



Additive Manufacturing of 3D Microfluidic MEMS for Labon-a-Chip applications

www.m3dloc.eu

M3DLoC Project Open Day 2020

Final Report

V1.0

Date: 23rd January 2020

Venue: Crowne Plaza Hotel - Le Palace Rue Gineste 3. 1210 Brussels. Belgium



























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Abstract

Cambridge Nanomaterials Technology Ltd (CNAT) as leader of work package 8 was responsible for organising the 1st Open Day Workshop. The 1st Open Day Workshop event was held on the 23rd January 2020 at the Crowne Plaza Hotel, Rue Gineste 3, 1210 Brussels, Belgium.

The aim of this workshop was to bring together experts, developers and end-users, to discuss exciting new developments in the project and in the field of microfluidic biomedical devices, development of 3D printing equipment and use of nanomaterials such as graphene for 3D printing applications. The workshop was a unique occasion for networking, related EC project clustering and enhancement of exploitation opportunities.

Participants of the M3DLoC Open Day 2020 Workshop and Exhibition were senior members coming from leading bio-medical and healthcare organisations such as: GSK, GE Healthcare (Whatman), Viscofan, Fluigent, Keralty among others. Fluigent is coordinator of the HoliFAB project with a similar aim and the meeting was an opportunity for discussion of project clustering.

Introduction

The 1st Project Open Day Workshop and Exhibition took place on the 23rd January 2020 at the Crowne Plaza Hotel (Rue Gineste 3, Brussels, 1210 Belgium). This hotel was chosen for its excellent location and great rooms for the conference and exhibition. The conference and exhibition rooms were located in the 8th floor, which was exclusively for the use and access of participants to the M3DLoC Open Day.







Information on the M3DLoC Project Open Day 2020 Workshop and Exhibition was published on the project website, on 3 different pages, where the announcement, registration form and preliminary agenda were available for downloading.

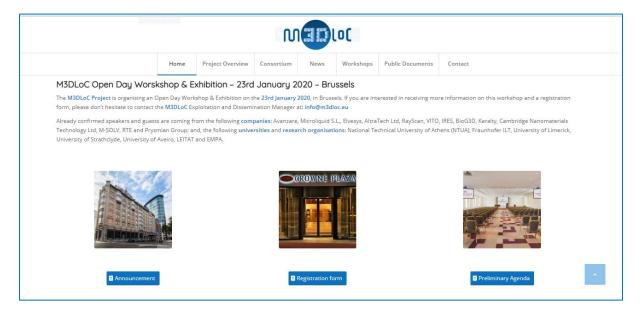






Fig 5 Home Page

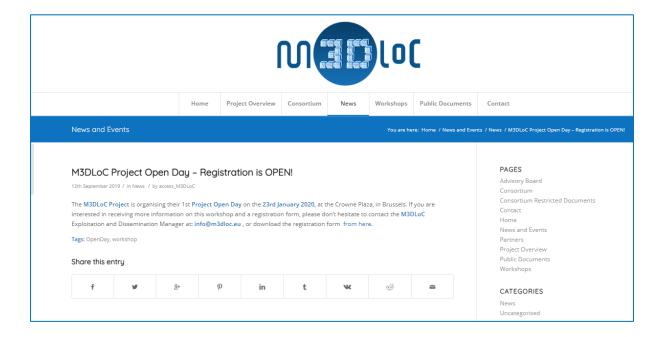


Fig 6 News Page



Fig 7 Workshops Page

An extensive mapping of the relevant stakeholders was conducted by CNAT, this included an extensive email campaign to invite relevant external delegates. Individual email invitations were sent to mapped stakeholders, in addition to relevant CNAT contacts who were also invited by individual addressed mails. M3DLoC Project partners were also encouraged to promote the event among their contacts.

