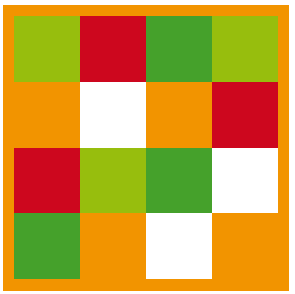

Unity

I Introduction

This book is about life sciences in the Netherlands – past, present and future. It looks back at what has been achieved, and ahead to what the life sciences may mean for our society and economy in the future. But most importantly, it takes a close look at ourselves – scientists, researchers, business men and women, entrepreneurs, citizens, consumers, innovators – and to what we can do to build on today's strengths and deliver tomorrow's promise.

This book is about innovation. It is about policy. It is about partnership. In the life sciences, you will not achieve much on your own. Life sciences innovation involves a chain of connected activities that typically takes more than fifteen years. Knowledge must be *generated, translated* into practical applications, and *delivered* in the form of products, processes and services that are actually used in real life. This chain stretches from basic research in academia to R&D in corporations and start-ups, to safety and efficacy tests, to prototyping, regulatory approval, production ramp-up and up-scaling, market introduction and more. To be successful, you need partners.

This book looks at the entire chain, but with a particular focus on where partnership has come to play a vital role: public-private partnerships. Since the turn of the century, the Netherlands has seen collaboration between academia, business and government occur on an unprecedented scale. In these public-private partnerships (PPPs), science and business come together. Basic science is translated into practical applications that can then be delivered into the hands of private and professional users, thus realizing social and economic value. Accounting for 40% of all PPP investment in the Netherlands, the life sciences exemplify the purpose, character, successes and failures of the public-private partnership model.

This book itself is a testimony to partnership. Much of the life sciences community has come together to write it. The book embraces many shapes and sizes, with (scientific) disciplines, market sectors, and public and private players uniting in a shared vision of the future, and of what public-private partnership can do to help make that future a reality. We invite you to join the discussion and share in our commitment to achieving the social and economic value that the life sciences promise.

Before we embark on our journey through the life sciences and the public-private partnerships of yesterday, today and tomorrow, we will provide some background: the life sciences and the socio-economic challenges they address, public-private partnerships, the concept of a single "bioregion" and the setup of this book.

A. Life sciences

We have entered the life sciences age. Increasingly, living organisms and biological processes are used to develop and deliver products, processes and services that improve our quality of life. This, in itself, is nothing new. We have used yeast for thousands of years to make bread and beer. But in the last 40 years or so we have made vast leaps in our understanding of life and its building blocks: cells, the molecules that make them, the proteins that are their workhorses and especially the DNA that is the code of life.

Our definition of life sciences
The studies of living organisms and biological processes and their use to develop products, processes and services that have social and economic value

The next wave of entrepreneurial activity

In 1953, James Watson and Francis Crick described DNA's double helix structure. Scientists have since unraveled its genetic code, have learned how to change and reproduce it, and how to insert bits and pieces into various organisms. This has created an undreamed-of toolbox that can help us manipulate and utilize (parts of) organisms for the benefit of humankind.[1] The use of this toolbox is that part of the life sciences called biotechnology.

The applications are many. The first biologically made drug was approved in 1982: human insulin produced in genetically modified bacteria. Today, about 120 biopharmaceuticals have obtained market approval and two are among the top 10 drugs sold today.[2] Tailored microorganisms are now used as small factories in a range of industries, producing products like chemicals, biofuels, pharmaceuticals, cosmetics and food ingredients. In 1997, the first weed and insect resistant crops made their way to the market. Today, crops improved through breeding techniques which were made possible thanks to the life sciences grow throughout the world.

Food, health, agriculture, chemicals & energy – all of these sectors are served by the life sciences. Together, these sectors account for over EUR 200 billion, well over a third of total GDP in the Netherlands. Their application of the life sciences is growing rapidly and is often combined with other new and existing technologies to develop and deliver products, processes and services. Worldwide revenues of dedicated biotechnology companies alone exceeded USD 85 billion in 2007 and are growing by 17% per year.[3] That is just from companies doing nothing but biotech. Factor in the widespread use of fermentation in large chemical companies, or the biologics divisions of big pharmaceutical companies, and the total commercial application of the life sciences is extraordinary. If the 90s belonged to Silicon Valley and dot.coms, then the 21st century belongs to life sciences entrepreneurs. It is the next big wave of entrepreneurial activity (Figure 1).

