

Science & Technology Value Creation (STVC) 2015 Panel Report

High Value Manufacturing



Science and Engineering
Research Council



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Acknowledgements

Acronyms and Abbreviations

Executive Summary

Manufacturing has been and remains a key pillar in Singapore's economy, contributing more than 1/5 of the country's Gross Domestic Product (GDP) in 2008. From the labour intensive operations of the 1960s, through the skill intensive investments of the 1970s, to a capital intensive followed by an increasingly knowledge based approach, the manufacturing industry in Singapore has both adapted to, and driven the transformation of the Singapore economy. That the industry has demonstrated its resilience is almost self-evident. In the face of an economic transformation that has seen Singapore moving from a truly low cost manufacturing base to one where some of the world's most sophisticated high technology manufacturing is carried out, the industry continues to account for close to a quarter of the country's GDP even while its share of the labour force continues to drop. Today there is a critical mass of highly innovative manufacturing talent in Singapore that can move with agility from the manufacture of high end disk drives to the design and manufacture of fuel cells or pharmaceutical products.

Nevertheless the accelerating pace of technology exploitation coupled to societal drivers such as economic globalisation and an aging demographic in consumer countries suggest that the industry faces an exponential rate of change that is likely to couple new technology with a continuing fragmentation of processes, encouraging specialisation, an associated complexity of global value chains and the rise of intangibles such as design, branding, and R&D. High value in Manufacturing will come not just or even primarily from the content of the processes available the ability to integrate value chains and the intangibles such as brands, trust, and conformance to standards. This is illustrated in the continuum from the iPod, a high volume high brand value product which can be manufactured with fairly conventional processes, for which Singapore has no competitive advantage, to a yet-to-be-developed, necessarily low cost, disposable diagnostic chip for Influenza A(H1N1) that may require a knowledge intensive set of manufacturing processes in microfluidics, the early development of which may confer a sustainable advantage to Singapore.

The High Value Manufacturing panel adapted the methodology of the Siemens Picture of the Future (POF) approach. In navigating the considerable distance in the mapping from societal and economic trends to specific research programmes in manufacturing science and technology, the panel recognised that research and development (R&D) in the latter, while important, is a small part of a complex value chain.

Nonetheless it is clear that drivers such as the need for sustainability, the limits of technology as today's electronic devices reach nanoscale dimensions, the ability to measure and analyse an enormous amount of data in real time as well as the convergence of much interdisciplinary knowhow will provide opportunities for step improvements in manufacturing technologies that serve



societal needs. Furthermore, functional aspects such as precision, flexibility, cost reduction, reliability and speed remain invariant with eras.

A*STAR and Singapore have invested and continue to invest in research in key vertical sectors such as the disk drive industry, the microelectronics industry, the pharmaceutical industry as well as other sectors of the economy today. This panel takes a horizontal cross-sectional view – to focus primarily on identifying a new set of capabilities that will be needed to manufacture the products of the future and to outline the research programmes that could lead us to those capabilities.

The following paragraphs outline proposals for a set of research thrusts to develop these capabilities.

Nanomanufacturing of Multi-functional Products and Devices

It is a continuing trend for the next generation of devices and products to decrease in critical dimensions. Today, manufacturing processes in silicon electronics while very successful, are approaching fundamental limits beyond which even the latest industry roadmaps are silent. Manufacturing of these nanostructured/nanoscale devices will pose nontrivial multidisciplinary challenges with key technologies still to be identified. This panel recommends that Singapore leverage its existing strengths to develop two key areas – fabrication of nanostructures and instrumentation at the nanoscale – in parallel so as to integrate the formulation of engineering rules for nanofabrication scale-up, proof-of-concept of nano-products/devices, and innovative nanoscale analytical devices.

Pervasive Microfluidics

The Pervasive Microfluidics Programme will target the development of high volume manufacturing of microfluidics based devices. While much research is still needed on the basic knowledge of fluid behaviour at the micro and nano metric scale, the priority will be on creating a library of process capabilities, laying down standards for device design and manufacturing, innovating cost effective manufacturing technologies viable for mass production, and putting in place a technology platform for application testing.

Printable Electronics

The Printable Electronics programme will develop materials, electronics and large area process capabilities towards the manufacture of high value printable electronics in Singapore. This capability is complementary to today's capital intensive manufacturing technologies built around silicon electronics. In this programme, cross-cutting technologies from A*STAR's SERC and the universities will be utilised to develop the materials, technology platforms, application prototypes, and large area manufacturing processes.

Enabling Intelligent Manufacturing

One characteristic need for high value manufacturing industries is the need for high mix low volume manufacturing. This thrust aims to develop and demonstrate new equipment, tools and methods to support a wide range of industries in their data and knowledge acquisition, validation, storage, organisation and exploitation across their design and manufacturing activities. To focus the programme scope, the pharmaceuticals and aerospace sectors will be initially selected for development of this capability in “pilot” form.

Biological Manufacturing (Tissue Engineering)

Unlike the first previous recommendations, this research thrust serves as a demonstrator for integrating the outputs of biomedical research with technologies for high quality and consistent, reliable mass production. The panel proposes to consider a subsector, the manufacturing opportunities of tissue engineering. We propose research into the manufacturing value chain, consisting of the cell source, scaffold, and growth factor and identifying the manufacturing issues as well as solutions.

Sustainable Manufacturing

The panel considers that a sixth thrust, to develop manufacturing practices that are consistent with the global trend towards waste reduction, life cycle sustainability to address resource constraints and to take advantage of information availability to achieve these goals, is a vital thrust for Singapore. In the interests of brevity, and since the Sustainable Development Panel is also recommending a similar programme, this panel has elected to provide its inputs on this subject to that report instead.

Chapter 1 Introduction of STVC Theme

1.1 Definition and scope

Manufacturing is an important part of the Singapore economy, representing the largest industry contributor and forming 22% of GDP in 2008¹. A*STAR supports key sectors of the manufacturing industries with capabilities at its research institutes (RIs). Institutes such as the Data Storage Institute (DSI), the Institute of Microelectronics (IME) and the Institute for Chemical and Engineering Sciences (ICES) engage with important vertical sectors of industry – in a continuous synergistic interaction that contributes to keeping Singapore industry in those sectors up to date with technology and people while at the same time doing the research that anticipates medium term needs. The growth in knowledge intensive manufacturing in Singapore in these sectors has been concurrent with the growth of domestic research capabilities in these sectors. This panel notes that the existing mechanisms support continuing linear growth in each of the vertical sectors referred to and notes that despite the recession and the rise of local business costs, Singapore still remains a choice location for manufacturers, with companies such as Abbott, Neste Oil and Illumina recently announcing their investment here.

In looking for over-the-horizon opportunities within existing sectors and new opportunities beyond today's sectors, the panel adapted the Siemens Pictures of the Future (POF) approach, the components of which will be outlined later in this section.

The panel concluded that high value in manufacturing will come from the ability to make to scale, with reliability and quality, using processes that are knowledge intensive and conform to standards, products that are designed for sustainability in the entire life cycle. Furthermore, scale in future will increasingly be beyond mere volume to product mix, flexibility and setup speed. Activities in a high value manufacturing value chain would typically be highly automated, employ a highly skilled workforce, utilize cutting-edge technology, and be environmentally friendly.

1.2 Key drivers and trends

In common with the Siemens approach, the first step was the identification of key drivers leading to expected change and the resulting global trends that are discernible or might ensue.

¹ EDB RSU Census & Surveys

² Phillips sense and simplicity

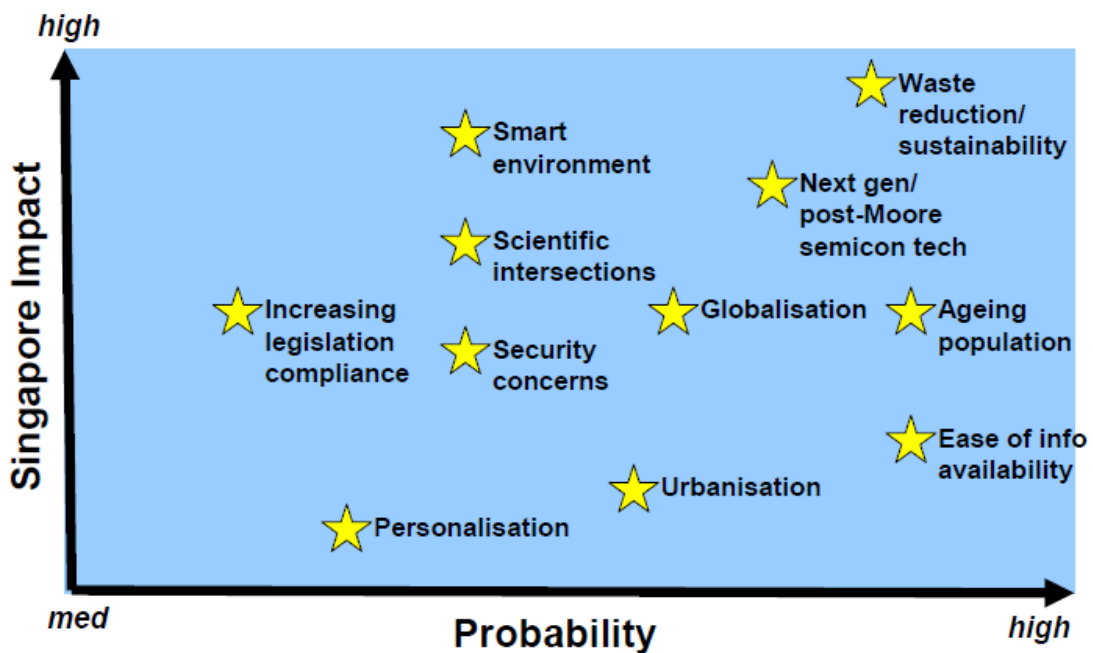
The drivers that the High Value Manufacturing (HVM) Panel identified as having significant impact in changing world trends are as follow:

1. Aging population – in Singapore and in most of the major economies of the world
2. Climate change
3. Consumer empowerment – rising expectations of range, quality and quantity
4. Structural shift to Asia – with the global weight and rate of growth of economic activity in this region
5. Resource constraints – on raw materials and energy
6. Globalization – of talent and knowhow, as well as capital
7. Urbanization – with more people living in cities than ever before

These drivers provide a long term perspective for analysing the impact on manufacturing of trends arising from these and other drivers.