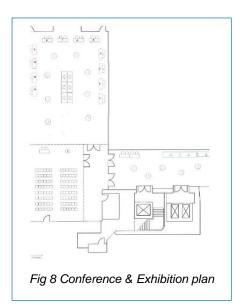




A preliminary agenda with participating organisations was prepared and circulated to all M3DLoC Partners, prior to send it to all Open Day participants. This agenda was also uploaded to the project website and has been regularly updated.



Fig 7 Preliminary Agenda sent to external delegates



M3DLoC Partners were given the opportunity to have an exhibition stand at the Open Day. Partners who expressed interest, were allocated a desk according with their specific requirements in the Vision Room. Poster displays and extra power sockets were requested to the venue, in order to cater to those who needed.

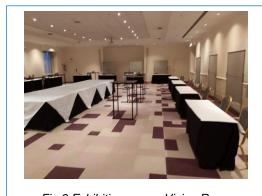


Fig 9 Exhibition area - Vision Room





Fig 10 Foyer- Reception area – Fig 11 Clarity Room (Conference)





M3DLoC Open Day 2020 - Agenda

The agenda below was distributed electronically and printed for all delegates attending the Open Day Workshop, ahead to the meeting.

08:30 Exhibition set-up

09:30 Participants arrival and registration (coffee and refreshments)

09:45 Welcome and M3DLoC Open Day Introduction

Dr Bojan Boskovic, Managing Director, Cambridge Nanomaterials Technology Ltd (CNT), UK **M3DLoC** Open Day 2020 Organiser

Prof. Costas A. Charitidis, M3DLoC Project Coordinator, NTUA, Greece

10:00 Overview of the n-M3DLoC Project

Prof. Costas A. Charitidis, M3DLoC Project Coordinator, NTUA, Greece

10:30 Dr Julio Gomez Cordon, Avanzare Innovacion Tecnologica S.L. Spain

Title: Graphene inks for Inject Printing

Graphene inks for inject printing have been develop in M3DLOC project. The low viscosity and high conductivity obtain, open a new field of application in the printing of flexible electronics. New graphene materials and Graphene/PLA masterbatchs for Fuse Filamentent 3D printing have been develop and prepared.

10:45 Dr.-Ing. Michael Krumm, RayScan Technologies GmbH, Germany

Title: X-ray CT Systems for a Wide Range of Industrial and Scientific Applications

RayScan is a leading CT-manufacturing company, facing technical challenges, partly in form of system specific innovations, partly in first-time accomplishment of completely new applications and evaluation of specifically designed systems and testing concepts. RayScan is a private owned company in Germany. The latest developments are RayScan systems for industrial cone beam tomography (3DCT) and fan beam tomography (2DCT) of outstanding performance. RayScan has been the first X-ray CT (XCT) system developer using high precision granite manipulators as used by CMMs. Its specialty is the high level of system integration and optimization supported by its own hardware and software development department. Besides XCT systems, radioscopic systems and automatic analysis software for fully automatic manufacturing control have been developed. Several times RayScan has proven its ability to develop specialized XCT systems which solve completely new demands. Outstanding successes are the mobile XCT system for inspection of the closed accelerator ring LHC at CERN in 2008, the successful design and implementation of the NanoXCT scanner in 2015, as well as the development of the RoboTom system. With regard to the project, RayScan has allocated specialists who have in total more than 100 years of experience in development of advanced X-ray inspection systems and computed tomography.

11:00 Coffee break and exhibition

11:30 Dr Noémi Thomazo, Elvesys – Microfluidic Innovation Center, France

Title: Elvesys - Microfluidic Innovation Center





Elvesys is an innovative French company dedicated to microfluidic instrumentation and flow control. In this presentation, we will present the company, its mission and its range of product. We will also introduce the research activities of the company, mostly based on its involvement in collaborative European research projects. The general fields of applications of microfluidics and some of our outgoing projects will be presented.

