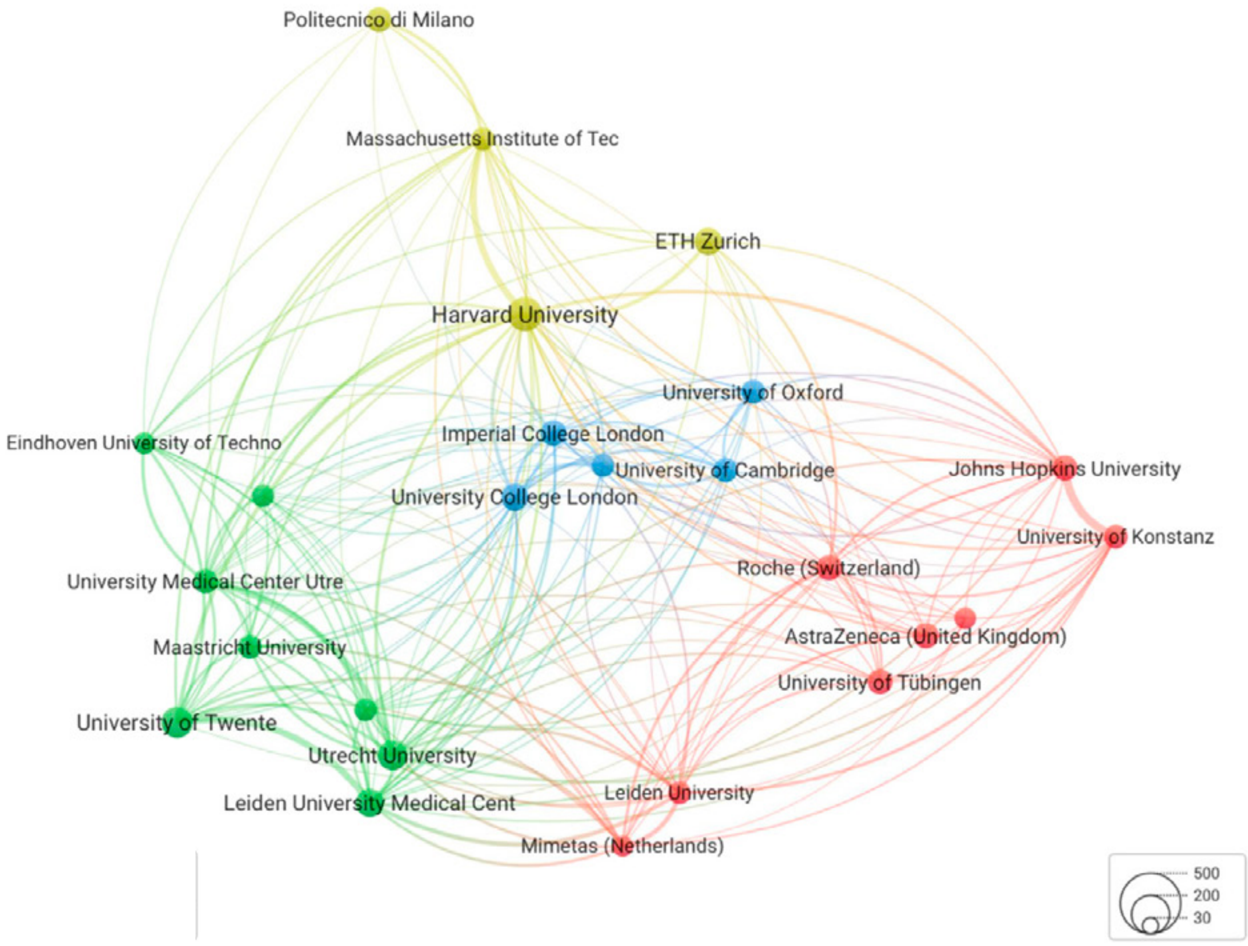


Number of Organ-on-Chip publications per country, 2003 - 2022, taken from: da Silva (2022), Organ Chip Research in Europe: Players, Initiatives and Policies

Ecosystem opportunities

Global impact of Dutch research
Outside of the number of articles Dutch knowledge institutes publish, the network the publications have across the globe can be highlighted. Within the Dutch knowledge cluster, many universities and medical centres collaborate on publications. This also is expanded to other clusters across the globe, demonstrating the added value of research being conducted in the Netherlands in the OoC space.