Figure 1 below identifies these trends and attempts a qualitative assessment of the probability of occurrence and its impact on Singapore within the next 7-10 years. The global trends identified and considered to have impact on the Singapore economy and the probability of occurrence are as follows:

Figure 1. Trends -Impact on Singapore vs Probability of occurrence



Resource constraints, particularly in energy and in some of the materials common to next generation technology, are already a given today and hence a high probability trend for *Waste reduction* and a philosophy of *sustainability* that will have a high impact on Singapore manufacturing. This is consistent too with concerns on climate changes.

An *ageing* population and *urbanisation* on a global scale both mean that the profile of products and services to cater for the needs of populations that have better access to information and higher expectations for quality of life (in possibly *smart environments*) will change dramatically. At the same time, scientific knowledge from many disciplines find many more *intersection* points that should enable the delivery of this new profile of products and services.

With *globalization*, the pressure on industry to successfully compete in global markets will require rapid responses to continuously changing business environment. Notwithstanding recent economic turmoil, the networked global economy will be increasingly driven by rapid and largely unrestricted flows of information, ideas, cultural values, capital, goods and services, and people. With its open economy, the shape of Singapore manufacturing industry, more than most is susceptible.

Security, a growing market for *personalised* products and services, and compliance with more *legislation* (even with or because of globalisation) are trends that are likely to have similar impact on the Singapore economy though the timing of their impact and hence probability of occurrence in the period under review differ greatly. What is almost certain is that all are better served with the certainty that the *ease of information availability* will increase.

In the Singapore context, it is difficult to avoid a specific technology trend towards seeking out the next generation semiconductor technology as technical challenges associated with Moore's Law and the scaling down of device feature size appear to be reaching a fundamental limiting point. This is almost a certain event and will have a high impact on Singapore's manufacturing industry.

Chapter 2 Vision

2.1 Vision and overall goals

The goal of the High Value Manufacturing Panel is to anticipate those capabilities that will be needed to envision, equip, and enable, the factories of the future the near future and to propose research programmes that will develop such capabilities in the medium term.

In the spirit of the Siemens POF approach, the impact of these trends was assessed in the context of user segments, living spaces and desired function, represented in Figure 2.

User Segments

This dimension identifies users of future technology. In the Singapore context, five main industry clusters were identified as:

1. Biological Manufacturing
2. Electronics
3. Precision Engineering
4. Chemicals
5. Manufacturing Systems/ Services

In associating trends and the innovation responses, the panel subdivided these to reflect specific segments within the larger cluster. For example, Tissue Engineering was considered as a specific segment under the Biological Manufacturing Cluster.

Living Spaces

The panel chose to examine the different parts of the manufacturing value chain to pinpoint “Spaces” where exactly the opportunities for technology research into the factories of the future lay. The resulting “Living Spaces” are as follows:

1. Sales and Marketing Dept
2. R&D Labs
3. Design Office
4. Shop Floor
5. Disposal / Recycle
6. Maintenance, Repair and Operations (MRO)

These living spaces are further broken down into specific domains for each of the research thrusts to be identified in Chapter 3.

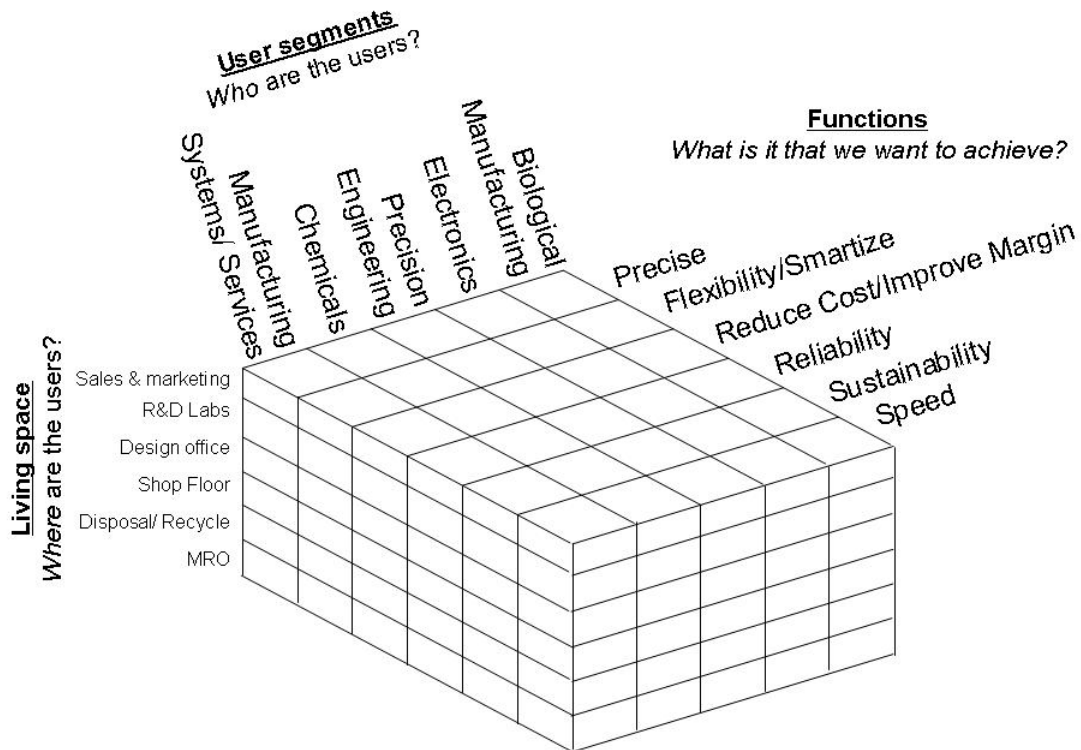
Functions

This dimension lists those functional features expected of future manufacturing capabilities that require improvement. They are:

1. Precision – in physical dimensional scales

2. Flexibility/Smartize – of products, processes and entire manufacturing chains
3. Reduce Cost / Improve Margin
4. Reliability
5. Sustainability
6. Speed

Figure 2. User Segments, Living Spaces and Functions



2.2 Identify key global / local needs and challenges to be addressed

As all the trends flagged in

Figure 1 pose challenges and opportunities for Singapore. The history of the Singapore economy over the past 40 years demonstrates that manufacturing typically gravitates to countries of lowest overall cost. As the Singapore economy morphed from a low labour cost to a higher labour cost economy, the profile of manufacturing activity in Singapore has dramatically changed. At the same time, more than most economies perhaps, Singapore has taken advantage of the opportunities from being able to keep a competitive cost advantage over the entire value added chain.

The factors that influence this value chain are dynamic. Some of these reshaping manufacturing value chains include:

- The accelerated pace of technology exploitation
- The increasing complexity of global value chains
- The fragmentation of processes, encouraging specialisation
- The importance in intangibles such as design, branding and R&D

Investment in mission -oriented R&D is a necessary (though not sufficient) condition for addressing all these factors.

2.3 Economic potential value capture and value add

Manufacturing is a significant contributor to Singapore economy with 22% of GDP. It is the stated aim of the government to maintain manufacturing at around one quarter of Singapore's GDP in the medium to long term. The value added from the manufacturing sector in 2008 was S\$47.9 billion. Its contribution to Singapore's total employment as of Dec 2008 is 19.9%. Beyond these numbers, manufacturing is a key demand driver for other sectors in Singapore, including logistics, and financial services. The recent sharp fall in container traffic through the Port of Singapore is a salutary reminder of this strong nexus.

To differentiate ourselves it is imperative that Singapore is not just an efficient, lower cost manufacturing base, but also provides manufacturing capabilities able to meet the needs of the future growth industries, such as biomedical sciences and clean energy. Furthermore one of the most tried and tested strategies to capture value and employment opportunities from R&D are to translate technology outcomes to products and services that are made and consumed. Thus research investments in opportunities arising from societal drivers such as urbanisation, health and wellness as well as ageing need to be complemented by investments in the capabilities that will enable the manufacturing of the products needed.

Singapore has important differentiators for the introduction of the new manufacturing capabilities proposed. In addition to the well known advantages of stable efficient government, good geographical location as a gateway into Indian and Chinese markets, flexible business models, first-class infrastructure and excellent connections to the world, Singapore's robust intellectual property (IP) protection and management regime provide extra competitiveness. This "trust" factor is especially crucial for applications in the health industries or in responding to social factors such as the risk management of nanotechnology.

2.4 Recommendations for key enabling technologies

The following pages outline recommendations for five groups of programmatic thrusts. They are:

1. Nanomanufacturing of Multi-functional Products and Devices
2. Pervasive Microfluidics
3. Printable Electronics
4. Enabling Intelligent Manufacturing
5. Biological Manufacturing (Tissue Engineering)

The first four thrusts take a horizontal cross-sectorial view in identifying the new capabilities that should be developed in Singapore to manufacture the likely products of the future. The fifth has the nature of a demonstrator that addresses opportunities in the introduction of capabilities for volume production of technologies arising from the trend towards scientific intersections identified earlier.

The panel considers that a sixth thrust, to develop manufacturing practices that are consistent with the global trend towards waste reduction, life cycle sustainability to address resource constraints, and to take advantage of information availability to achieve these goals, is a vital thrust for Singapore. In the interests of brevity, and since the Sustainable Development Panel is also recommending a similar thrust, the panel has chosen to provide its inputs for incorporation into that panel's report instead.

A*STAR and Singapore have invested and continue to invest in research in key vertical sectors such as the disk drive industry, the microelectronics industry, the pharmaceutical industry, as well as other sectors of the economy today. This panel takes a horizontal cross-sectorial view – to focus primarily on identifying a new set of capabilities that will be needed to manufacture the products of the future and to outline the research programmes that could lead us to those capabilities.

Each of this panel's five thrusts will develop platform capabilities that apply to more than one of the key industries previously identified. Each programme is also explicitly inter-RI, and its importance to the research landscape and to Singapore's manufacturing landscape as a whole is elaborated in the following chapter.

Chapter 3 Proposed Programmes

3.1 Nanomanufacturing of Multi-functional Products and Devices Programme

3.1.1 Description of programme

The role of nanosciences and nanotechnologies in many areas such as health care, information technologies, materials sciences, manufacturing, instrumentation, energy, environment, security and space as well as its importance for the improvement of economic competitiveness and quality of life is well recognized around the world². In Singapore, the Science and Engineering Research Council (SERC) initiated a thematic investment in R&D with the development of a nanoscience initiative in 2002 followed by a Thematic Strategic Research Programme (TSRP) on nanoelectronics in 2004 and the launch of a Visiting Investigator Programme (VIP)³ in interconnection technologies in 2006.