11:45 Dionysios Tsimourtos, BioG3D – New 3D printing Technologies, Greece

Title: Advanced 3D Printing Technologies and Smart Composite Materials towards Personalised Fabrication

3D printing technologies represents a significant breakthrough in an era of customized fabrication and could allow shifting of production and distribution processes closer to consumers. Indeed, by exploiting possibilities of 3D printing systems, personalised on demand fabrication could be achieved, designed to cover the specific requirements of each application in many industrial fields. When combined with the development of advanced smart materials, they undeniably consist one of the main driving forces of the transition from traditional manufacturing routes to the era of personalized innovative solutions. 3D printing technologies has begun to embrace the range of sizes and materials that appeal to the developers and reflect the recent advances in polymer-based systems, where no etching or dissolution processing is required and are thus more environmentally friendly and economically efficient. This indicates that in the near future, many industrial products will move away from the conventional raw materials and use polymers as due to the wide range of low-cost polymeric materials available on the market and their highly adjustable physicochemical characteristics, which can be tailored to address the specific needs of different applications. Additionally, 3D printing can be combined with Generative design to enhance the development of personalized products with advanced functionalities and complex geometries.

12:00 Georgios Gkoulionis, NTUA-AMDC - Lavrion Technological and Cultural Park, Greece

Title: Lavrion Technological and Cultural Park and its Work

The aim of this presentation is to show the history of Lavrion Technological and Cultural Park and to bridge the old times with the present activities. In addition, it highlights the role of Science Parks and they are also presented the ongoing projects that take place in LTCP.

12:15 Dr Elias P. Koumoulos, IRES, Belgium

Title: 3D Printed Lab-on-a-chip Diagnostic Systems - Developing a Safe-by-Design Manufacturing Approach

The aim of this study is to provide a detailed strategy for Safe-by-Design (SbD) 3D printed labon-a-chip (LOC) device manufacturing, using Fused Filament Fabrication (FFF) technology. At first, the applicability of FFF in lab-on-a-chip device development is briefly discussed. Subsequently, a methodology to categorize, identify and implement SbD measures for FFF is suggested. Furthermore, the most crucial health risks involved in FFF processes are examined, placing the focus on the examination of ultrafine particle (UFP) and Volatile Organic Compound (VOC) emission hazards. Thus, a SbD scheme for lab-on-a-chip manufacturing is provided, while also taking into account process optimization for obtaining satisfactory printed LOC quality. This work can serve as a guideline for the effective application of FFF technology for lab-on-a-chip manufacturing through the safest applicable way, towards a continuous effort to support sustainable development of lab-on-a-chip devices through cost-effective means.

12:30 Dr Stefanos Koutsoumpis, National Technical University of Athens, Greece





Title: Multi-Material Additive Manufacturing of Microfluidic BioMEMS for Lab-on-Chip Applications: Challenges and Future Perspectives

Due to its capability of manipulating extremely small quantities of liquids, microfluidics technology has been widely employed in biochemical analysis in the past decades. Many of the current challenges in realising the full potential of BioMEMS devices require a paradigm shift in multi-scale and multi-material integration in a single process. From the first generation of inorganic glass, silicon and ceramics microfluidic devices, fabricated using techniques adapted from the microelectronics industry, to diversely competitive polymers and multi-material Additive Manufacturing (AM), the emerging materials and microfabrication processes dedicated to the next generation of microfluidic biosensors is a key enabler for scalable, low-cost production while maintaining good reproducibility and performance. We present an overview of a modular, hybrid manufacturing process and tailored materials developed within H2020 project M3DLoC and their application in the fabrication of polymeric microstructured devices for point-of-care testing.

12:45 Dr Lluis Quintana Frigola, Viscofan BioEngineering, Germany – Guest Speaker

Title: Development and industrial-scale production of novel collagen biomatrices

An introduction to the Viscofan BioEngineering, a business unit of Naturin Viscofan GmbH – a company of the Viscofan group, would be given. The company applies partly proprietary technologies and standardized extraction methods to process collagen from bovine skin for the development and industrial-scale production of novel collagen biomatrices in research, medical and food grade. The combination of premium products with an exceptional scientific support positions Viscofan BioEngineering at the forefront of regenerative medicine.