Network of Research Organisations publishing Organ-on-Chip research



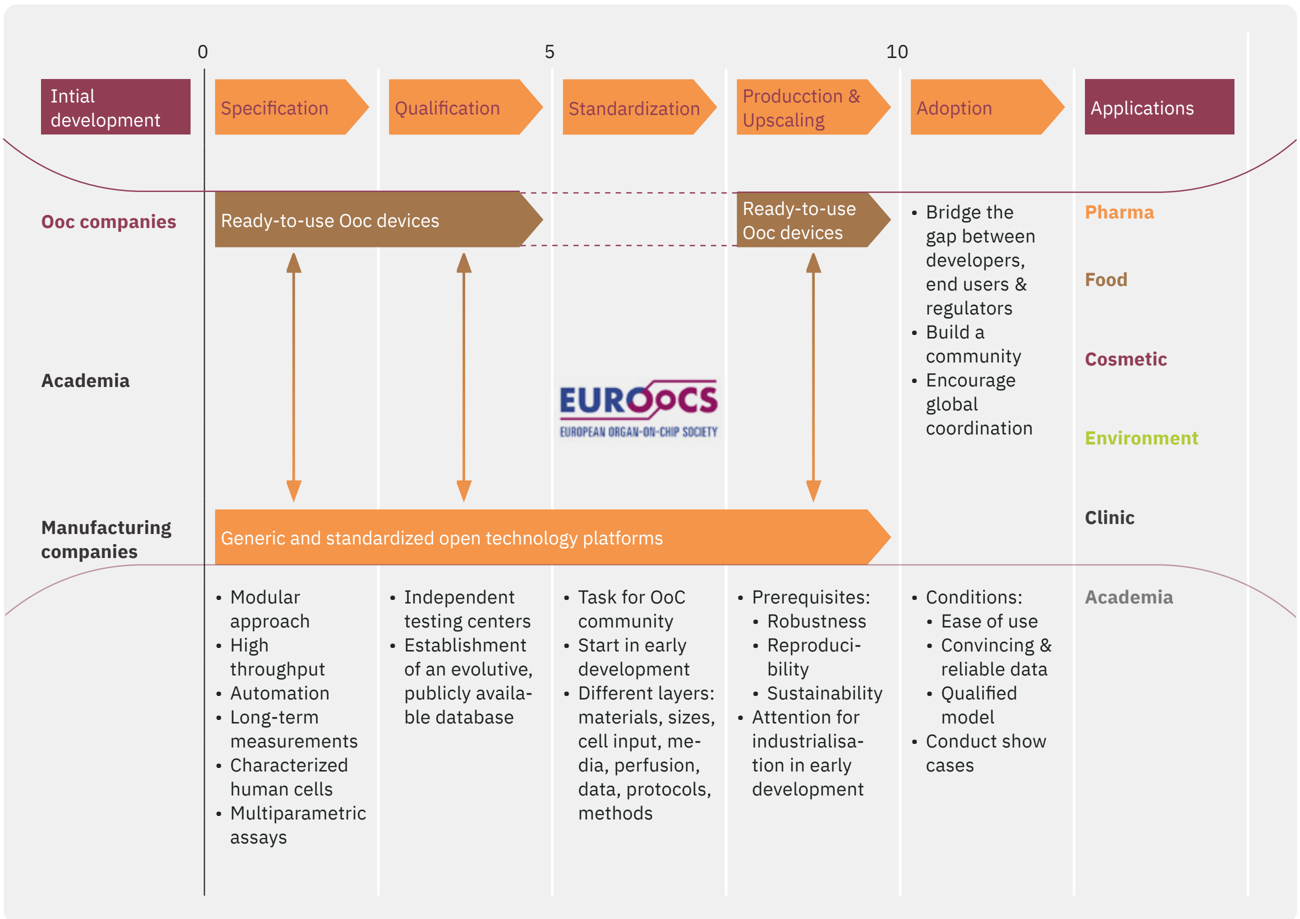
Taken from: da Silva (2022), Organ Chip Research in Europe: Players, Initiatives and Policies

BECKMAN COULTER
Biomek i5
Automated Workstation

Ecosystem opportunities

European ecosystem for Organ-on-Chip
Although Organ-on-Chip technology has been developing over the past 10 years, one point which has caused issues in the translation towards increased commercial applications is the lack of standardisation of the technology. The European Organ-on-Chip Society (EUROoCS), of which hDMT is a member of, published a roadmap towards the standardisation of terminology and elements of OoC systems in the summer of 2024. Building from an earlier publication on the ORCHID roadmap for OoC development, the Netherlands is poised to take a leading role in the road towards standardisation.

EUROoCs Roadmap towards Enabling Organ-on-Chip Commercialisation'

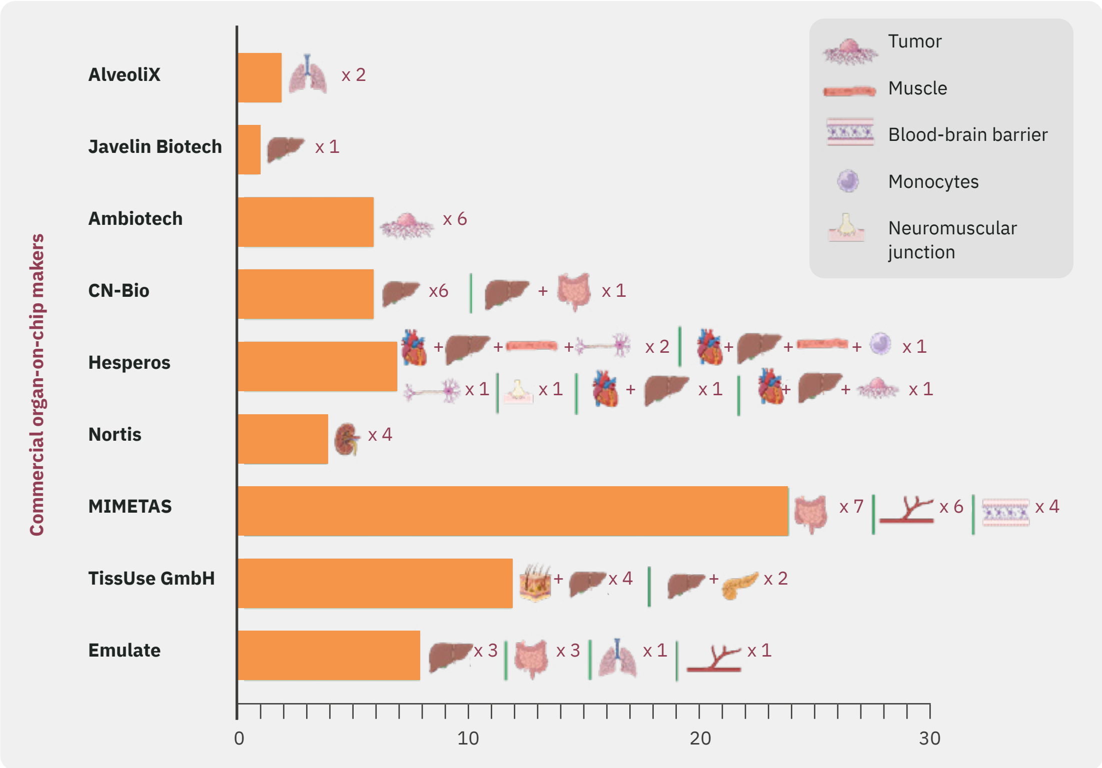


Taken from Mastrangeli (2019) Building Blocks for a European Organ-on-Chip Roadmap

Translating OoC research into commercialisation
Notwithstanding the academic output demonstrated across multiple Dutch universities, the OoC start-up that has been successful in publishing its latest developments is MIMETAS, dwarfing other competitors in the OoC start-up scene.