While there has been sustained investment in understanding the science and inventing the technology that exploits nanoscale phenomena and functionalities, research into the tools and capabilities needed for the scaled production of nano features, whether by top-down or bottom-up approaches, imaging and manipulation at atomic precision remains a nascent field. A first international attempt to define a technology roadmap for productive nanosystems was published by Battelle Memorial Institute and the Foresight Nanotech Institute in late 2007⁴. The roadmap notes that while prototype scanning probe based systems exist in the laboratory and demonstrate atomic precision operations on semiconductor systems, nanoscale production systems exist in nature and fabricate uniquely complex nanostructures in enormous quantities. It identifies some of the improved technologies that will enable development of next generation atomically precise manufacturing systems.

Figure 3 below depicts the nanoscience and nanotechnology issues in materials, devices, modelling and characterisation. While it is now well established that nanotechnology and nanoscience have huge potential in the next generation of devices and products, much research is still needed to

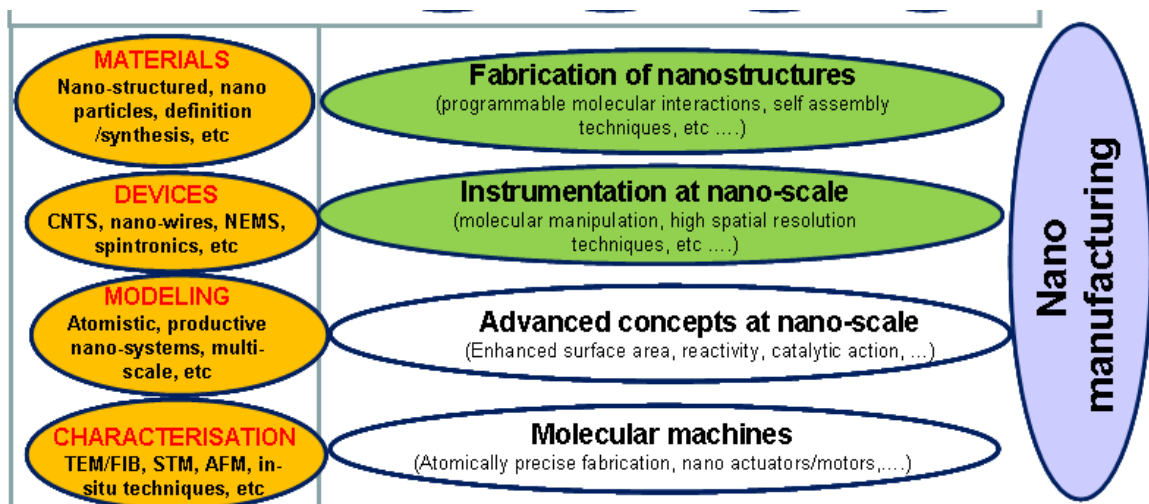
² Council of European Union 2891st COMPETITIVENESS Council meeting Brussels, 26 September 2008

³ The VIP represents SERC's commitment to excellence in scientific research by attracting eminent scientists and researchers to participate in our local scientific capabilities development. These high calibre scientists are invited to develop and lead research programmes in areas that are part of Singapore's S&T 2010 roadmap. The statement tenure of awards is three years.

⁴ SERC participated in this roadmapping effort from 2006 leading to "Productive Nanosystems: Launching the Technology Roadmap" launched by the Society of Manufacturing Engineers and the Feynman Institute on 9 Oct 2007.

translate this potential to manufacturing. Even while there is much ongoing research in fabrication technology, some known challenges are repeatability, scalability, safety and standards development for producing in a manufacturing environment. This is further compounded by the fact that there is a dearth of instrumentation and few in-line metrology tools to monitor the process and yield of the end products.

Figure 3. Nanoscience and nanotechnology issues in materials, devices, modelling and characterisation



To establish an early mark in nanomanufacturing, A*STAR can build from its initial investments and leverage on strategic partnerships. Two key areas namely, the “Fabrication of nanostructures” and “Instrumentation at nanoscale” are proposed as priority areas for developing Singapore capability in nano manufacturing. Each key area can draw upon the capabilities of A*STAR RIs as well as the capabilities built up in nanoscience initiatives at both the National University of Singapore (NUS) and the Nanyang Technological University (NTU); as well as leverage on the international networks and partnerships that have already been established at the Institute of Materials Research and Engineering (IMRE) and the university initiatives. As indicated in the Battelle/Foresight roadmap referred to earlier, no country or region yet dominates in this new field. Nevertheless the research communities in East Asia in particular are investing heavily. Singapore’s position in this region and its reputation for trust gives us a potential competitive advantage to take a leadership position. This panel hence strongly recommends that these two key areas be of high priority for the seven years to the end of the 2015 financial year.

Using the POF method described in Chapter 1, Table 1 lists the various technology living spaces and potential user segments for which economically viable manufacturing technologies at the nanoscale could have high impact. These provide the basis for the ensuing discussion on opportunities and recommendations.

Table 1. Living spaces, functions, and user segments for Nanomanufacturing Programme.

Living Space	Functions/Trends	Some User Segments ⁵
<ul style="list-style-type: none"> • R&D labs • Innovation centers • Design and Engineering office • Production area 	<ul style="list-style-type: none"> • Precision • Flexibility • Reduced cost • Reliability • Biocompatibility • Smart features • Lightweight • Rigid • Speed • Post Moore devices • Smart environment • Scientific intersections • Miniaturization • Personalization • Waste reduction • Ageing population 	<ul style="list-style-type: none"> • Photonics, electronics, storage, precision engineering, chemicals, pharmaceuticals, biological manufacturing, energy storage, energy conversion, photovoltaics, Water treatment and remediation, Disease diagnosis and screening, Drug delivery systems, Food processing and storage, Air pollution and remediation, Construction, Health monitoring etc • Known examples from these segments include: <ul style="list-style-type: none"> a) Clothing industry uses nanotech to make stain-repellent fabrics. Socks that are made with nano-silver particles give anti-microbial protection, preventing bacteria and fungus b) Carbon nanotubes can make composite coatings for car bumpers. The tubes absorb hydrogen, enabling more efficient storage of future fuels c) Surface of active glass coated with titanium oxide nano-particles breaks down dirt. d) Nano-sized zinc oxide particles used in sun creams make the lotion transparent and smooth e) Hairs on gecko feet make sticky tape lined with gecko-like synthetic hairs

3.1.2 Opportunities and Impact

Various reports have produced estimates of the size of the market for products engineered to take advantage of nanoscale phenomena that range from hundreds of millions to a trillion USD. Lux Research⁶ for example, predicted sometime ago that from 2010 onwards, nanotechnology will become commonplace in manufactured goods, with revenues rising to \$2.6 trillion in 2014. The report expected that healthcare and life sciences applications will finally become significant in this period as nano-enabled pharmaceuticals and medical devices emerge from lengthy human trials.

Notwithstanding the uncertainties that bedevil such predictions, it is clear that much of the products and services identified in the other STVC panels will only be available at an economic scale if we have the capabilities to manufacturing high volumes of devices and systems designed to exploit nano scale phenomena.

⁵ Source: <http://news.bbc.co.uk/2/hi/science/nature/4421867.stm>

⁶ Source: http://www.luxresearchinc.com/press/RELEASE_SizingReport.pdf

This section describes some of the critical technologies to be developed in each of the two key areas:

Fabrication of nanostructures

- The underlying technology bottleneck in nanofabrication lies in the lack of ability to realize precise nanostructures at large production-scale. Bearing in mind the need to engineer nanostructures at such scale, a new generation of nanosynthesis methodologies needs to be developed for the ease of scaling-up and mass production. Such methods would provide the impetus of breakthroughs across a wide range of industries such as pharmaceuticals, specialty chemicals, precision engineering, electronics and photonics.
- Computational design is prerequisite to boosting the efficiency in designing new nanostructures. The development of new atomistic modeling techniques is needed to provide higher accuracy and broader scope than the current models based on molecular mechanics and dynamics, which are similar to macroscale modeling and design.
- Self-assembly of nano-particles, which is the fabrication of ultrafine structures beyond the limits of conventional lithography, is expected to play a significant role in the realization of futuristic nanotechnology. An important step towards realization of nano devices is self-organized nanopatterning of functional structures called “chemical lithography”, enables the regular assembly of optically active nanoparticles on a silicon surface.⁷
- Chemical formulation techniques that vary the degree of structural order or disorder at nanoscale can possibly tailor-make specific functional properties in novel medicinal and specialty chemical products. Methods include amorphization (creating liquid-like disorder in solids), supramolecular chemistry (co-crystallizing two or more different molecules), nanocrystallization, use of mesoporous excipients and intelligent science-based design of desired functional properties. They can potentially address two major technological limitations in today’s pharmaceutical industry, i.e. insolubility (or poorly aqueous soluble drugs) and instability of new drug candidates leading to poor bioavailability. They would serve to maximize the current shortage of new drug candidates in research pipeline.

Instrumentation at Nanoscale and Metrology

- In order to scale-up nanofabrication, a new generation of Process Analytical Technologies (PAT) at different length- and time-scales needs to be developed to address quality assurance. In- and on-line characterization technologies are key to mass continuous processing of nanoscaled and nano-structured materials. Such advanced PAT

⁷ Source: Nanowerk Spotlight <http://www.nanowerk.com/spotlight/spotid=707.php>

enables monitoring and feedback control for corrective actions during manufacturing with benefits of high throughput, waste reduction, reliable and consistent product quality. Continuous processing of pharmaceutical products also allows good adherence to strict protocols required by regulatory agencies, e.g. the U S Food and Drug Administration (FDA).

- Combination of refined processes such as electron beam lithography and molecular beam epitaxy, to allow the deliberate manipulation of nanostructures, leading to the observation of novel phenomena in nano regime.
- New methods for the manipulation of atoms based on the Atomic Force Microscope (AFM) that make it possible to build stable atomic structures at room temperature. Using the atoms at the tip (that are chemically different to those at the surface) as “ink”, it is possible to “write” or “draw” with the microscope. This interchange process can be repeated in different positions over the surface to form complex structures very efficiently.⁸
- Placement of specific dopant elements in the best position on semi-conductive surfaces to increase the efficiency of nanometric transistors or magnetic atoms would open the possibility of developing devices based on the control of the spin of an electron. These techniques could also bring the possibility of “nano-facturing” of qbits, which are the basic components of what could eventually become a quantum computer.