Addressing the big questions together

Food supply, chronic diseases, energy security and climate change – these are the major challenges of our time. We need to find ways to feed a world population that is projected to grow to more than nine billion by 2050, when nearly one-sixth of today's 6.8 billion are already hungry and undernourished.[4] We need to care for and treat an ageing population, increasingly suffering from chronic diseases like cancer, diabetes and dementia. In the Netherlands alone, current trends point to rises of up to 40% in major chronic diseases by 2025.[5] Our energy demand is expected to grow by 44% from 2006 to 2030, while fossil resources are limited and often come from unstable parts of the world.[6] Last but not least, all of this places a huge burden on our environment. We need to meet our food, health and energy needs responsibly – i.e. safely and sustainably: protecting ecosystems, humans and animals, and reducing energy consumption and greenhouse emissions.

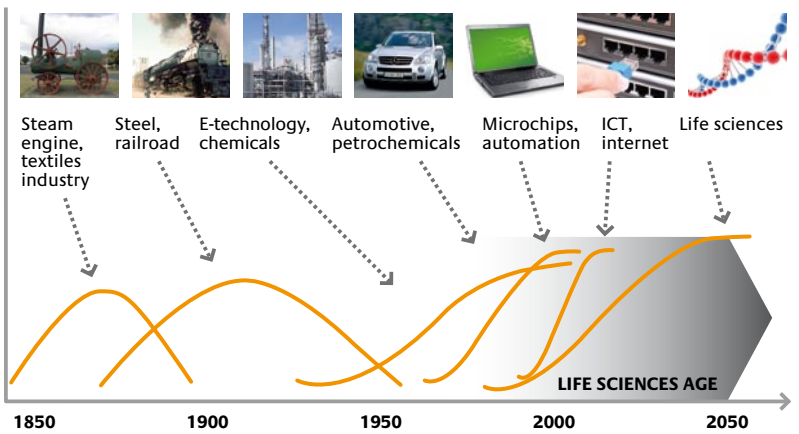

Figure 1: Waves of entrepreneurial activity

Life sciences promise to play a major role in overcoming these challenges. They are revolutionizing plant breeding in agriculture, building resistance against climate and disease and increasing yields while reducing the need for fertilizers and pesticides. They are improving the taste and nutritional value of food. They are increasingly employed in the discovery, development, testing and production of new diagnostics, drugs and medical devices. They are an important enabler in the sustainable production of energy, chemicals and materials, with less energy use and less harmful emissions of greenhouse gases.

These are not separate challenges. They impact each other and none can be resolved in isolation. What is more, they require multidisciplinary solutions in which several sectors work together utilizing the full breadth of their technology base. A good example can be found in the health challenges we currently face. As healthcare depends increasingly on prevention (e.g. diagnosing risk factors, countering and containing them), diet has become a major factor. Food companies can make healthier foods, or better tasting healthy food. The health sector can help food companies better understand and tailor their foods to dietary needs. Agriculture also plays a role. A recent Dutch innovation

The importance of social studies

The life sciences not only provide solutions to challenges of today and tomorrow. They also, like many new technologies, raise new questions and create new risks – many of which we cannot foresee today. The effects of the new life sciences and technologies (including benefits and risks, but also possible changes in social relations) need to be identified as quickly as possible. Once identified, scientifically-founded and democratically legitimate and acceptable policy choices can be made. We propose that "social programs" accompany all life sciences initiatives. Such programs begin with the observation that knowledge, risk and benefit mean different things to different people and in different contexts. By exploring such multiple meanings and interests, social programs will generate debate on the social impact of life sciences innovations. Innovations cannot exist without being embedded in society, and interactive involvement of various relevant social groups in such debates will improve the success rate of innovations. This does require a joint, multidisciplinary and public approach in which the innovators take the lead, but in which they are prepared to listen to outsiders and to consider adapting their designs.

grew tomato with a high concentration of antioxidants that may play a preventive role against cancer.

That same multidisciplinary approach is needed to secure our energy supply and petrochemical industry while preserving the environment. There are many sustainable alternatives to fossil resources, but neither sun nor wind contains the molecules needed to make chemicals and materials. Biomass is a promising solution. It can be eaten, turned into energy, fermented into biofuels or separated through biorefinery into building blocks for pharmaceuticals, base and specialty chemicals, and materials. This requires a joint approach by the agriculture, chemicals and energy sectors, combining life sciences technologies with others, like catalytic and separation technologies, thermochemical conversion and process engineering, and resolving competition issues with the use of biomass for food supply.