When looking at multinationals, a growing number of companies are presenting their ongoing work in OoC. Of note, some of the pharmaceutical partnerships are in conjunction with MIMETAS and Hubrecht Institute/HUB Organoids

Multinational end-users of Organ-on-Chip models



Taken from BioPharmaTrend report 'How Industry Embraces Organ-on-Chips: A 2024 Status Report

Multinational end-users of Organ-on-Chip models

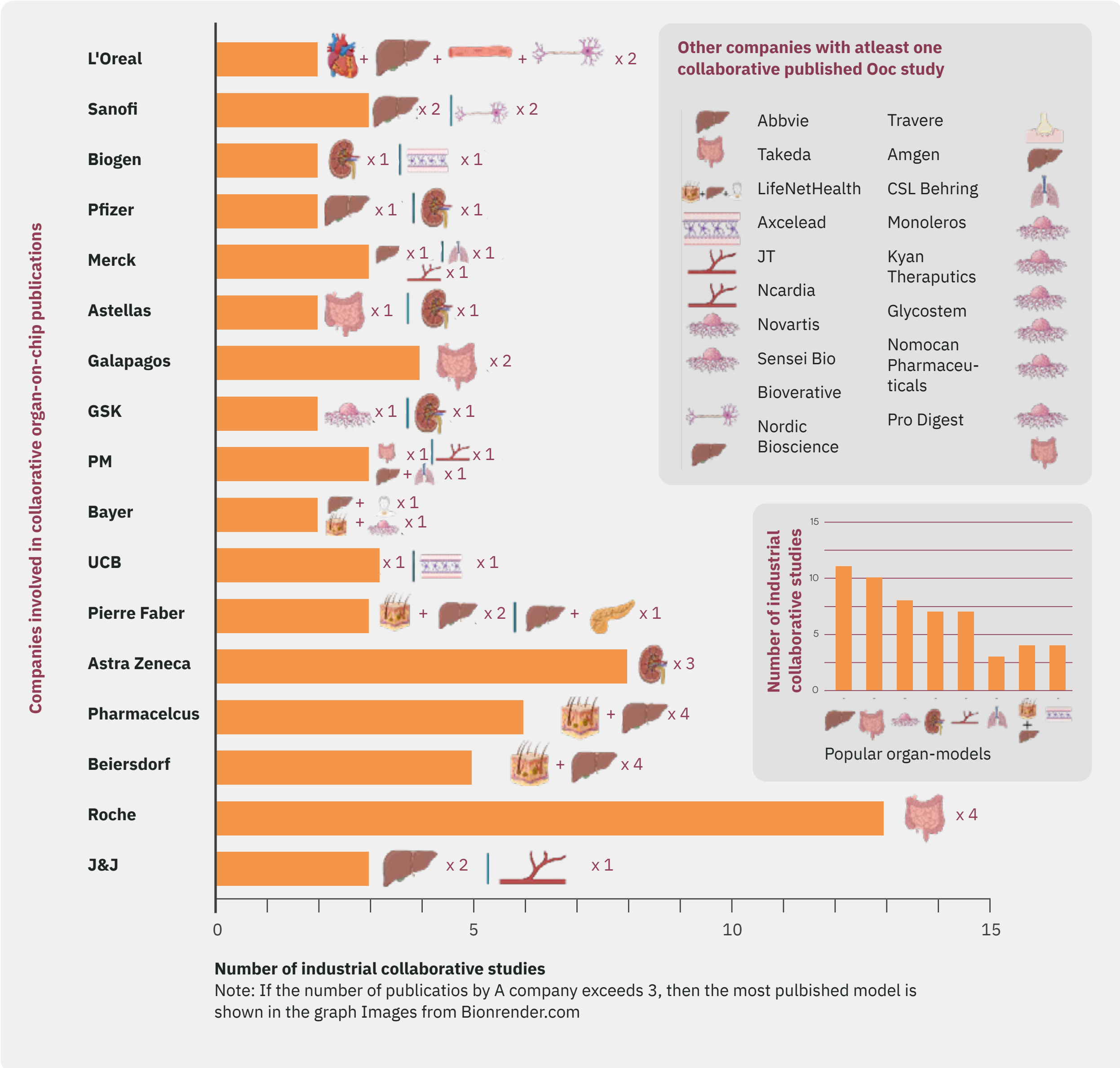


Figure 2. Data from the industry standpoint: Details of the organ-model used by the industries, Taken from BioPharmaTrend report 'How Industry Embraces Organ-on-Chips: A 2024 Status Report


SET1/2

What is the missing the puzzle piece for funding?
When enquiring start-up C-suite on what is missing, funding is always a pressing issue. This also holds true within the start-ups interviewed, with a highlighted focus on the difficulty of addressing the speciality that LoC, OoC and Biosensing technologies fall under. Encompassing multiple technological areas, it presents a challenge on how to present the start-up to investors.

For this report a breakdown of funding in healthcare, within the Therapeutics and MedTech domains in the Netherlands and its comparison to funding in Europe and the US has been outlined. While the report looks to encompass the three technology areas addressed, as most of the companies work within the healthcare space, the funding section highlights the challenges presented in the domains.

As advances in technology have facilitated microfluidic applications to enter the forefront towards commercial applications, a historical breakdown between the two domains is compared.

While this section focuses mainly on fundraising in healthcare domains, the overarching pain point regarding the narrative on fundraising in a multidisciplinary technology remains.

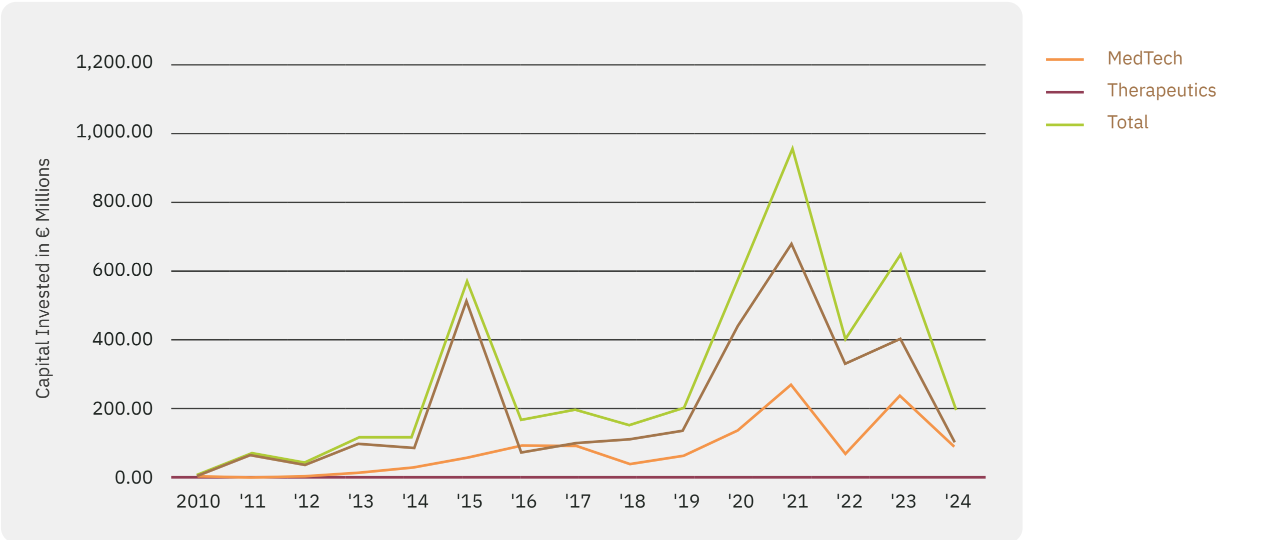
What funders are saying
The technologies presented within the LoC, OoC and Biosensor domains are interesting for the funders interviewed. However, the main issue raised lies in the use case presented to investors. The commercialisation of technologies presents a high hurdle that has not been convincing as of yet. Although technologies are maturing to the point of increased uptake by non-academic users, the scalability of current platform presents a difficult roadmap towards viable commercialisation.