Potential to leverage on user segments in Singapore to validate or demonstrate technologies

The key areas identified require research competencies across disciplines: chemistry, material science, chemical, mechanical and electronics engineering, pharmacy, biology, physics, and applied mathematics. Most of the discipline competencies already reside as capabilities at RIs⁹ across both of A*STAR’s research councils¹⁰, and at, NUS’s Departments of Chemical & Biomolecular Engineering, Chemistry, Material Science and Physics.

Singapore has the unique advantage of having the RIs of SERC and BMRC, NUS, and the National University Hospital (NUH) within such close proximity, that new nano manufacturing ideas and concepts can be evaluated and developed with expertise from different disciplines much more efficiently and effectively than in other research organizations.

⁸ Universidad Autónoma de Madrid (2009, January 21). Scientists 'Write' With Atoms Using An Atomic Force Microscope. ScienceDaily. Retrieved May 24, 2009, from <http://www.sciencedaily.com/releases/2009/01/090109083455.htm>

⁹ These research institutes include DSI, ICES, the Institute of of High Performance Computing (IHPC), IME, IMRE, SIMTech, the Institute of Bioengineering and Nanotechnology (IBN), and the Institute of Molecular and Cell Biology (IMCB).

¹⁰ The two research councils at A*STAR are the Science and Engineering Research Council (SERC), and the Biomedical Research Council (BMRC).

Furthermore Singapore has a mix of small and large firms that are already in networked relationships with Institutes of Higher Learning (IHLs) and RIs

The user segments identified in Table 1 are either existing participants in Singapore industry or sectors that are being developed. Both public and private research laboratories, as well as technologically sophisticated industries such as the data storage and microelectronics industries are already adopting manufacturing of devices that exploit nanoscale phenomena. The following list illustrates some of the current and near future applications:

- Bit Patterned Media is fabricated with lithography technologies (nano dimensions) and meant for next generation magnetic recording systems with ultra-high areal density.
- The 'spin' of the electron is being exploited rather than its charge to create a remarkable new generation of 'spintronic' devices which will be smaller, more versatile and more robust than those currently making up silicon chips and circuit elements.
- Nanowires made of semiconductor materials are being used to make prototype lasers and light-emitting diodes with emission apertures roughly 100 nm in diameter--about 50 times narrower than conventional counterparts. Nanolight sources may have many applications, including "lab on a chip" devices for identifying chemicals and biological agents and scanning-probe microscope tips for imaging objects smaller than is currently possible¹¹.
- Metamaterials that could light the way toward high-powered optics, ultra-efficient solar cells and even cloaking devices¹².
- Nanotube nanomotor, which is a molecular device capable of converting energy into movement. The device can typically generate forces in the order of piconewtons. Nanomotors have also been made using synthetic materials and chemical methods, and have a potential application in healthcare to carry drugs into cells.

3.1.3 Assessment and Stocktake of R&D capabilities

The capabilities that need to be developed have been summarised in

¹¹ National Institute of Standards and Technology (2006, May 26). Growing Glowing Nanowires To Light Up The Nanoworld. ScienceDaily. Retrieved May 24, 2009, from <http://www.sciencedaily.com/releases/2006/05/060525192830.htm>

¹² Rice University (2009, March 19). Nanocups Brim With Potential. ScienceDaily. Retrieved May 24, 2009, from <http://www.sciencedaily.com/releases/2009/03/090313171318.htm>

Table 2. The focus should be on fabrication of nanostructures and the development of instrumentation with a goal towards manufacturing scale, governed by the need to have the appropriate metrology and conformance that are today still missing in the world.

Table 2. Capabilities to be developed for Nanomanufacturing Programme, and relevant RIs.

Challenges	Potential R&D topics	Institute with relevant capabilities
Fabrication of Nanostructures	Computational Design	IHPC
	Self Assembly of Nanoparticles	IMRE, ICES, IBN
	Lithography	IME, DSI, IMRE
	integrated analytical techniques	IMRE, ICES
Instrumentation	Process Analytical Technologies	ICES
	Probe Microscopy and Imaging	IMRE
	Precise positioning of dopants	IME, DSI, IMRE

As flagged in the introduction, there has been worldwide investment in nanoscience and nanotechnology research. There has been much less attention paid to manufacturing issues. With SERC participation in the development of the international roadmap, Singapore is well placed to make key and strategic early investments in R&D for nanomanufacturing.

At A*STAR RIs, work is being conducted on single molecule devices and molecular machines. This is with the aim of achieving controlled manipulation and fabrication of single molecule devices and molecular machines connecting them to the 'outside world'. The approach has been by the manipulation of single molecule by low temperature STM, single crystal nano-island manipulation via "destabilisation" and to meet the atomic scale cleanliness requirement by nanostencils. "Bottom-up" approach is being undertaken to synthesize inorganic nano-fibers and wires with controllable aspect ratios via low-temperature steam-assisted solid-phase crystallization. Nanostructured metals, oxides and carbon nanotubes are being investigated for hydrogen storage and fuel cell application. Synthesis of the world's first tri-continuous mesoporous nanoscale silica with potential applications in catalysis, separation and drug delivery was recently reported. Drug deposition inside nanoscale pores of mesoporous excipients is being studied to overcome drug insolubility. In the area of scanning tunnelling microscopy (STM) and atomic force microscopy (AFM) the main foci has been imaging and characterization of organic molecules which are self-assembled on a surface. It has the potential to measure the properties of electronically single molecules, which could contribute to molecular electronics. Ballistic electron

emission microscopy (BEEM) is another technique which enables imaging and spectroscopy of interfacial electronic properties at nanoscale.

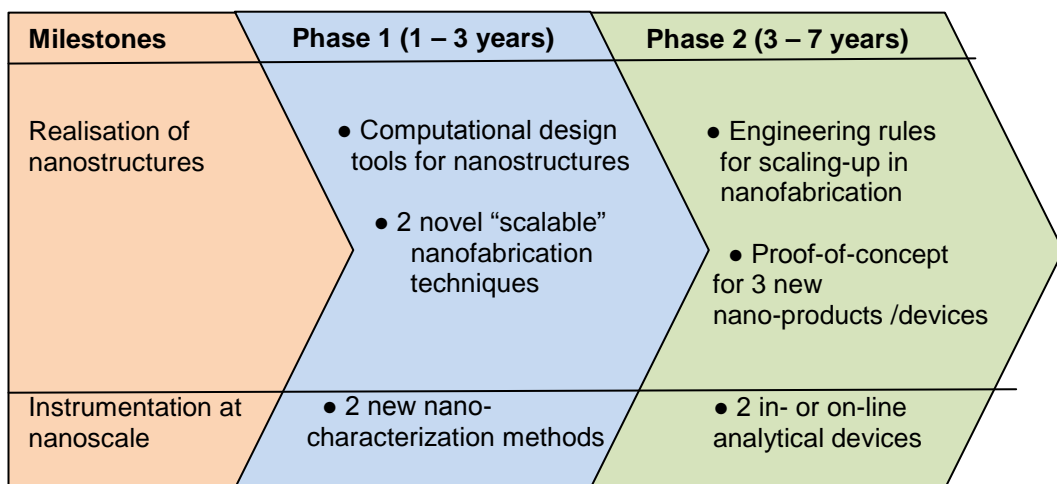
At NUS, the Nanoscience and Nanotechnology Initiative (NNI) involves some 70 faculty and research staff from 20 research labs around NUS; working on some S\$14 million worth of research grants. Areas of work in NNI include molecular self-assembly and devices, nano-structure formation, and in-situ nano-characterisation instrumentation with applications to photonics, silicon nanodevices, information storage materials, nanoscale materials and systems, bio-nanotechnology

At NTU, the Nanoscience and Nanotechnology Cluster (NanoCluster) has close to 90 faculty members from all disciplines of science & engineering, a wide network of research centres with shared facilities for nanofabrication, nano characterization, and exploitation of nanotechnologies working in microelectronics & photonics, microelectromechanical systems (mems) , precision engineering, advanced materials, analysis & characterization, testing & simulation.

3.1.4 Recommended Programme Roadmap and milestones

Figure 4 outlines a broad timescale for milestones. Phase 1 (1-3 years) requires heavier commitment of basic sciences framed by the needs of “scaleability”. In Phase 2 (3–7 years), it is likely that engineering takes over programme ownership to continue with proof-of-concepts and pilot-scale investigations.

Figure 4. Nanomanufacturing Programme milestones



During Phase 1, nanofabrication methods that have the potential to be scaled-up for industrial production will be identified and developed. These include self-assembly of nanoparticles, lithography and chemical formulation techniques in altering nanoscale structures. Nanocharacterization techniques with potential to support subsequent high volume manufacturing will be identified, developed and tested at bench-scale. Advances in atomistic modelling is expected to contribute towards raising the efficiency of both

process and product design. At the end of Phase 1, it is envisaged that at least two novel nanofabrication and two nanocharacterization methods should be ready for proof-of-concepts studies.

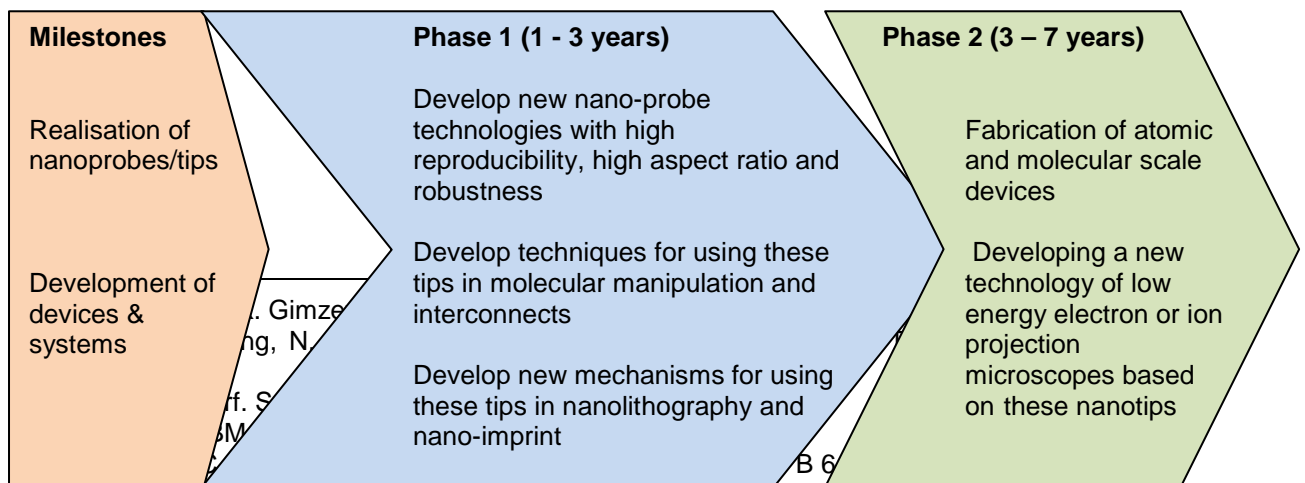
Phase 2 involves the engineering design of nanofabrication techniques into full-fledged manufacturing processes. Demonstrator products or devices with unique functional attributes will be designed and manufactured at pilot-scale. Research output includes establishing new engineering rules pertaining to scale-up of nanofabrication techniques, which are presently not available.