13:00 Lunch, exhibition & networking (Vision Room)

14:30 Mike Szymonikm, VITO, Belgium

Title: Design and Testing of Integrated Microfluidic Devices for the Detection of Oncogene Mutations from Liquid Biopsy

Development of lab-on-a-chip diagnostic devices presents a number of complex manufacturing challenges. To address these, the M3DLoC consortium is developing a hybrid manufacturing process, combining extrusion-based additive manufacturing and inkjet printing with micromachining and laser processing in an integrated, modular pilot line, with advanced in-line monitoring techniques. Using this process, we present the design and testing of integrated microfluidic devices for the detection of oncogene mutations from liquid biopsy. Liquid biopsy samples are of great clinical value for minimally-invasive monitoring of cancer, but present a particular challenge for mutation detection as they contain a minority of tumour-derived mutated DNA within a large background of DNA from healthy tissue. We focus on mutations in the EGFR gene which are of interest in the treatment of non-small cell lung cancer. To detect such lowabundant mutations using a surface hybridization-based approach, we designed optimal recognition probes using a theoretical framework and microarray experiments, enabling the detection of single-nucleotide polymorphisms at a level below 0.1% of the total DNA. To reduce device costs and complexity we demonstrated the performance of the isothermal recombinase polymerase amplification (RPA) technique within a prototype microfluidic device. This approach showed rapid, high-yield amplification even with low copy number DNA samples. The low reaction temperature allows for simpler hardware, decreased power draw and enables the use of materials not compatible with traditional PCR approaches.

14:45 Patrick Gretzki, Fraunhofer ILT, Germany





Title: Process Development and System Requirements for Small Scale Structuring and Functionalization of PLA Substrates

15:00 Coffee break & exhibition

15:15 Dr Wenlong Chang, University of Strathclyde, UK

Title: High precision machining process for Freeform and Micro/Nano Structured Surfaces by self-developing a compact ultra-precision hybrid micro-machine

High precision miniature and micro products which possess 3D complex structures or free-form surfaces are now widely used in industries. These micro products are usually fabricated by several machining processes in order to apply for various materials such as hard-to-machine steel and ceramic etc. The integration of these machining processes onto one machine becomes necessary since this will help reduce realignment errors and also increase the machining efficiency. In this research, an ultra-precision hybrid micro-machine which is capable of micro milling, micro grinding, micro turning, laser machining and laser assisted micro-machining has been designed and commissioned. This hybrid micro-machine can manufacture microfluidic devices, superhydrophobic surface, Fresnel lens, micro lens, and any customised micro-products in various materials.

15:30 Tim Cummins, AltraTech Ltd, Ireland

Title: DNA & RNA Detection: Electrochemical \leftrightarrow Capacitive. CMOS Semiconductor \leftrightarrow 3D-Printed.

This presentation will give an overview of emerging Electrochemical and Capacitive methods for DNA & RNA detection. These electronic methods are smaller and more compact than optical detectors which currently dominate the market. The Electrochemical Detection (ECD) readers developed in M3DLoC will be described, including their advanced CV, EIS & BiPot modes. Capacitance-versus-beads data for AltraTech's CMOS semiconductor capacitive bead detector will be presented. These will be compared with results from M3DLoC 3D-printed PLA prototypes with ink-printed electrodes.

15:45 Dr Martin Hajnsek, Joanneum Research, Austria

Title: Sensor Technologies for Special Applications in Point of Care Testing

16:00 Dr Gabriel Leen, PolyPico Technologies Ltd. Ireland

Title: Printing Materials with PolyPico Technology

Printed deposition of functional or biological materials enables the realisation of many existing and novel devices. Printable inks are non-trivial complex engineered fluids with properties which must both fit within the operational envelope of the print technology used and fulfil the requirements of the application at hand. A high-level overview will be provided in regard to designing inks and brief discussion of the inks designed for the M3DLoC project will be provided.