Revenue start-ups are generating is an essential validation marker. More specifically, having repeat clients with increasing commercial project sizes and positive feedback are important to demonstrate the capacity of growth for start-ups in the technology domains. Patent portfolios demonstrate the uniqueness of the technology being developed, future-proofing opportunities for developing their technology into a commercial use case.

Other considerations
It has been highlighted that investing in therapeutics presents a clearer roadmap to exiting, which remains elusive to define a singular roadmap for MedTech. More broadly, as MedTech encompasses multiple technologies, including but not limited to digital health, robotics and telemedicine platform, for start-ups developing LoC and OoC, the broad definition of MedTech presents a challenge as competition of limited funding is .

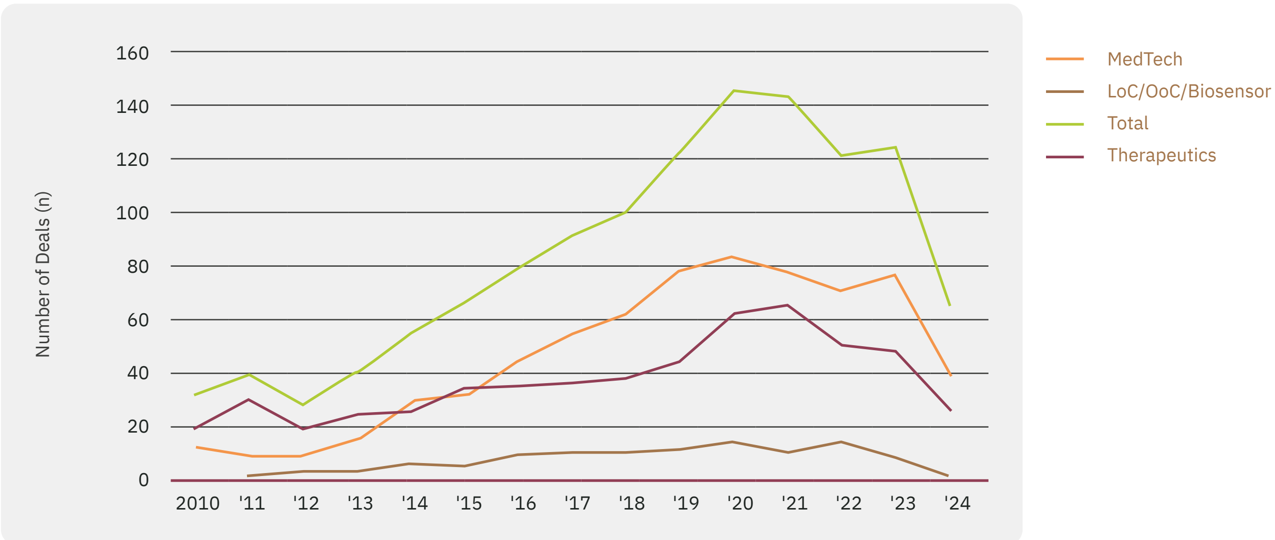
Breaking down capital investments in the Netherlands in Healthcare
Capital invested in therapeutics has almost always exceeded that in Med tech. However, from 2016 onwards, the number of MedTech deals is greater than the number of Therapeutic deals. When comparing the number of deals in the technology domain of this report (i.e. LoC, OoC), the number of deals was increasing steadily until 2022.

Total Capital Invested in NL (€ M)



Data extracted from PitchBook by Invest-NL data team. Note: figures of '24 are not yet complete.

Total Number of Deals in NL (n)



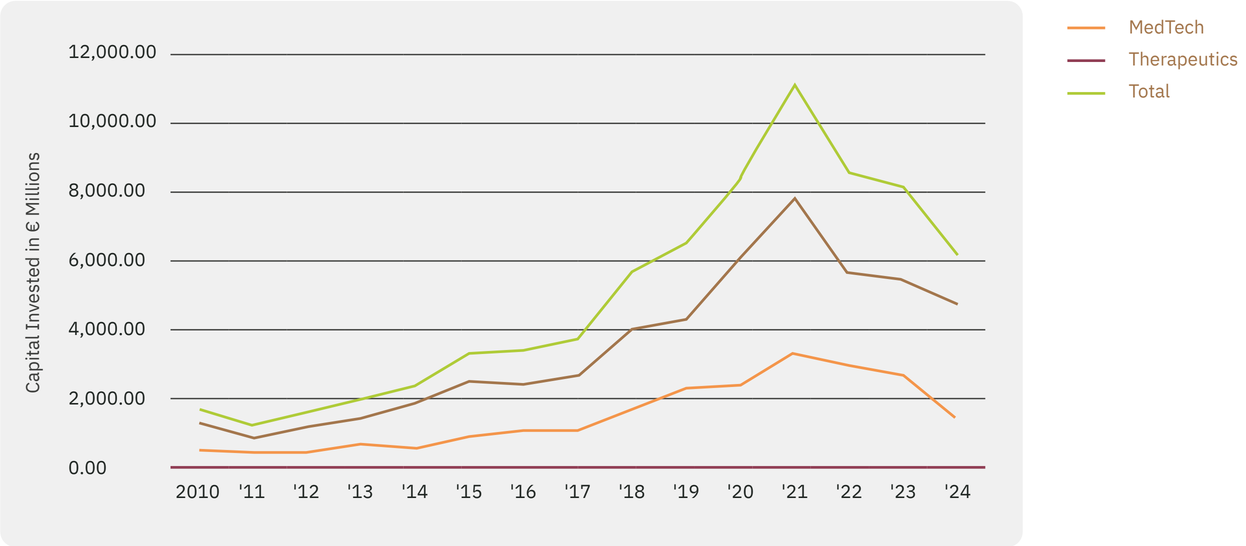
Data extracted from PitchBook by Invest-NL data team. Note: figures of '24 are not yet complete.