A blend of colors

These four sectors – food, health, agriculture and chemicals & energy – are not only connected by their application of life sciences, they are also united by the technology itself. All base themselves on the same (biological) principles and processes. All employ the same toolbox of genomics (genes), proteomics (proteins), metabolomics (cellular processes), bioinformatics (data processing), systems biology (integration) and more. As such, they are all "biotech". The use of life sciences techniques in health is commonly referred to as "red biotechnology", in chemicals & energy as "industrial" or "white biotechnology", and in agriculture and food as "green biotechnology" (although in this book we shall distinguish between "dark green" agriculture and "light green" food to reflect both their commonalities and differences).

However, as clear as the similarities or the need to collaborate may be, an integrated approach is far from simple. Sectors have very different dynamics. The chemicals sector is based on large-scale industrial processes and carefully optimized, global supply chains, whereas agriculture relies on local environmental conditions and is accustomed to wide supply variations due to seasonality and unpredictable harvests. Even within sectors the dynamics can vary. The health sector, for example, is tightly regulated and dominated by (semi-)public institutions. But within this sector, medical devices must satisfy other criteria than drugs for market approval. Food companies wishing to introduce healthy foods may not relish the thought of having to first undergo lengthy trials. On the other hand, they operate within a consumer industry more exposed to (bad) publicity and fickle tastes than others.

These sectors are thus united in diversity. Bound together by applications and underlying life sciences, but each with its own path to take and story to tell. This book presents both.

B. Public-private partnerships

Innovation is a lengthy and risky process requiring large investments over time. This holds especially true for the life sciences, where the path from scientific breakthrough to marketable application is typically 15 years or more for all sectors. Chances of success are often low, investments high and the range of knowledge and competences required wide and varied. It is all but impossible for a single company or research group to realize a life sciences innovation from beginning to end alone. Cooperation is vital. Note that for simplicity we often sketch a somewhat linear process of innovation. In reality, it is not linear at all. It is an iterative process, it branches, sometimes steps are skipped, sometimes repeated and knowledge from innovations on the market is used for the development of others. This last characteristic has made some people refer to innovation as a cyclic process.

Innovation is sometimes described as a three-stage rocket: you need basic science in the first stage to achieve lift off; in the second stage you apply science to real-life problems, propelling you into the "orbit" of markets and companies; and in the final stage the "payload" – a new or improved product, process or service – is delivered to end users. In the Netherlands, the first stage, basic science, is first rate. Dutch science ranks in the top three worldwide in terms of scientific impact – and fields relating to the life sciences are among our top performers.[7] We are, however, not so successful in the final stage: delivering innovations to markets, realizing their value to users and society and making money off of them. Here we are a follower at best,[8] and this may be due in part to failings in the second stage.

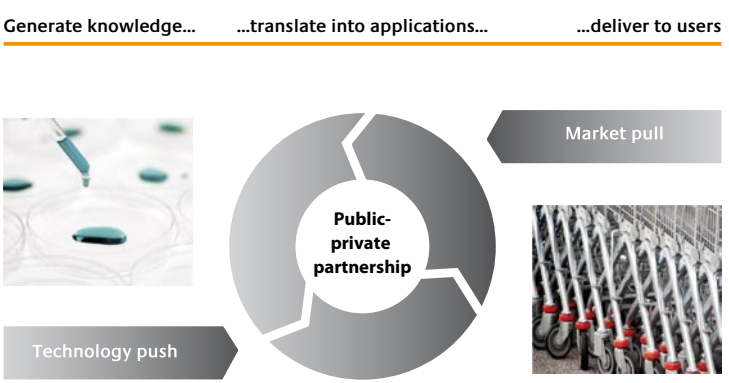

Figure 2: Public-private partnerships combine technology push with market pull

Basic science is the domain of academia: universities, university medical centers and (semi-)public research institutes. It is public and publicly funded. Markets and (large-scale) production are the province of industry – the private sector. To develop and deliver innovation successfully you often need both, and the second stage, where scientific knowledge is translated into marketable applications, is where they meet.