16:15 Dr Ehtsham-Ul Haq, University of Limerick, Ireland

Title: Metrology, the science and act of measuring

Metrology, the science and act of measuring, is required not only from a technological confidence point of view but is also a market requirement and would become a legal and financial requirement for the products that would be sold in the market. The measurement or characterization of functional, dimensional, structural, mechanical and physico-chemical properties of the 3D printed devices and its constituent materials underpins process





optimization, inspection and monitoring, and product quality assurance. While 3D printing can make some very complex and unconventional shapes and structures by additive manufacturing, a robust quality assurance scheme still alludes manufacturers due to the lack of availability of appropriate and enough tools, methodologies and characterization expertise. Such characterization or metrology can be in line, on line and off line. Currently the primary focus of characterization is on the functionality and dimensional tolerances of the manufactured device or product. It is however also important to control and optimize a manufacturing process especially for its primary and secondary raw materials. The success of 3D printing in creating shapes and structures into useful products depend on how firmly one can assure that properties in the desired shape or structure actually meet certain accepted, pre-defined standards as well as the cost of production remains competitive. Thus characterisation of materials, surface and interface properties is a Key Enabling Technology for MEDLOC in realising its goal to use existing pilot lines for a complete manufacturing process of microfluidics devices combining inkiet 3D printing, fused filament fabrication (FFF) technologies and laser processing strongly underpinned by innovative thermoplastic nanocomposite and carbon-based inks. University of Limerick team is using the combination of state of the art and custom-made characterisation tools, methodologies and expertise that are unique and provide a critical strength for both offline and on-line measurement capability towards polymer based 3D printed devices. The custom-developed systems (IR nanoscope and microscope, CARS and confocal Optical Birefringence (c-OBF)) are truly ground breaking and provides UL the unique capability to combine high-resolution chemical, structural and optical imaging at the ambient. Of particular importance is the c-OBF technique, which UL has recently constructed for high throughput nondestructive imaging for both lateral and depth imaging. The robust open construction of this imaging facility enables integrating this with commercial deposition and printing systems for on line 3D monitoring of defects.

16:30 Dr Adam Brunton, M-Solv, UK

Title: "Development of 3D printing robots for scale-up and pilot production "

16:45 Angel Del Pozo, Research Institute @Keralty, Spain - Guest Speaker

Title: Open Innovation Test Beds for Medical Technologies: SAFE-N-MEDTECH Project

Society and clinical practice pose a growing demand on novel biomaterials, ICT, micro and nanotechnologies for innovative medical devices and in vitro diagnostics (Medical Technologies-MTs). In order to balance between the rapid development of innovative MTs and the safety and/or efficacy aspects, the new EU Medical Device Regulation was published in May of 2017, addressing, among other, issues, patient safety and the use of nanomaterials in medical devices. This changing framework has opened a multiple challenge for the Medtech Industry, R&D institutions, public administrations and healthcare providers, including the need of standardised methodology, equipment and facilities for up-scaled production, characterization, testing, clinical validation and certification, as well as business development of novel medical materials and devices. To address the existing challenges (characterization, production, preclinical and clinical research, market access, business development), the SAFE-N-MEDTECH consortium aims to bring a strong cooperation to compete in the market for a coordinated OITB for nano-enabled MTs. SAFE-N-MEDTECH will build an innovative open access platform to offer to companies and reference laboratories the capabilities, knowhow, networks and services required for the development, testing, assessment, upscaling and market exploitation of nanotechnology-based Medical and Diagnosis Devices. This OITB will offer a multidisciplinary and market oriented innovative approach to SME's, Healthcare providers and Industries for the translation to the market of MTs, based on a deep understanding and knowledge of the material-nano-properties, their advanced use and applications in MTs and any other aspects involved in MTs safety

17:00 End of workshop





M3DLoC Open Day 2020 Workshop - External Participating Organisations

GSK Vaccines

Web: www.gsk.com



GSK Vaccines are a science-led global healthcare company with a special purpose: to help people do more, feel better, live longer. We have 3 global businesses that research, develop and manufacture innovative pharmaceutical medicines, vaccines and consumer healthcare products. Our goal is to be one of the world's most innovative, best performing and trusted healthcare companies.

