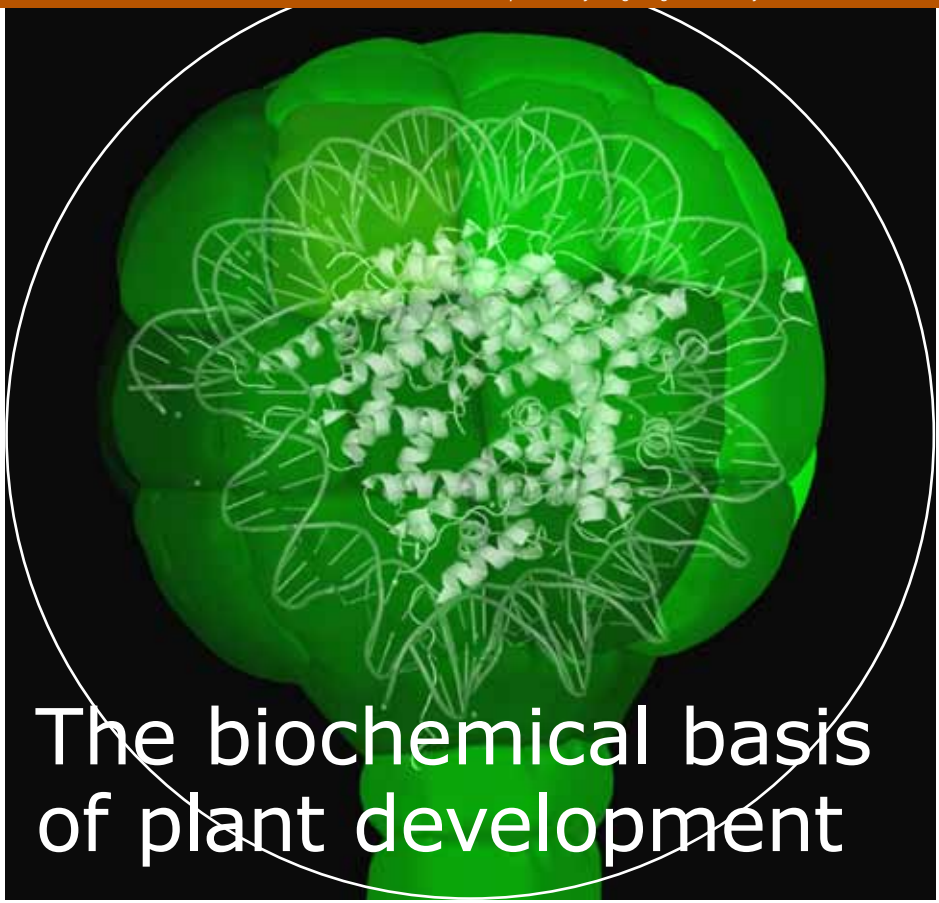

The biochemical basis of plant development

Prof. dr Dolf Weijers

Inaugural lecture upon taking up the post of Personal Professor of Biochemistry of Plant Development at Wageningen University on 13 June 2013

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Dear deputy rector, colleagues, friends, family, ladies and gentlemen,

You probably have not realized that the invitation you have all received is a symbolization of one of the biggest challenges in the study of living systems. And when I say living systems, I mean all living systems. Although this may sound strange, the same problem applies to the study of life at the level of molecules and cells, and the level of animals, plants and their ecosystems. The problem I refer to is that of linking the scales.

Scales in the living world

There is probably no better way to illustrate this problem than to show you an excerpt of a film made by people at the company IBM in 1977, called "Powers of ten" (www.youtube.com/watch?v=ofKBhvDjuyo). In this film, every few seconds we zoom in one order of magnitude, or power of ten, deeper into the skin of the hand of a man that takes a nap after lunch. As we dive deeper into this man's hand, we encounter the skin, a blood vessel, and within it, a white blood cell. Going deeper, we see the nucleus, which carries the genetic material, the DNA, which we can see when we enter. As we zoom in on the DNA, we start to see the famous double helix, and next we see the individual bases, or letters of DNA. Finally, we can see the carbon, hydrogen, oxygen, nitrogen and phosphorus atoms from which the DNA is built. As I hope you appreciate, we have now traveled 9 orders of magnitude, yet what we observe at the level of this quietly sleeping man, is the result of all the processes happening at the deeper levels.