The second stage is absolutely key. You cannot just give ready-to-use academic knowledge to industry. It has been tried. It does not work. It is too much like trying to force a square peg into a round hole. You need more than a simple handover, which is why the second stage must in some sense be transformative, creating practical applications of cutting-edge science and technology that are of value to real people. That means combining the technology push from academia with the market pull from society and industry (Figure 2). It also means (intense) collaboration between public and private players. This is never easy, and results are neither certain nor predictable. Innovation is more intractable than that. However, if not a sufficient condition, it is a necessary condition that the public and private domains of science and enterprise meet and interact.

It is in the space of this second stage that public-private partnerships were conceived. Over the last decade these so-called PPPs have taken major leaps in the Netherlands.

In PPPs, academia, industry and government join forces to translate basic science into marketable applications with social and economic value. Public-private partnership can take many forms: it can be one-on-one; it can involve many parties, from large corporations to small and medium-sized enterprises (SMEs), from universities to (semi-)public or private research organizations, from charities to governments; it can be physical, co-locating teams of researchers on a single campus or in a single building; it can be virtual, combining the efforts of researchers from different organizations and locations; or it can be something else entirely. Although there is no single definition of PPPs and we will not attempt to develop one, all PPPs share a number of traits:

- They are **collaborative** – one partner does not simply pay another for a piece of research or to do a job; rather, partners work together and contribute knowledge and resources;
- They are **precompetitive** – research has clearly progressed to a focus on commercial application, but not to the point where a single company will demand exclusivity;
- They are **partnerships** – partners share the risks and the rewards, all contribute their share of funding (be it cash or in kind) and all receive their share of the intellectual property generated.

PPPs serve different purposes and have different advantages and disadvantages for individual stakeholders. Typically, for industry, they involve a trade-off between leverage (government matching of funds) and exclusivity (pre-competitive, sharing IP). In academia, a balance must likewise be struck between opportunities for additional funding and the threat of withdrawing scarce resources from basic research. Government, meanwhile, wants to see the different parts of the innovation chain connected and resources concentrated on areas that are important for society. It wants to give direction without infringing on the judgment and entrepreneurship of either academia or industry, and without creating a "subsidy fest".

PPPs are especially suited to the life sciences, with their long development horizon, multidisciplinary nature and collaborative, "open innovation" paradigm. More than EUR 2 billion has been committed to Dutch life sciences PPPs over a period of approximately five years. That is more than 40% of all PPP investment in the Netherlands,[9] which is why the life sciences are a good place to study PPPs as a model for innovation. Now is a good time, too. The life sciences PPPs are gaining momentum and starting to deliver results. Other countries are taking note, following the Dutch model as a best-practice example.

In this book we review the history and origins of PPPs, draw lessons from our collective experience in setting up and operating these PPPs, and describe the challenges we see ahead of us. Although it may be too early for a final evaluation of the PPP model, we believe both the life sciences themselves and society at large will benefit from the critical review in this book. Government has played a crucial role in realizing the PPPs, matching the investments made by academia and industry. That is tax money. It is time that we explain what we are doing with it and why we think it was wisely invested. Moreover, we hope that our successes and failures, and the lessons and recommendations we present, will be of value to government in future policy and funding decisions.

C. One bioregion

The Netherlands is well-positioned to play a leading role in the life sciences age. As we pointed out before, our knowledge base is excellent – among the best in the world. What is more, the industry sectors impacted by the life sciences have a strong presence in the Netherlands. Our plant breeding industry is a global leader. We are the petrochemical gateway to Europe, with one of the strongest chemical and energy sectors on the continent. Our medical infrastructure and academic hospitals are world-class, and we have a dynamic and fast-growing pool of biotech entrepreneurs. We are home to some of the most innovative companies in food and food ingredients. Uniquely, all of this is located on just 42,000 km^2. That is only about double the Bay Area, the Massachusetts life sciences cluster or Denmark's "Medicon Valley". The Netherlands is packed with not one, but several life sciences-intensive sectors, thirteen universities and an unparalleled number of public-private partnerships. In this book we will argue that the Netherlands should be seen as one "bioregion": a single cluster, with a strong tradition of (multidisciplinary) cooperation.

The Dutch polder model is being renewed and applied to innovation in the life sciences PPPs. One lesson of successful (innovation) clusters is not to try to do everything, but to concentrate energy and resources on a select few topics. This creed is commonly summarized as "focus and mass". That is the future we see for the Netherlands: the life sciences polder. A small country with excellent science, strong sectors and real partnership in a multidisciplinary field with huge social and economic promise. In this book we will show why that is both desirable and achievable, and we will set out the routes to reach this goal.