Example: Nano-probe technology for scanning probe and electron/ion microscopy

The advent of scanning probe microscopes in the early 1980's created a continuous demand for fabricating well defined nano-tips with a minimum apex area for achieving the optimum resolution. Beyond the conventional use of these nanotips for imaging it turns out that these tips can be used for manipulating and charactering atoms, molecules and nano objects, paving the way for the era of atomic and molecular technology. Furthermore, fabrication of atomically sharp nanoprobes with a high aspect ratio in a controlled manner is quite crucial for forming multiple inter-contacts with extremely small objects, for instance: molecules or nano-islands settled on metal or semiconductor surfaces^{13,14,15}. In addition to their importance in scanning probe microscopes nano probes are also highly needed in electron and ion microscopy as well as in ion and electron lithography as their sharp end can be used to produce confined electron and ion beams. In fact, several methods have been developed to fabricate nanotips^{16,17,18,19} but they are associated with serious limitations related to the reproducibility, robustness and tip shape. Consequently, improving this technology is attracting worldwide attention because it has a direct impact on all nanotechnology aspects.

Figure 5 illustrates possible milestones for this aspect of a programme.

Figure 5. Nano-probe technology for scanning probe and electron/ion microscopy roadmap



¹³ (a) M. Rezeq, J. Pitters and R. Wolkow, J. Chem. Phys. 124, 204716 (2006)

(b) M. Rezeq, J. Pitters and R. Wolkow, United States Patent 7431856 (2008)

¹⁹ E. W. Muller and T. T. Tsong, Field Ion Microscopy: Principles and Applications, American Elsevier Publishing Company, Inc. (1969)

3.2 Pervasive Microfluidics

3.2.1 Description of Programme

Microfluidics deals with the behaviour, precise control and manipulation of fluids that are geometrically constrained to a small scale ranging from sub-millimetre to sub-micrometer dimensions.

Microfluidics is one of the fastest growing technology areas worldwide, integrating multi-disciplinary technologies for a wide range of applications in diagnostics, genetic analysis, drug development, chemical analysis, energy, and food, water and environmental monitoring. It is poised to become the most dynamic and enabling technology for nanotechnology and biotechnology. As shown in Table 3 microfluidic devices and systems can be used in many user segments, in particular, the chemical, electronics, and biomedical manufacturing segments. It is predicted that disposable device applications will be the most significant market segment for microfluidics. However, amongst other issues, the high manufacturing cost and lack of design and manufacturing standards for large volume reliable manufacturing of microfluidic devices have thus far prevented their widespread commercial adoption.

This programme will target the development of these manufacturing technologies. It aims to tap multidisciplinary capabilities in A*STAR RIs for the design, manufacturing, testing, and implementing microfluidic systems for applications in biotechnology, medical diagnostics, chemical processing, new energy and water monitoring/treatment.

Table 3. Living space, functions and user segments for microfluidics technologies.

Living space	Functions	User Segment
<ul style="list-style-type: none"> • Design office & shop floor of pharmaceutical companies for drug discovery • R&D laboratories • Clinical diagnostic and analysis • Food and beverage industry for quality assurance • Water & environmental monitoring & analysis • Personalized healthcare 	<ul style="list-style-type: none"> • Reduce cost • Fast test for point-of-care applications • Miniaturization and weight reduction • Integrated system • Handling of minimal amounts of fluids • One-stop solution and multi-functions • Disposable & environmentally friendly • User-friendly 	<ul style="list-style-type: none"> • Chemical <ul style="list-style-type: none"> ○ Pharmaceuticals/generic drugs ○ Nanoparticles / materials ○ Biotech (chemicals, polymers) ○ Specialty chemicals • Electronics <ul style="list-style-type: none"> ○ Semiconductor ○ Plastic / opto- electronics ○ Bio-compatible electronics ○ Sensors • Biological Manufacturing <ul style="list-style-type: none"> ○ Organs ○ Biopharmaceuticals ○ Tissue engineering, stem-cell ○ Hospitals and clinics ○ Food and environmental control

3.2.2 Opportunities and Impact

Potential to develop new industry sectors and grow existing sectors

Microfluidics is a key technology for molecular diagnostics and Point-of-Care (POC) medical treatment. According to Yole Développement²⁰, the microfluidic biochip market alone is expected to grow at 25% per year between 2009 and 2014. Pervasive industrial manufacturing capabilities in microfluidic systems are required if these predictions are to be realised.

In Singapore, the biomedical manufacturing sector is one of the five manufacturing pillars. Microfluidic devices and systems will provide an opportunity for Singapore to grow this sector by setting up a new industry platform that will take advantage of generic precision manufacturing skills already available in the engineering and electronics companies in Singapore.

Although considerable research work has been conducted worldwide for selected applications, there is so far no industrial platform base established looking at the whole set of capabilities necessary for volume manufacturing of microfluidics products and systems. Setting up this Pervasive Microfluidics Programme will not only enable A*STAR RIs to establish a unique technology platform to support the development of the growing microfluidics industry in Singapore, but will also help upgrade the technologies of Singapore companies in materials, manufacturing, electronics, and equipment development areas to compete in the global market. The success of this programme will put Singapore at the forefront of microfluidics industrialization technology and microfluidics applications.

Potential to leverage on user segments in Singapore

Singapore has established a strong industrial base in microelectronics, pharmaceuticals, bio-medical products and systems, and chemicals. There is great potential to leverage on these user segments in Singapore to aid development of integrated microfluidic capabilities and systems.

A number of companies in Singapore are developing microfluidic devices. Fluidigm has set-up a manufacturing base here for their micro-channel network systems. ES Cell International, a locally-based subsidiary of BioTime, is a regenerative medicine company and a leading provider of products & technologies derived from human embryonic stem cells. STMicroelectronics and Veredus Laboratories have developed Vereflu, a fast, point-of-care DNA-based diagnostics kit to quickly detect strains of Avian Flu and other influenza viruses that was evaluated with the NUH.

²⁰ Emerging Markets for microfluidic Applications in life Sciences and In-Vitro Diagnostics (EMMA 2009), July 2009, www.yole.fr

Other competitive advantages for Singapore

The skilled workforce in precision engineering, microelectronics, chemicals, pharmaceuticals and biomedical manufacturing will provide competitive advantages for Singapore to embark on the establishment of a microfluidic industry cluster. The large number of well-trained engineers from the above industries will provide a unique strength in meeting manpower needs for the take-off of volume microfluidics manufacturing during the course of industry transformation to high value added and high volume microfluidics activities.

In addition, the government's push to expand the bio-medical sector in Singapore is creating great potential for microfluidics applications, in particular, in the area of medical diagnostics, bio-research & drug discovery. EDB has identified diagnostics as one of five key development segments in the Singapore medical technology industry.

3.2.3 Assessment and Stocktake of R&D Capabilities

Design and manufacturing of microfluidics products requires knowledge and technical capabilities in materials, design, manufacturing processes, and micro fluidic sample handling, sensing, detection and analysis technologies. In this programme, technological capabilities cutting across A*STAR's SERC and BMRC as well as local universities, shown in

Table 4 are needed to develop microfluidics manufacturing technologies for the targeted applications.

Competitive landscape viz key research groups globally

While there is as yet no known large scale research programs dedicated to manufacturing issues, microfluidics technology itself is an active research area that has attracted considerable interest in recent years from both academia and industrial communities worldwide. The U.S. is leading the research in both device fabrication and applications. Leading players include the research groups from Stanford University, the University of Washington, the Massachusetts Institute of Technology (MIT), and the University of Michigan. In Europe, research work has mainly focused on Si-based devices for bio-sensing and bio-medical applications. Active research groups include those from the University of Glasgow - UK, Lund University-Sweden, Ecole Normale Supérieure -France, Department of Microsystems Engineering – Germany (*Institut für Mikrosystemtechnik*, IMTEK), University of Freiburg – Germany, and the Ecole Polytechnique Fédérale de Lausanne – Switzerland. In Asia, research activities have been reported from China, Japan, Taiwan, Korea and Singapore. Singapore is one of the pioneers and active players in the field, represented by the research work from Singapore–MIT Alliance (SMA) and MicroMachines Centre (MMC) NTU on Si-based Micromixers, MEMS micropumps, plus other devices and systems.

Table 4. Existing relevant research capabilities

Institute/university	Core capabilities	Research areas
SIMTech	Manufacturing technologies covering forming, machining, joining, surface engineering, mechatronics & measurement	Polymer based microfluidics manufacturing, scale-up processes, cost-effectiveness, system integration, applications
IMRE	Synthesis & processing of polymer materials, micro- & nano-fabrication, bio-sensing	Tailored polymer materials for microfluidics, device design, fabrication, and testing
IME	Silicon manufacturing, micro-electronics design, micro-fabrication, sensors and photonics, characterisation	Si-based microfluidics – design, prototyping, testing, applications (drug screening, biomarker detection, clinical diagnostics)
ICES	Chemical reaction engineering, process analytical expertise, catalysis, pharmaceuticals and special chemicals	Microfluidic devices for mixing, crystallization, phase behavior, searching for polymorphs, analytical methods & systems.
DSI	Fluidic behavior in micro-/nano-channels, nano-fluidics for information storage.	Molecular bonding, transfer & control of fluids, sensing and measurement technology.
IHPC	High performance computing, modeling and simulation	Modeling and simulation of fluid behavior.
BMRC RIs	Biomedical analysis, diagnostic and bio-imaging applications. Examples: IBN-regenerative medicine, GIS-pyrosequencer & nanosensor	Microfluidics for biomedical analysis, diagnostics and bio-imaging, bio-mimicking materials, bio-engineering and bio-testing
NTU and NUS	Extensive research activities on microfluidics by the teams in SMA for healthcare technologies, in the	Device fabrication and integration in both Si-based and polymer based components, testing and



	Micromachines Centre of NTU on platform capabilities for microfluidics/MEMS devices prototyping, etc.	characterization, applications
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Research challenges and gaps viz capabilities which need to be developed

The major challenges or gaps in microfluidics research include manufacturing of microfluidic devices and systems at low cost using polymer or polymer silicon/glass hybrid systems, which can be drilled down to following categories.