To be a bit more precise: Interactions of atoms determine the structure of molecules, such as proteins. Molecules in turn can interact to make for example protein complexes, which localize to and form the cell organelles. All molecules and organelles together make the cell, while cells together build organs. Ultimately, these organs form the organism (Figure 1). In all living systems and organisms, this series of scales can be found, and in each, the higher scales are a consequence of processes happening at lower scales. One of the key challenges of the field of Biochemistry is to describe and understand how cellular and organismal properties follow from atomic and molecular scale properties and interactions.

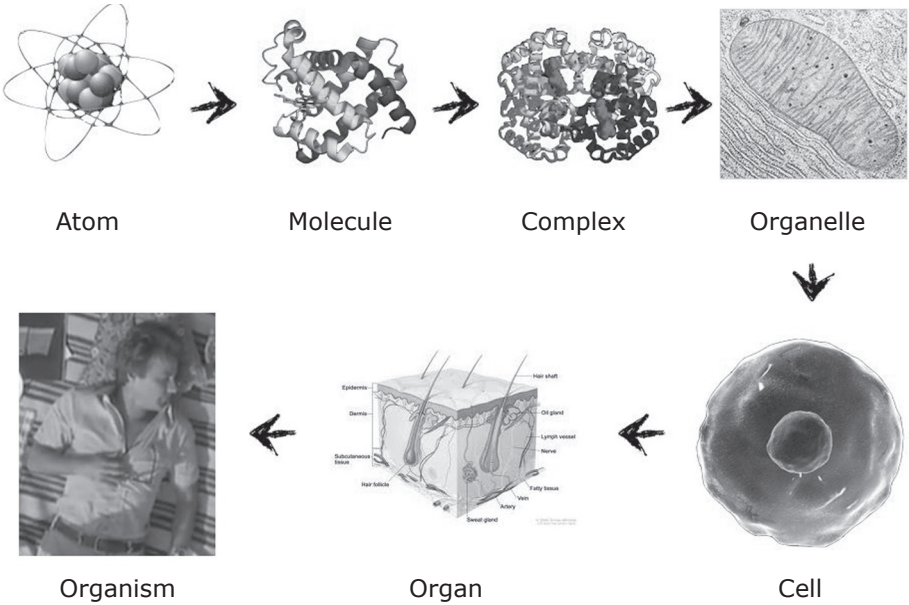

Figure 1. Scales in the living world.

What is true for the sleeping man in this example is true for any multicellular organism, and this includes the entire plant kingdom. Also these organisms are built from organs, which are made from cells that are in turn made of molecules. As I will outline during this lecture, especially this green kingdom offers wonderful opportunities to link the different scales in the living world. But before I do that, I should first explain what plants are actually made of. One advantage of studying plants is that, even though the diversity of forms and shapes is overwhelming, the diversity *inside* the plant is very limited. Whether we cut through a leaf, a stem or a root, we always find only three basic types of tissue, being from the outside to the inside: epidermis (or skin), ground tissue and vascular tissue. And this is true whether we look inside a giant oak or a tulip.