How does Healthcare investing fare in the EU and US?

Capital invested in Europe and the United States presents a similar picture, albeit the number of deals and capital invested per deal are greater in the US. When looking at the number of companies within LoC and OoC space in Europe, a health competitive environment can be found across multiple countries (specifically, Germany, France, Switzerland and United Kingdom). However, the gap in funding raised between these companies and those in the US is high. Emulate in the US leads the way with $227 million raised, while InSphero (Switzerland) has raised $35 million in a similar timeframe.

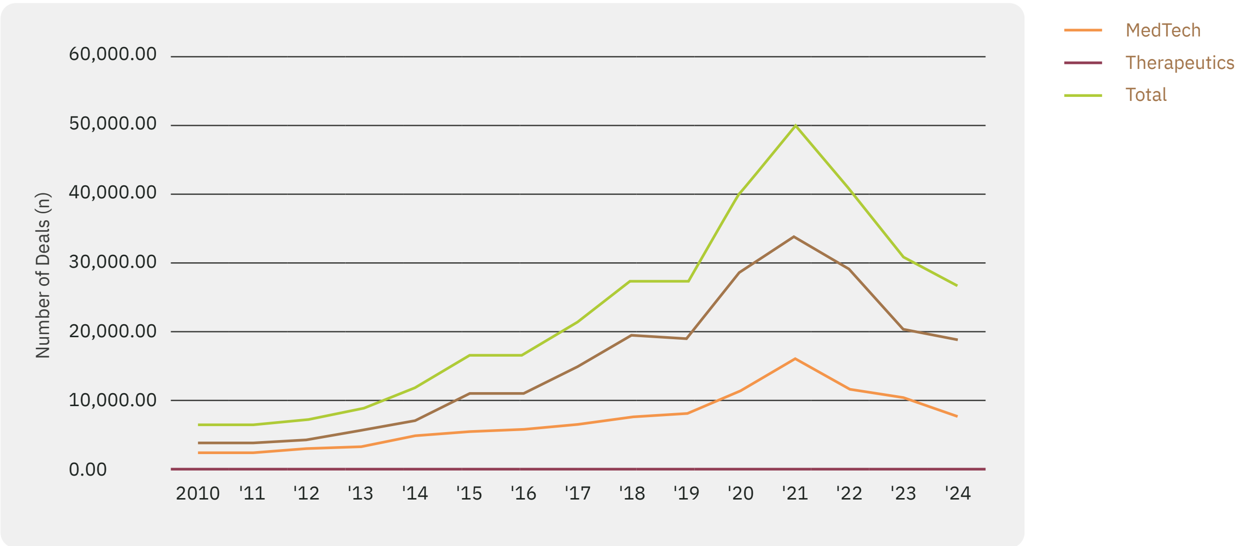
The September 2024 Draghi report on EU competitiveness highlighted the gaps found within the Innovation Landscape in Europe, when compared to the US and China. Specifically highlighting the lack of €100 bn companies starting in the last five decades, the worrying trend of 30% of unicorns leaving the EU-block since 2008 demonstrates the stifling environment start-ups face in Europe. Of the unicorns that left, the reason for leaving was presented as the lack of facility and opportunity to scale-up within the continent.

Total Capital Invested in EU (€ M)



Data extracted from PitchBook by Invest-NL data team

Total Capital Invested in US (€ M)