- Process technologies for precise manufacture of microfluidics devices
- New materials and processing for microfluidic device manufacturing
- Micro and nano channel network design and fabrication
- Hybrid microfluidic system (polymer, silicon, ceramics, etc.) development
- Metrology solutions for micro and nano structures
- Bio-photonics integration
- Sensor and actuator development
- Integration and packaging of biological components and products
- Implantable devices and biocompatibility

A major advantage of microfluidics is that multi-functions can be carried out within a system such as sample mixing, pre-treatment, virus detection and disease diagnosis. Challenges and gaps related to integration and device manufacturability are yet to be overcome for practical applications. In particular, holistic and collaborative efforts are needed to establish a set of standards for device design and manufacturing.

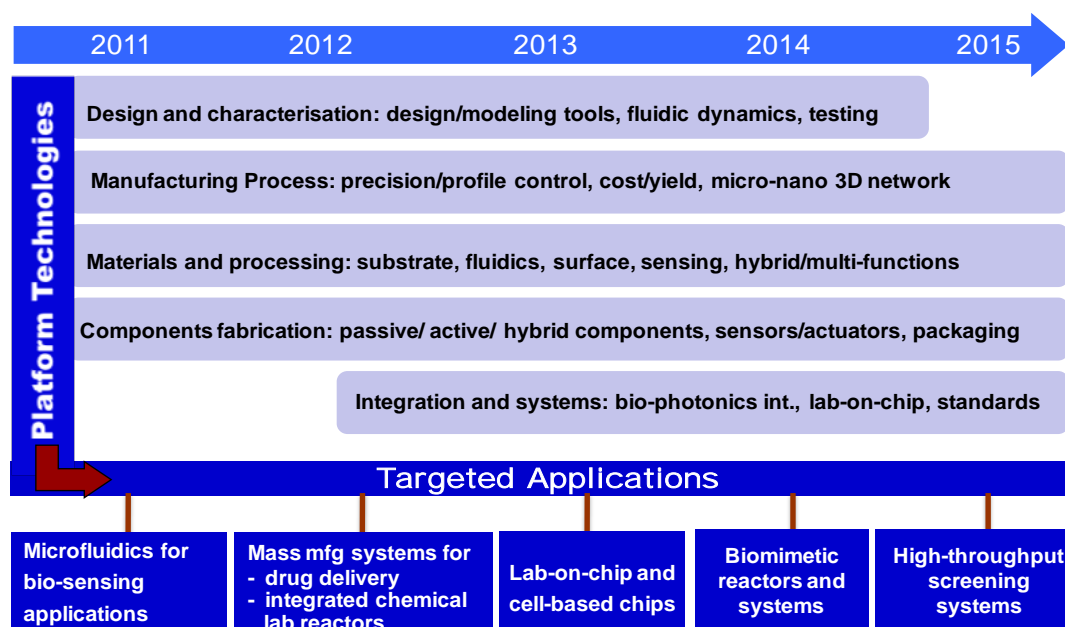
3.2.4 Research Roadmap and Milestones

The key driving thrust for commercial success of microfluidics technologies is cost-effective mass manufacturability for fabricating various devices or products required at large scale. Based on the level of technical challenges in large scale device fabrication, a roadmap is outlined in Figure 6 to prioritize/organise research activities to establish platform technologies in microfluidics manufacturing while Table 5 summarises the key technical competencies to be developed.

Table 5. Competencies needed for Pervasive Microfluidics

Key competencies to be developed	Target applications	Programme goals
<ul style="list-style-type: none"> • Microfluidics design and characterization • Manufacturing processes • Materials and processing • Components fabrication • Integration and systems 	<ul style="list-style-type: none"> • Microfluidics for bio-sensing applications • Mass manufacturing systems for <ul style="list-style-type: none"> ○ drug delivery ○ integrated chemical lab reactors • Lab-on-chip & cell-based chips • Biomimetic reactors & systems • High-throughput screening systems 	<ul style="list-style-type: none"> • Knowledge of microfluidics behaviors at micro and nano metric scale • A library of process capabilities • Standards for device design and manufacturing • Cost effective manufacturing technologies viable for mass production • A technology platform for application testing

Figure 6. Pervasive Microfluidics Programme roadmap



3.3 Printable Electronics Programme

3.3.1 Description of Programme

Printable electronics is a technology that uses additive printing methods to deposit functional electronic materials only where needed, and allows the use of low-cost flexible substrate materials such as polymers and even paper. Living spaces, important functions addressed and potential user segments are tabulated in Table 6.

Printing electronics at a small scale can utilise inkjet printing processes, although at a larger scale it is expected to use higher through-put printing processes, such as screen printing, flexography, gravure, and offset lithography. Instead of printing graphic arts inks, families of electrically functional electronic inks are used to print active devices, such as thin film transistors. Printed electronics is expected to facilitate widespread and very low-cost electronics useful for applications such as flexible displays, smart labels, animated posters, and active clothing. Printable electronics integrates knowledge and developments from printing technology and electronics as well as from chemistry and materials science, especially from organic and polymer chemistry.

This programme will develop materials, electronics and large area process capabilities towards the manufacture of high value printable electronics in Singapore. It is aimed to tap on capabilities cutting across various A*STAR RIs relating to materials development, prototyping, large scale manufacturing, and implementing printable electronics for applications in medical sensing and clean technology.

Table 6. Technology Functions, User Segments and Manufacturing Issues to be Addressed in area of Printable Electronics

Living Space	Functions	User Segments
<ul style="list-style-type: none"> • R&D labs • Innovation centers • Design and Engineering office • Production area 	<ul style="list-style-type: none"> ○ Flexibility, conformability ○ Intelligence ○ Energy efficiency ○ Space efficiency ○ Advanced electromagnetic sensitivity 	<ul style="list-style-type: none"> ○ Clean Technology, e.g. OPVs, batteries ○ Consumer, e.g. lighting ○ Medical, e.g. printed sensors for detecting pathogens

3.3.2 Opportunities and Impact

Economic and Technological Opportunities and Impact

According to IDTechEx, the global market for printable electronics will be US\$1.92b in 2009, and grow at a Compound Annual Growth Rate (CAGR) of 40% to US\$57.16b in 2019, and to about US\$300b in 2029. In order to leverage on these market opportunities, we should aim to develop a low cost, scalable printable electronics platform that can be a global standard, specifically in high growth applications such as clean technology and medical technologies. It will also provide an additional avenue of growth for existing sectors including the electronics, precision engineering, and chemicals sectors, providing opportunities for manufacturing of devices, printing equipment and materials (refer to Table 7).

Table 7. Existing sectors that will benefit from Printable Electronics capabilities

Existing sector	Companies that will benefit
Electronics	<ul style="list-style-type: none"> - Semiconductor companies that develop or design printable electronics solutions - Printing, print head and publishing companies that adapt their technologies for printable electronics - Data storage companies that develop polymer storage solutions - Passive components companies that develop printable passive components
Precision Engineering	<ul style="list-style-type: none"> - Equipment companies that develop automation solutions for the manufacture of printable electronics
Chemicals	<ul style="list-style-type: none"> - Specialty chemicals companies that develop materials and chemicals for printable electronics

Competitive advantages of Singapore and potential to leverage on user segments in Singapore

Singapore has established a strong industrial base in electronics, precision engineering and chemicals companies that provides the capability base for Singapore in printable electronics. In addition, Singapore's strong foray in biomedical sciences and clean technologies provides an additional base of potential sophisticated users for application development.

Singapore has also started to make inroads in attracting companies to embark on printable electronics R&D activities. In this regard, several companies in Singapore are already developing printable electronics materials and devices. For example, BASF Corporation has an organic electronics R&D centre in Singapore, while Nitto Denko conducts R&D in integrated organic optoelectronics sensing devices. Bosch is setting up an R&D centre in Singapore with one of the areas of focus being the development of organic photovoltaics (OPVs).

3.3.3 Assessment and Stocktake of R&D Capabilities

Printable electronics is a multidisciplinary research field. The development and manufacturing printable electronics products requires knowledge and technical capabilities in materials, design, additive manufacturing processes, and in market applications.

Competitive landscape viz key research groups globally

Printable electronics has been a research area that has attracted interest in recent years from both academia and industrial communities worldwide.

The active research groups include VTT Technical Research Centre of Finland (started R&D in roll-to-roll processing for OLED in 2004), ITRI in Taiwan (pilot roll to roll processing for passive devices in 2006 and moving on to active devices), Korea Printed Electronics Centre, and Plastic Electronics Technology Centre UK. In Singapore, the initial capability base in our RIs was developed through the Polymer Molecular Electronic Devices (PMED) programme led by SERC in 2007, and SIMTech is embarking on a large area processing programme.

Research challenges and gaps viz capabilities which need to be developed

In this programme, cross-cutting technologies from A*STAR's SERC RIs and the universities are needed to develop the materials, technology platforms, application prototypes, and large area manufacturing processes. These capabilities and the respective potential contributing institutions are listed in Table 8.