Our values and expectations are at the heart of everything we do and help define our culture - so that together we can deliver extraordinary things for our patients and consumers and make GSK a brilliant place to work. Our values are Patient focus, Transparency, Respect, Integrity. Our expectations are Courage, Accountability, Development, Teamwork.

Fluigent

Web: www.fluigent.com



Fluigent is an international company which develops, manufactures and supports the most advanced microfluidic systems available. Whether your application is with droplets, cell biology, particle studies, or in other research areas, we have the expertise and knowledge to provide the most cost effective and technically advanced solutions to your fluid control needs.

Whatman - GE Healthcare Life Sciences

Web: www.gelifesciences.com/whatman



Whatman is a **GE Healthcare Life Sciences** brand specialising in laboratory filtration products and separation technologies. Whatman products cover a range of laboratory applications that require filtration, sample collection (cards and kits), blotting, lateral flow components and flow-through assays and other general laboratory accessories.

Viscofan

Web: www.viscofan.com



Viscofan, founded in 1975, is the global leader in the casing market with a market share of the 33% of the global market. Our headquarters are located in Spain. We are selling in more than 100 countries and manufacturing in 14 sites worldwide with 4.600 people. Viscofan is the only company offering casings out of the main technologies available: cellulose, collagen, vegetable, fibrous and plastic casings. As a result of our Diversification strategy, we have a business unit of Bioengineering located in our center of excellence for collagen products within the Viscofan group in Weinheim (Germany). We process collagen to obtain R&D and food grade products in different formats such as custom-tailored membranes, bio tubes, or as collagen suspension (Viscolma) and others (sponges, gels, etc). We have invested in our GMP plant to manufacture our collagen products in medical grade for biomedical applications





Viscofan BioEngineering

Web: www.viscofan-bioengineering.com



Viscofan BioEngineering is a business unit of Naturin Viscofan GmbH – a company of the Viscofan group. The modern production facilities including a plant for medical grade production are located in Weinheim, Germany. A dedicated international team covers the complete value chain from research to development and sales of novel collagen products. Naturin Viscofan is the center of excellence for collagen products within the Viscofan group. We apply partly proprietary technologies and standardized extraction methods to process collagen from bovine skin for the development and industrial-scale production of novel collagen biomatrices in research, medical and food grade. The combination of premium products with an exceptional scientific support positions Viscofan BioEngineering at the forefront of regenerative.

Keralty

Web: https://www.keralty.com/en/about-keralty



We are a value focused health company consisting of health insurance, health services and hospital and provider health care delivery organizations. **Keralty** also has educational institutions and socially focused companies that complete the "world of health" that we are offering society. We are a group committed to the health of our members, keeping them healthy, focusing on prevention and the identification and management of health risks and diseases. We are leaders in comprehensive health services in the countries where we are present, being recognized for our humane, scientific, technical and ethical focus.

Prysmian Group

Prysmian Group

LINKING THE FUTURE

Web: www.prysmiangroup.com

Prysmian Group is world leader in the energy and telecom cables and systems industry. With nearly 140 years of experience, sales of over €7.5 billion in 2016, 21,000 employees across 50 countries and 82 plants, the Group is strongly positioned in high-tech markets and offers the widest possible range of products, services, technologies and know-how. It operates in the businesses of underground and submarine cables and systems for power transmission and distribution, of special cables for applications in many different industries and of medium and low voltage cables for the construction and infrastructure sectors. For the telecommunications industry, the Group manufactures cables and accessories for voice, video and data transmission, offering a comprehensive range of optical fibres, optical and copper cables and connectivity systems. Prysmian is a public company, listed on the Italian Stock Exchange in the FTSE MIB index.