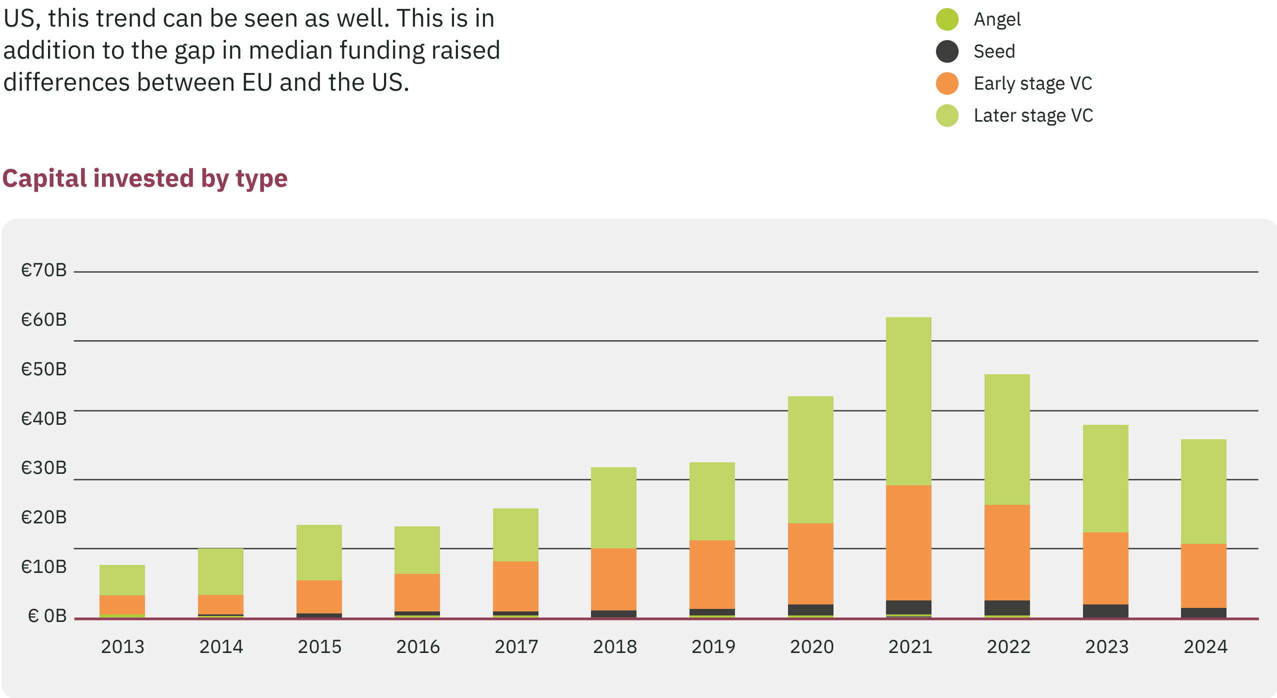


Data extracted from PitchBook by Invest-NL data team

Deal sizes across the years in MedTech
Breaking down the funding raised across MedTech in the Netherlands, an increase has been seen over the years, especially in later stage VC funding (i.e. Series B and onwards). However, when comparing to the deal sizes in Therapeutics, the median funding raised shows smaller ticket deal sizes.

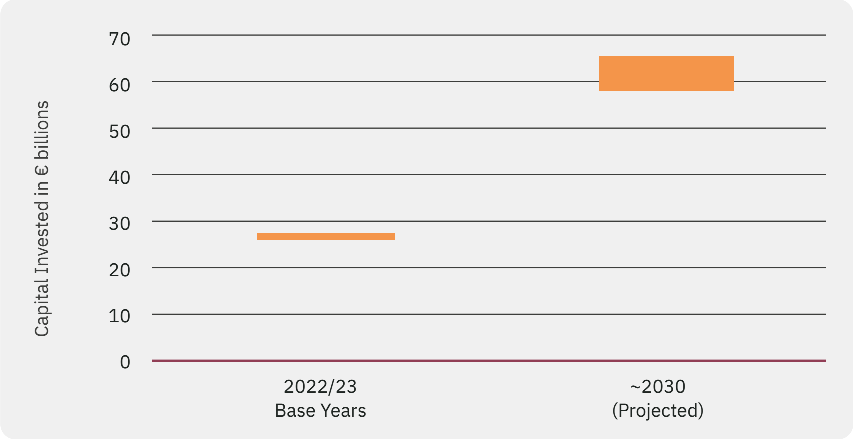
When comparing to deals in the EU and in the US, this trend can be seen as well. This is in addition to the gap in median funding raised differences between EU and the US.

Capital invested by type

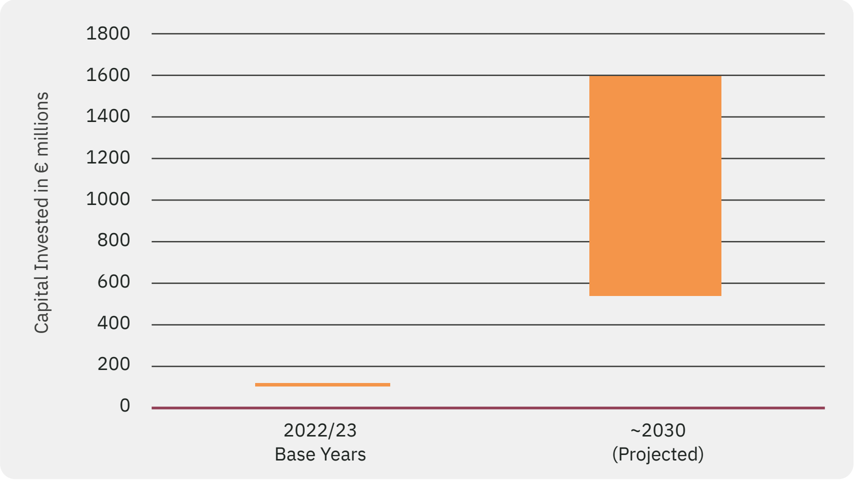


Data extracted from PitchBook by Invest-NL data team

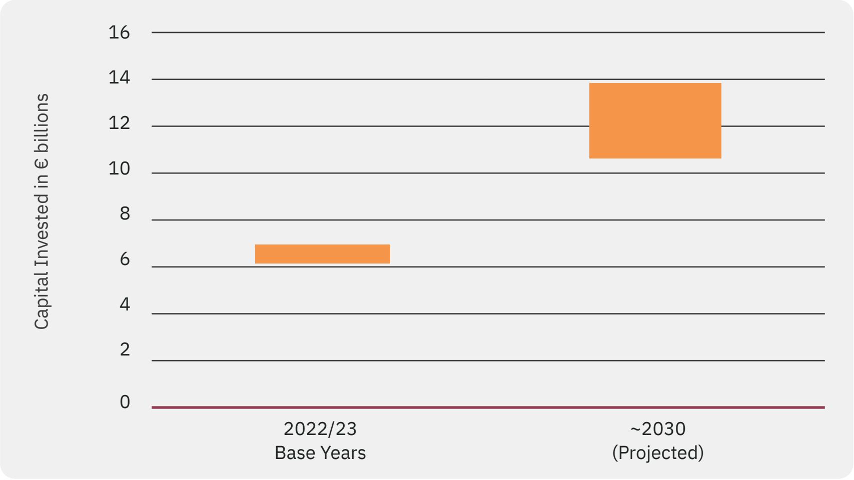
Biosensor Market Size Forecast



Organ-on-Chip Market Size Forecast (2022/23 - 2030)



Lab-on-Chip Market Forecast (2022/23 - 2030)