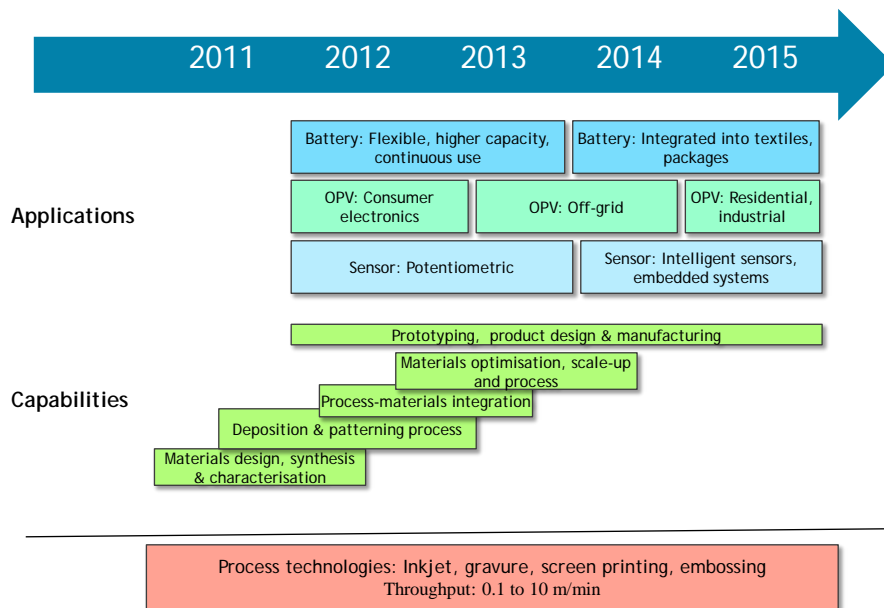
Table 8. Matching of capability requirement/gap to potential research performers

Capability requirement/gap	Potential RI/IHL
Materials development - A major challenge today is the development of electronics materials that provides the platform that enables high volume and low cost organic electronics devices	IMRE is developing materials for the enablement of polymer and molecular electronics devices. As a next stage, IMRE could develop materials-based technology platforms and prototypes for printable electronics. IHPC can contribute in the providing the necessary simulation tools. ICES could further study the manufacturing issues pertaining to the large scale production of the materials.
Circuit design - Circuit design for printable electronics products	IME's capabilities in CMOS circuit design could be extended to circuit design for printable electronics devices.
Processes and integration - For high throughput manufacturing, large area printing processes such as screen printing, gravure or multi-printhead inkjet will be required.	SIMTech is embarking on a Large Area Processing programme which can be applied to Printable Electronics. In addition, the work conducted in NUS on nano-gold and PEDOT:PSS printing using Litrex printer and in NTU on printing micro-sized features using embossing techniques

3.3.4 Research Roadmap and Milestones

Figure 7 illustrates a high level programme research roadmap which aims to establish process technologies in printable electronics. The applications are chosen in line with Singapore’s focus on clean energy and biomedical. Other application areas such as RFID and display are not listed as a number of other institutes and companies have already been embarking on these applications and it may be difficult for Singapore to differentiate itself in these applications. For large area processing technologies, a number of printing methodologies are listed as it is likely that multiple printing technologies will emerge to fit the requisite materials, applications and line widths.

Figure 7. Printable Electronics Programme Broad Roadmap



3.4 Enabling Intelligent Manufacturing Programme

3.4.1 Description of Programme

A characteristic of future manufacturing industries will be an increasing need for the combination of a high product mix with relatively small runs for each product. - high-mix low-volume manufacturing. Examples range from the production of personalised medication to the mass customisation of consumer goods, and in industry sectors such as the aerospace, pharmaceutical, specialty chemicals and high value electronic assembly sectors. While the technologies for these industries differ, they share common problems in the handling of complex and detailed technical and commercial information along multi-step supply chains. Many activities require substantial levels of scientific and techno-commercial understanding and high data quality for success. Transactions include supply chain design and management, process design, product design, outsourcing, troubleshooting, scheduling, operational control and many others.

Intelligent manufacturing exploits the trend towards smarter environments and increasing data availability to use knowledge-based analysis and precise response to maximize the effectiveness of such high-mix low-volume manufacturing operations. An early adopter has been the logistics industry, which has demonstrated the orders of magnitude improvement possible. There is a significant challenge in delivering similar improvements for much more complex manufacturing operations.

This programme will develop and demonstrate tools and methods to support a selected group of industries in their data and knowledge acquisition, validation, storage, organisation and exploitation across their design and manufacturing activities. The philosophy is to capture large quantities of data and information at low cost and to be able to exploit it to generate better understanding of the manufacturing process and equipment performance. By tailoring the system to the problems of a particular sector it is believed that step change improvements in manufacturing and overall business performance could be achieved. As the programme addresses step changes in manufacturing it inevitably reflects a long term view (with the full benefits being delivered in 10 years and beyond). However, it is clear that developments along the way will also bring direct benefit sooner than that.

The programme will focus on selected user segments where the products are of high-mix low-volume nature. In the Singapore context, this is most likely to be the pharmaceutical, specialty chemical and possibly the aerospace industry.

3.4.2 Opportunities and Impact

There is an opportunity to access step change improvements in manufacturing performance. For example, in pharmaceuticals, performance in final product manufacture typically attains 2-3 sigma levels, and the “cost of quality” has been estimated to be in excess of 20%²¹. By using more precise and more widespread data acquisition we expect to be able to observe things that are normally hidden in processing. By capturing and interpreting such data we can generate a deeper understanding of process performance at scales from processes within individual operations to plant-wide and supply chain. This can be used to enable improvements in a very wide range of activities: maintenance, troubleshooting, control, process optimization, production planning, modification etc. In other industries where highly reproducible manufacturing is already achieved an opportunity could be in the rapid set-up of new processes, reducing response times, better technology transfer to subcontractors, in reduced time or resource spent prototyping and/or more efficient supply chain design.

The IP generated could be exploited through manufacturing and selling measurement devices or whole systems to carry out the functions described above, as well as by their application to manufacturing industries in Singapore and beyond.

This programme will develop the means to have integrated data acquisition, knowledge generation and management in manufacturing. This would involve the coordinated development of

- Means to collect richer information from processes using novel instrumentation (“smart machines”);
- Means to analyse those data to extract information relevant to both managing current operations and designing new processes/machines (“the learning factory”);
- Means to deploy the information into a wide variety of manufacturing industry transactions (“information-driven design and analysis”);
- Means to make the information accessible to people in a usable form (“user-centred knowledge management”).

Potential to leverage on user segments in Singapore to validate or demonstrate technologies

There is a broad potential for Singapore’s pharmaceutical, process/engineering contracting, and electronic industries to be leveraged to test these technologies. Such technology might be deployed, for example, to support the technology transfer into Singapore of a new process, or to support the translation of a product developed in Singapore into manufacture. Initially, pharmaceutical and specialty chemicals may be good test cases.

²¹ P Suresh, P. K. Basu. Improving Pharmaceutical Product Development and Manufacturing: Impact on Cost of Drug Development and Cost of Goods Sold of Pharmaceuticals. J Pharma Innov, 3, 3, (2008)

3.4.3 Assessment and Stocktake of R&D capabilities

The expertise this programme would draw on broadly falls into six areas:

- Domain specific expertise in pharmaceuticals and chemicals (ICES), and precision engineering / aerospace (SIMTech, IMRE) including both manufacturing technologies and measurement methods relevant to manufacture and process development;
- Devices for data collection (IME, SIMTech, ICES);
- Data analysis methods – statistics, chemometrics, pattern recognition, data mining (ICES, I²R);
- IT integration, data warehousing, information transmission, storage and access, data integrity (DSI, I²R) ;
- Decision making (SIMTech, ICES) and
- User interface design (I²R)

Additionally, substantial local university expertise is available locally. In the area of knowledge management this includes the NUS Knowledge Management Laboratory and the Institute for Systems Science, the NTU School of Communication and Information (Knowledge Management Research Cluster, Digital Intelligence Research Cluster and Knowledge Organisation Research Group). Intelligent machines in manufacturing is an area that the NUS Centre for Intelligent Products and Manufacturing Systems (CIPMAS) can contribute to, mostly in the area of mechanical engineering.

The specific challenges to address would include the following.

- Design of advanced measurement devices to capture rich data (fast and/or multivariable and/or spatially distributed) from processing/manufacturing equipment at low cost and suitable for use in hazardous environments;
- Rich data collection in laboratory/prototype manufacture to improve manufacturing performance and reduce time to market, through both gaining more understanding early in the product life cycle and ensuring that laboratory/prototype measurement devices are also suitable for use in manufacture;
- Enhanced quality control in short production runs by linking rich processing measurements with prior knowledge obtained from laboratory, modelling or other sources;
- On-machine processing of the (rich) data collected to identify problems and to facilitate subsequent analysis/data mining;
- Intelligent agents to mine data and search for events and behaviours outside those expected or known, and/or to support/refine existing models of the process;
- Linking process models, data sources and archives to real transactions, e.g. scheduling, supply chain management, design, troubleshooting; and
- Integration of an information support system based on this that allows users to make maximum use of available information.

Clearly there are many organizations developing advanced instruments, corporate IT systems. Some companies have used major software suppliers

to deliver bespoke systems that provide relevant IT capabilities. For example, Pfizer's Catalyst data sharing system was provided by Microsoft. However, the integration from sensor to enterprise is not to our knowledge addressed in a coherent way anywhere. Some relevant "competing" activities are as follows.

Intelligent Manufacturing Systems (IMS) is an international organization looking at manufacturing technology innovation, and has been associated with projects such as Acceleration of Innovative ideas to Market (AIM) and Advanced Decision Support System for Chemical/Petrochemical Manufacturing Processes (CHEM). Both of these were EU-funded consortium projects. It appears that the consortium passed through a quiescent period but phase II was launched recently. Given that IMS is an open international partnership it would be logical for Singapore to join/participate through the vehicle of the proposed programme.

Singapore has an inherent advantage in providing an integrated solution because of the proximity of RIs, mechanisms for cross-disciplinary work and the proximity of many potential users. The skill sets available from the RIs mentioned above are an excellent starting point for the programme – there are no major gaps in capability.

3.4.4 Recommended Programme Roadmap and Milestones

The programme will develop the techniques for at least two locally important industry sectors, demonstrating the capability in "pilot" form at the collaborating RIs. The sectors could be pharmaceuticals and aerospace. It is expected that this work would bring benefits that would be available from two to three years onwards, though to provide a complete approach will take much longer, up to 10 years. This work would potentially benefit all business functions from marketing through product and process design to manufacture and end of life, but the direct effects would be in manufacturing.

Unlike the other programmes recommended, this research does not lack enabling capabilities. The key to this programme is choice and integration of appropriate technologies, and the accompaniment of an appropriate business model.

Rather than a technology roadmap, the panel recommends milestones to construct a research programme:

Eight milestones have been identified as key to the Programme:

1. Identification of at least two industry sectors to demonstrate the technology, e.g. pharmaceuticals, precision engineering;
2. Design of a number of pieces of "smart equipment" with on-board data collection and "learning" capability;
3. Demonstration of that equipment under realistic processing conditions;



4. Identification of a number of typical industrial transactions that are data and knowledge intensive, e.g. troubleshooting, process design, process control in a complex system;
5. Analysis, design and implementation of IT systems to collect and analyse data from measurements (laboratory and plant), modelling, prior knowledge for the selected industrial transactions;
6. Definition of key issues for user-system interaction;
7. Design of user interface for chosen transactions; and
8. Demonstration of transaction on pilot system.