enablingMNT Group

Microfluidic Association

enabling MNT micro nano technology

Web: enablingmnt.com

enablingMNT group provides industry, research organisations and government agencies with technical and business support in the field of microengineering and nanoelectronics. enablingMNT has expertise in market studies & business development, collaborative project management, funding strategies & proposal development, congress organisation, test & reliability engineering, standardisation, and both operational & supply chain management. We are a proud member of the Microfluidic Association. The Microfluidics Association (MFA) exists to encourage the development, coordination, and dissemination of engineering knowledge as well as market and technical information





on microfluidics. It provides industry stewardship and engages industrial, academic and government stakeholders to advance the interests of the global Microfluidics Industry Supply Chain.

Ampashield NV

Web: www.ampashield.com

AMPASHIELD®

Ampashield is a Joint Venture Company between Aurubis Belgium NV/SA and Cametics Ltd specialized in nano-carbon enabled coating solutions. Cametics is an R&D enterprise born out of the University of Cambridge. It was founded in 2014 by Prof. Krzysztof Koziol and Dr Marek Burda with the mission of bringing to the market innovative solutions in the field of advanced materials, such as nano carbons, metals and polymers. Aurubis is part of a leading global copper group, engaged in the business of producing high purity, high quality copper from copper concentrates and recycling materials, destined for various industrial applications. Initial contact and collaboration between Cametics founders and Aurubis has been established in the FP7 UltraWire project funded by European Commission to develop novel nanocarbon- copper conductors, and has been followed further after the end of the project. A collaboration of Cametics and Aurubis was formed to bring the great ability of nanomaterials to the copper market. The expertise of Cametics in the field of carbon nanomaterials and Aurubis' speciality in copper products led to a productive scientific research and development project.

Annexes

Photos exhibition



Fig 11 & 12 M3DLoC Open Day 2020 Exhibition







Fig 13 & 14 Discussions at AltraTech exhibition desk with M3DLoC Partners & GSK and Fluigent





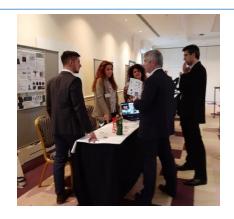


Fig 15 Viscofan at Bio3DG exhibition desk



Fig 16 Elvesys exhibition desk





Fig 17 & 18 Prysmian Group at PolyPico exhibition desk



Fig 19 Prysmian Group at Joanneum exhibition desk



Fig 20 Discussion: Fraunhofer, Viscofan, Fluigent









Fig 21 GE Healthcare at Elvesys exhibition desk

Fig 22 University of Strathclyde exhibition desk





Fig 23 GSK at Rayscan exhibition desk

Fig 24 Fluidgent at AltraTech exhibition desk



Fig 25 Viscofan in discussion with Avanzare



Fig 26 Discussion at Elvesys exhibition desk



Fig 27 Elvesys exhibition stand



Fig 28 Bio3DG exhibition stand





Photos from the event





Fig 29 M3DLoC Open Day sign at Conference room entrance Fig 30 M3DLoC Open Day Conference

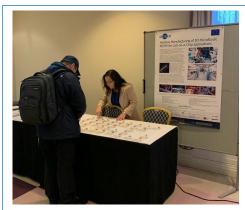




Fig 31 M3DLoC Open Day - Registration Desk



Fig 32 Opening of the workshop by Dr Bojan Boskovic, Open Day Organisers (CNAT)



Fig 33 Welcome & Introduction to M3DLoC Project by Prof. Costas A. Charitidis, Project Coordination (NTUA)









Fig 34 & 35 Presentation by Dr Angel Del Pozo, from Keralty, Guest Speaker





Fig 36 & 37 Presentation by Dr Lluis Quintana Frigola, from Viscofan BioEngineering, Guest Speaker





Fig 38 Presentation by Evesys

Fig 39 Presentation by Viscofan Engineering



Fig 40 Presentation by RayScan



Fig 41 Presentation by Avanzare