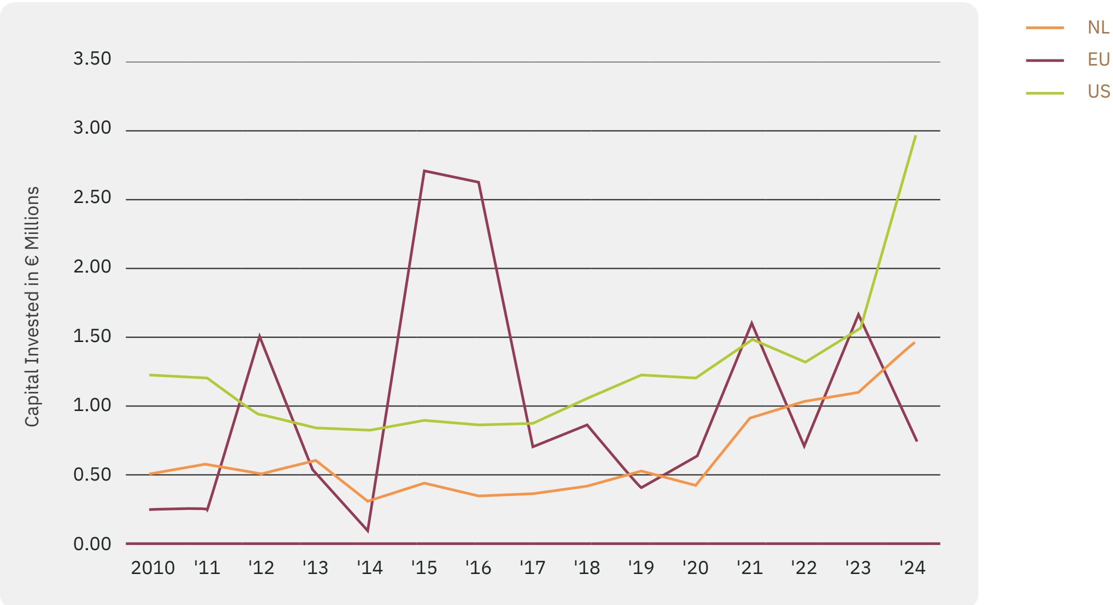


Data extracted from PitchBook by Invest-NL data team

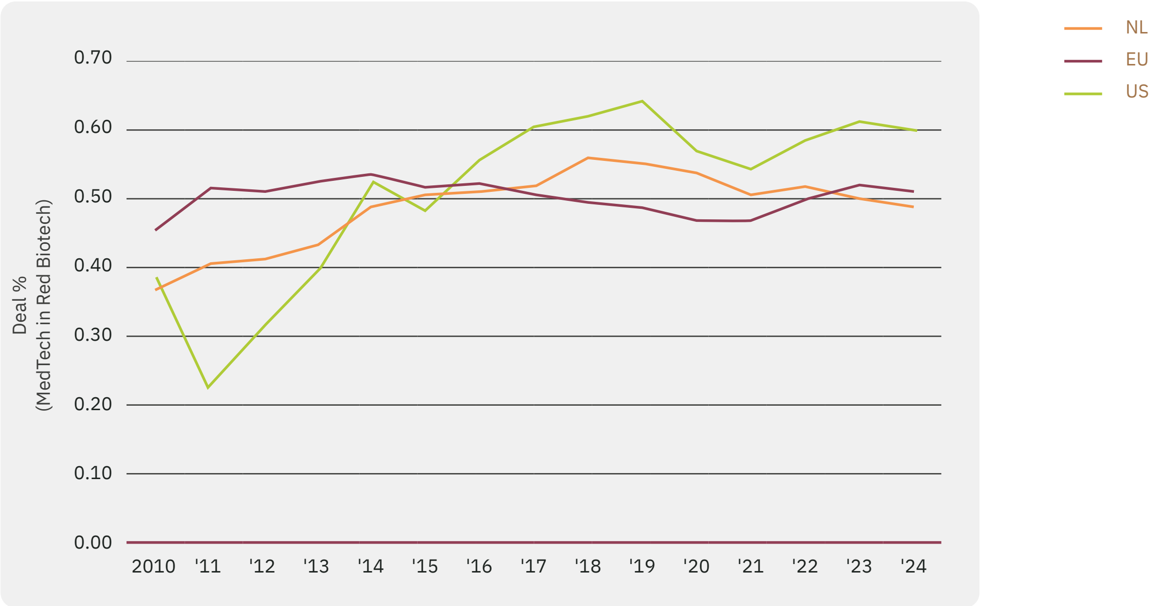
Comparing the Netherlands to Europe and the US

Focusing on MedTech fundraising, the Netherlands demonstrates a higher percentage of deals compared both the EU and the US. Specifically, this trend is seen from 2016 onwards, with MedTech deals floating around 60% of deals within the healthcare domain, with both EU and US at around 50%. Nevertheless, the percentage of MedTech capital invested is similar across the three comparison areas. Hovering around 30% of capital invested, MedTech has remained relatively stable in recent years. Of note, capital investment in the Netherlands presents the greatest fluctuation since 2010. On the other hand, MedTech capital invested presents a downward trend in the US. However, the median ticket size for MedTech deals is higher for the US compared to the Netherlands and EU. This highlights the strategy of start-ups towards incorporating a US focus for commercial strategies to present opportunities for future financing.

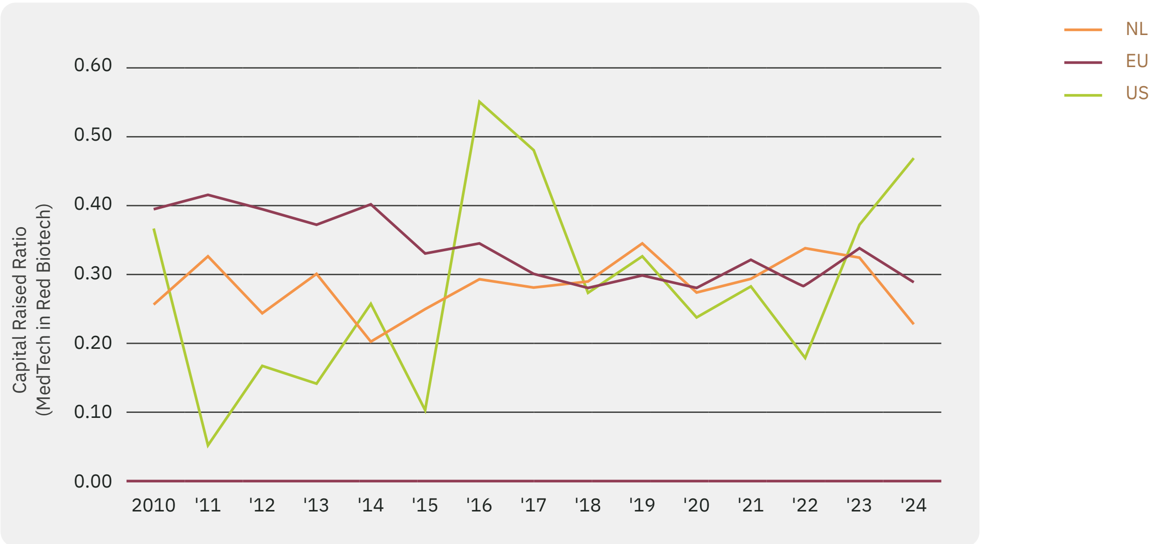
Median Ticket size of MedTech Deals (NL vs EU vs US)