3.5 Biological Manufacturing (Tissue Engineering) Programme

3.5.1 Description of programme

Biological manufacturing refers to the making of materials and devices for medical use. Today, the major categories of biomedical products in the market are: implant devices, tissue engineering (regenerative medicine), Sensing, and drug delivery systems. Among the four types of biomedical technologies, implant materials is perhaps the most successful in terms of commercialization success. The manufacturing of implants materials are mostly based on traditional processing techniques such as injection moulding and rapid prototyping technologies. In the area of biosensor and delivery systems, the fabrications of these devices are mostly based on the Silicon-chip processing technologies, and there have been some activities towards the commercialization of these devices in Singapore.

However, there has not been an active effort towards the manufacturing of tissue-engineered products. This report focuses on the manufacturing issues in tissue-engineering.

Although artificial implant is a common therapy today, its effectiveness over the long term remains a challenging problem. Often times secondary surgery is needed to replace the implant devices, this is not only costly to the patient but is also associated with higher risk for post-surgery recovery. Consequently, regenerative medicine (tissue engineering) is becoming a preferred therapy whenever possible. However, the commercialisation of tissue engineered product remains challenging. A roadblock to the commercialization of these products, include yet-to-be-proven clinical success and more importantly a cost effective way to scale up for mass production. To achieve this, there is a need for cell biologists to work closely with engineers or industries to consider manufacturing challenges even at the research stage.

This program aims to develop technology to realize tissue manufacturing in Singapore, by addressing the manufacturing problems inherent within each part of the tissue manufacturing value chain, including cell source, scaffold manufacturing, and growth factor.

Figure 8. Tissue Engineering Value Chain



The cell synthesizes matrices of new tissue, while the scaffold provides the appropriate solid support for the cell and the growth factor promote the cells to regenerate new tissue. Each of the value chain has its own sets of manufacturing challenges, as described below:

Cell source or cell-based products

There are a variety of different sources of cells used for tissue engineering for example autologous (patient's own cell), allogenic (donated by another person) and xenograph (from an animal). In allogeneic cell therapy, regardless of the source or type of cells, a required step before the cell is useful is to expand the cell numbers by cell culturing in a bioreactor. Generally the bioreactor must satisfy the requirements of a tightly controlled environment conditions, with efficient nutrient supply and appropriate mechanical stimuli. While the above mentioned requirements are generally well understood and reasonably well controlled in the lab-scale, there are unaddressed manufacturing issues:

- Product yield: balance between cell growth and proliferation;
- Product quality: culture-induced phenotypic, genetic or epigenetic changes;
- Multidimensional optimization needs real-time measurement, for instance, the use of mass spectrometry to quantify hundreds of proteins in parallel allows for culture system optimization. Other techniques include optical measurement technologies and flow cytometry for surface antigens;
- In-process testing at different points in the manufacturing line: cell banks, cell-seeding during expansion/differentiation of cells and cell seeding. Lab-scale testing of cell properties is most often done in 'open' culture media; this 'format' of testing is not suitable for integration into a manufacturing line. Alternative test 'formats' will be needed for in-process testing for 'closed' systems.
- Final product testing: viability, purity, potency
- Delivery: sterile containers, media for cell preservation and shipping media.

Scaffold products

The pre-requisite of scaffold products are biocompatibility and biodegradability. The technical challenge in this area is the production of scaffolds with controlled porosity, mechanical strength and 3-dimensional structures. Common manufacturing issues include:

- Integration of computer aided design in the processing line, especially with the increasing trend in personalized therapy;
- In process testing: porosity control;
- Final product testing: geometry, physical and mechanical tests.

Growth factors

While growth factors are cell signalling molecules, their production is more akin to pharmaceutical processing technology, which can be adapted from the pharmaceutical industries. However, potential production issues include biological activity, protein stability, and aggregation.

In addition to the above-mentioned challenges in the individual value chain, integration of three parts of the value chain to achieve a more readily usable tissue engineering product poses another set of manufacturing challenges.

3.5.2 Economic and technological opportunities and impact

The current market for tissue engineering products is in the area of skin, bone and cartilage. According to open access data, the market for tissue engineering products was estimated to be about 1 billion USD in 2007 and was expected to have a compound annual growth rate of more than 20%. The market is dominated by the U.S. and Europe, but the demand from Asia is expected to grow substantially.

Tissue manufacturing represents a potential new growth engine for the biomedical sciences cluster in Singapore. In addition, it is clearly multidisciplinary, requiring capabilities in materials, bio and chemical processing, and three-dimensional design and simulation.

3.5.3 Assessment and Stocktake of R&D capabilities needed

Competitive landscape viz key research groups globally

Tissue engineering has been a research area that has attracted significant investments especially in Japan and US.

In Japan, the Cell Sheet Tissue Engineering Center (CSTEC) is a public-private partnership programme to address the manufacturing of cell sheets for tissue engineering. The technology started as a photopolymerized scaffold with promising tissue engineering potential – it is called cell sheet because of the multilayer structures that gives it a three-dimensional structure. The project is now funded by the Japanese Ministry of Education, Culture, Sports, Science and Technology (MEXT) and the Japanese Geothermal Energy Development Department (NEDO). It consists of three industrial partners that constitute the value chain of cell sheet manufacturing: CellSeed (for cell culturing), Dai Nippon printing and Olympus. The manufacturing issues being addressed include automatic cell-culture container and dish traceability, and mass production of the thermo-sensitive dish.

In the U.S., the *Advanced Technology Program* (ATP) on tissue engineering under NIST was started in 1999 with a fund of about USD 50 million from the U.S. government agency with nearly equal fund from industrial partners.

Research challenges and gaps viz capabilities which need to be developed

In this programme, cross-cutting technologies from A*STAR's BMRC and SERC, and the universities are needed to address the challenges facing the realisation of lower cost tissue manufacturing. These challenges and the respective potential contributing institutes are listed in

Table 9.

Table 9. Matching of SERC RIs with research challenges

Challenges	Potential R&D topics	Institute with relevant capabilities
❖ biocompatibility of implants	❖ new materials, bio-based materials	❖ IMRE, ICES, IBN
❖ 3-D scaffold	❖ surface texturing ❖ 3-D fabrication	❖ IMRE, SIMTech
❖ Non-standard scaffold geometry	❖ Computer aided design	❖ IHPC
❖ in-process testing	❖ integrated analytical techniques	❖ IMRE, ICES
❖ Cell expansion	❖ Scaleability of culture systems	❖ BTI ²²
❖ Differentiation	❖ Purity and functionality of differentiated cells ❖ Functionalised surfaces and ligands for differentiation	❖ IMB, BTI
❖ Purification	❖ Negative selection of embryonic stem cells and positive selection target cells	❖ BTI
❖ Preservation	❖ Large scale stable preservation of differentiated cells for delivery, low toxicity	❖ None, except in NUS

Finally, the most important success criteria is a close collaboration between clinicians, cell biologists, material and process engineers even prior to the pre-clinical study stage.

General References:

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²² Bioprocessing Technology Institute

Chapter 4 Conclusion

This report has recommended a set of research thrusts to develop important new capabilities for manufacturing. In deliberately taking a horizontal cross-sectorial view, the panel anticipates that these capabilities will enable the creation of new manufacturing activities that have high knowledge content, use highly integrated supply chains, employ a highly skilled workforce, utilize cutting-edge production technology, and have environmentally friendly life-cycles. In particular, the panel notes that recommendations from concurrent panels, looking into Health, Wellness and Aging and Urban lifestyles have yielded recommendations for a research into a portfolio of products, the economic delivery of which will depend crucially on the ability to manufacture nanotechnology based products, microfluidics and alternatives to electronics manufacturing such as printable electronics.



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High Value Manufacturing Panel Recommendations for Research Thrusts

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Acronyms and Abbreviations

A*STAR	Agency for Science, Technology and Research, Singapore
AFM	Atomic force microscopy
AIM	Acceleration of Innovative ideas to Market
ATP	Advanced Technology Program
BEEM	Ballistic electron emission microscopy
BMRC	Biomedical Research Council, A*STAR
BTI	Bioprocessing Technology Institute , A*STAR
CAGR	Compound Annual Growth Rate
CHEM	Chemical/Petrochemical Manufacturing Processes
CIPMAS	NUS Centre for Intelligent Products and Manufacturing Systems
CSTEC	Cell Sheet Tissue Engineering Center
DSI	Data Storage Institute , A*STAR
EDB	Singapore's Economic Development Board
ETPL	Exploit Technologies Pte Ltd, A*STAR
GDP	Gross Domestic Product
HVM	High Value Manufacturing
I2R	Institute For Infocomm Research , A*STAR
IBN	Institute of Bioengineering and Nanotechnology , A*STAR
ICES	Institute Of Chemical And Engineering Sciences , A*STAR
IHPC	Institute Of High Performance Computing, A*STAR
IMCB	Institute of Molecular and Cell Biology, A*STAR
IME	Institute Of Microelectronics, A*STAR
IMRE	Institute Of Materials Research And Engineering, A*STAR
IMS	Intelligent Manufacturing Systems
IMTEK	Department of Microsystems Engineering – Germany (Institut für Mikrosystemtechnik)
IP	Intellectual property
IT	Information technology
MEMS	Microelectromechanical systems
MEXT	Japanese Ministry of Education, Culture, Sports, Science and Technology
MIT	Massachusetts Institute of Technology, Massachusetts, U.S.A
MMC	NTU MicroMachines Centre
MRO	Maintenance, Repair and Operations
NanoCluster	NUS Nanoscience and Nanotechnology Cluster
NEDO	Japanese Geothermal Energy Development Department
NIST	National Institute of Standards and Technology
NNI	NUS Nanoscience and Nanotechnology Initiative
NTU	Nanyang Technological University, Singapore
NUH	National University Hospital, Singapore
NUS	National University of Singapore, Singapore
OPVs	Organic photovoltaics



PAT	Process Analytical Technologies
POF	Picture of the Future
R&D	Research and development
RI	Research institute
S&T	Science and technology
SERC	Science and Engineering Research Council, A*STAR
SIMTech	Singapore Institute of Manufacturing Technology, A*STAR
SMA	Singapore–MIT Alliance
STM	Scanning tunnelling microscopy
STVC	Science and Technology Value Creation
TSRP	Thematic Strategic Research Programme
VIP	Visiting Investigator Programme