D. This book

This book is about life sciences in the Netherlands. It is about partnership. It is about what can make a small country great. Obviously, we will talk about more. The life sciences cannot be seen in isolation from other technologies or the industry sectors they serve. Public-private partnerships should not be separated from the larger innovation system of which they are part. Basic research is crucial. Its excellence needs to be sustained and its interaction with and participation in PPPs secured. Industry needs to take an active and leading role to take PPP results and bring them to users and markets. (Small, new) entrepreneurs will be a major factor in realizing innovations through new ventures and new business models. Nor are we alone. The life sciences field is an international field, with other countries, companies and universities both competitors and potential partners. But like the life sciences, we have chosen focus and mass: *life sciences PPPs in the Netherlands*.

This is a book in two parts. This, the first, reflects on the impact of life sciences on our lives and the past, present and future of Dutch life sciences PPPs. Chapter II will sketch our world in 2020. What will life be like if the life sciences deliver on their promise? This chapter will be a pastiche of images. Not predictions or ironclad guarantees, but likely future applications and directions. We are not attempting to be 100% accurate or exhaustive. Chapter III is devoted to a case study of Dutch life sciences PPPs. Where did they come from? What have we learned? What challenges await? We will describe successive generations of R&D and innovation policy, draw lessons, point out trends and next steps, and lay out the main recommendations. Chapters II and III are each self-contained and can be read independently from each other. We invite you to read them in the order that you see fit, or pick the one that most interests you.

After these "overview" chapters, individual life sciences sectors will present their perspectives in Part II of this book. Part II will describe in more detail where the sectors are going and how PPPs may help them get there. Each life sciences sector (food, health, agriculture and chemicals & energy) will tell its own story. These stories are bound together by "cross-links" – common elements that unite and span the sectors: enabling technologies, education & training, valorization and social aspects. Each cross-link has its own chapter in Part II. The book concludes with a postface written by Herman Wijffels. Throughout this book, stakeholders from politics, industry, academia and society are invited to share their thoughts about this book, the life sciences, PPPs, or anything else they wish to share.

This book is both a tribute to and an exercise in partnership. It is a polder or an ecosystem in itself, inhabited by different "breeds" and perspectives and benefitting from both their unique contributions and collaboration. We hope this book shows both the unity and diversity of the life sciences. Many people from the many sectors of the life sciences field came together to present a single vision and ambition, to paint the future. Even if not everybody sees it in the same shades or agrees on all details, this book provides a clear and shared sense of direction and a powerful base and stimulus for (continued) collaboration. It is meant to unite and inspire.

Finally, this book is dedicated to you: our fellow citizens, our prospective customers, the people we hope will benefit from the innovations we foresee. We will account for the public funds entrusted to us. We will tell you how they are spent and why we think they are well-spent. And we will offer our experience to the government. Throughout the book we will share recommendations and lessons learned in the hope that this may inspire and support future decision makers in setting policy and allocating funds for innovation – whether in the life sciences or beyond. We invite everybody to join the discussion and contribute to realizing our shared vision.

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A job half done

This is an important book. This book shows that impressive results have been achieved in stimulating innovation in the life sciences in the Netherlands in recent years. There is every reason for Dutch policymakers, Dutch knowledge institutions and private companies to congratulate themselves on half a job well done. Through cooperation and investments from all parties, the groundwork has been laid for a sector that may well develop into the preeminent bioregion in Europe in the years to come. TNO is a proud member of many of the public-private partnerships that together form this Dutch bioregion. Its mission, to help turn fundamental research into innovations that benefit society, aligns perfectly with the mission of life sciences PPPs. In the next phase of the life sciences PPPs, TNO aims to expand on its ambition of valorizing the scientific results obtained in PPPs.

The main value of this book is, however, that it reveals that the job is only half done. The groundwork has been successfully laid, but unless we keep fostering innovation in the life sciences, we will not reap the rewards. Continuity of commitment and investment and the willingness of all partners to keep cooperating are key to future success. This book shows how we can successfully finish the job we started. We all, government, knowledge institutions and private companies, should follow its advice and recommendations. ”

Tini Colijn, Member of the TNO Board of Management

Diederik Zijderveld, Director of Research at TNO Quality of Life

Quote from Tini Colijn ...

... and from Diederik Zijderveld