Percentage of MedTech Deals (NL vs EU vs US)



Percentage of MedTech Capital Invested (NL vs EU vs US)



Conclusion

Recommenda-tions and next steps

Courtesy of MIMETAS

Concluding thoughts

The Dutch ecosystem in the LoC, OoC and Biosensor sectors is thriving, and the forecast of commercialising developments can be seen as positive. A clear channel of nurturing innovation in leading academic institutions to developing commercial enterprises through TTO/KTOs is well defined. For up-and-coming start-ups, the early-stage network of incubators, advisors and administrative support to develop the technology towards defining commercial use cases are facilitated. Nevertheless, the innovation gap remains a chasm to be crossed.

Providing financial support

Highlighting differences in the quantity and size of investments between Therapeutics and MedTech, increasing funding opportunities within MedTech would reflect the ongoing developments in the field. A dedicated MedTech fund in the Netherlands has been raised as a point that would address the funding gap faced in start-ups that have secured seed funding and looking at further financing. While it would not address all bottlenecks faced, a MedTech fund would address the issues highlighted by start-ups on the lack of dedicated local funding for larger ticket sizes. This presents an opportunity to future proof the development of these technologies in the Netherlands than losing innovative start-ups in the early stages of development to overseas locations.

This said, MedTech would only encompass start-ups focused on OoC and LoC. With budding start-ups in Biosensors, which does not fall wholly under MedTech, considerations towards the hurdles faced when funding is

Fostering collaboration for sustained growth

Fostering collaboration for sustained growth

With the opportunity for start-ups in this space flourishing, extending support outside the initial start-up phase would facilitate better navigation towards scaling-up. The ecosystem presents a unique opportunity where larger stakeholders, i.e. NXTGEN Hightech, Health~Holland (Project ADOPT), can provide a roadmap to bridge the challenges faced. Through sustained collaboration with these stakeholders, start-ups can leverage strengths of these organisations to solidly the use case for commercial scalability and navigate challenges that hinder growth in start-ups. The recently established BioMicroSystem Innovation Hub between TNO and University of Twente in Enschede is one opportunity of fostering collaboration within this ecosystem. By positioning the Dutch ecosystem as the hub for innovation in LoC, OoC and Biosensor technologies, commercial end-users are better positioned to make decisions on up taking the products.

Strengthening start-up teams

In recent years, focus on educational opportunities within academic settings for budding entrepreneurs to start their own start-ups has increased. As more entrepreneurial courses are offered and incubator programs provide roadmaps on how to establish and develop a start-up, one area that could be strengthened is incorporating commercial experience in founding teams to tailor initial technology development. This enables better alignment and development planning to what end users can readily apply within their development programs. By understanding how a start-up's commercial proposition fits within a larger companies' product development and portfolio, start-ups can avoid circular discussions on how their technology enables improvements to current internal capacities and work to improve towards commercialising their technology.

Investment strategy Invest-NL Deep Tech Fonds

The Invest-NL Deep Tech Fonds aims to strengthen the Deep Tech ecosystem in the Netherlands by co-investing with private investors in Deep Tech start-ups. This scope includes areas such as micro-nanofluidics, biosensing, and nanobiotechnology, which are part of the Netherlands' Key Enabling Technologies (KETs).This study has been conducted to map out the ecosystem in the Netherlands related to these technologies and to formulate an investment strategy for the Deep Tech Fonds. The Deep Tech Fonds is open to investment proposals from technology start-ups in the Netherlands. The Fund co-invests with private and public investors in start-ups deemed attractive based on criteria including:

- **Team, business case, financials** and other elements in a standard due diligence process;
- **Global competitive position**, assessing how state-of-the-art the technology is and the company's ability to maintain or enhance its competitive standing;
- **Impact on the Dutch ecosystem**, considering factors like interdependence with other ecosystem players, number of fte, R&D expenditures, company size, and overall business case;
- **Developing key enabling platform technologies**;
  - Hold a strong IP position;
  - Have an extended timeline to reach their intended market;
  - Require substantial capital, often tens of millions, to reach commercialization.


3-LANE 64
MIMETAS

Courtesy of QuiX Quantum

Afterword

This report was undertaken to determine the maturity of technologies falling under the Key Enabling Technology field of nanotechnology. Specifically focusing within bionanotechnology and microfluidic applications, the time I spent discussing with the Invest-NL Deep Tech Fund team on how to shape this report was most illuminating.

Due to the overlapping nature of the terminology used over the years and current terminology encompassing multiple technologies, it was an interesting jigsaw puzzle to put together this report. Nevertheless, the culmination of hours of literature reading and countless interviews have been compiled into this report. It always brings great enthusiasm to see a diverse network of stakeholders, all of whom hold different pieces of the puzzle, coming together and culminate in a concerto of technological innovation. While the report ended up focusing more on Organ-on-Chip and growth in red biotech, the opportunities that lie across the other technologies and biotech domains is not to be dismissed.

I hope the reader finds just cause to understand that for innovation in the field of Lab-on-Chip, Organ-on-Chip and Biosensor technologies to flourish, a melting pot of innovators, network support and patience is required. As the saying goes, Rome was not built in a day, the ongoing developments within the field in the Netherlands has borne fruit and commercial users are more readily becoming believers in the technology.

Many thanks for taking the time to read this Deep Dive on Lab-on-Chip.

It was my pleasure to work with the sharp minds at Invest-NL and interview the brilliant innovators across the Netherlands and their supporters.

Taichi Ochi
taichi@spasianbio.com

Copyright & disclaimer

We thank Databridge, Future Market Insights, Global Market Insights, Market Data Forecast, Nova1Advisor, Markets and Markets, Allied Market Research, Massimo Mastrangeli, Renan da Silva, BioPharma Trend, and PitchBook data extracted by the Invest-NL Data team for allowing to use some of their reports’ graphs (accredited on the respective pages).

Deep Tech Fonds, Invest-NL
www.invest-nl.nl
Kingsfordweg 43-117
1043 GP Amsterdam