Plant stem cells

How then, can we find such amazing plant diversity if the basic ingredients are so simple and similar. Anyone who has ever sown seeds and observed how a seedling emerges from it and grows, has witnessed the power of stem cells. Even the largest plants start as a small seedling, but at the tips of shoot and root, the plant has cells that continuously divide to make new cells for new organs. By organs I mean leaves, roots, stems, flowers. It is the activity of these stem cells that is different between plant species and that sculpts the shapes we are so familiar with. Like in human and

animal stem cell systems, cell division must be very strictly regulated to prevent uncontrolled growth. In plants, this works through so-called organizer cells that sit right next to the stem cells and, as was demonstrated by professor Ben Scheres, keep the stem cells in their stem cell state (Van den Berg *et al*., 1995). Now please keep in mind that, in order to fulfill this task, the organizer cells need to sit *right next* to the stem cells.

Even though talking about stem cells in plants may sound awkward, we witness their activity every day. Not only do these cells make all the organs of the plant transforming a minute seedling into a large tree, they also are the basis behind the amazing developmental flexibility in plants. The roots that are formed on a cut stem in a vase are also the product of newly activated stem cells.

An old recipe for success

As I mentioned, despite the stunning diversity of plant forms, the basic ingredients are very simple: 3 tissue types and stem cell systems. What is even more striking is that this recipe for development is a very old one. The forest in the image (Figure 2) may seem a bit strange. The reason is that it is an artists' impression of what North America looked like about 350 million years ago, based on fossils from that period.

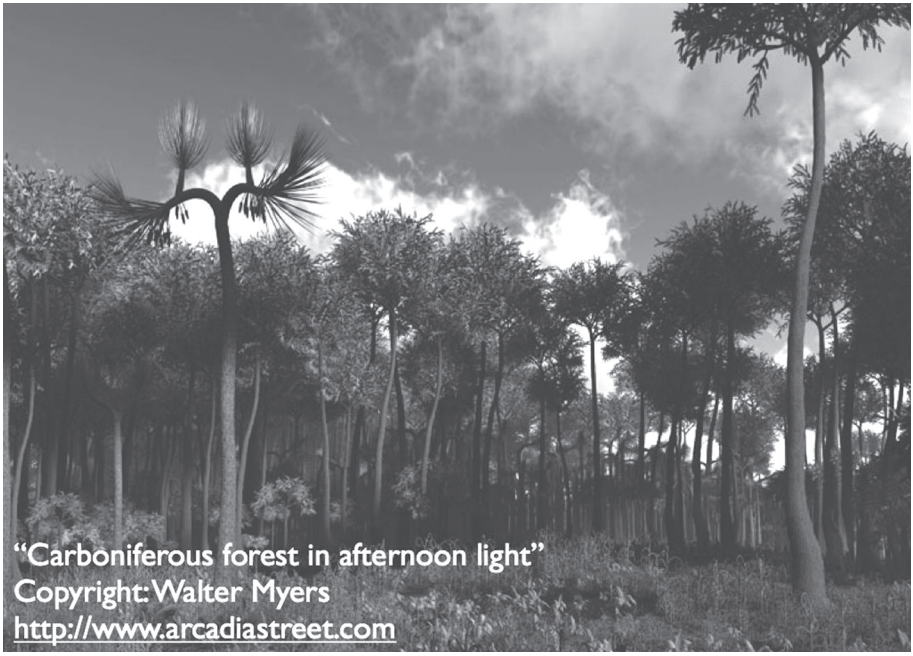

Figure 2. An old recipe for success.

Already in these fossils, one can recognize the same elements, the 3 tissues and the stem cell systems. In other words, this arrangement is a very old and very successful one, as it has been maintained for hundreds of millions of years. Therefore, if we want to understand the fundamental principles of plant development, one of the key challenges will be to define how the arrangement of tissues and stem cells is controlled. I see it the task of my field of *Biochemistry of Plant Development* to reveal how the properties of molecules in cells instruct the basic recipe for how to make a plant.

But before I will describe to you what I believe is the way we should address this problem, I would first like to remind you why it is actually a good idea to study plant development, in addition to satisfying curiosity and generating fundamental knowledge. Up to this point in my lecture, each of you has inhaled about 10 liters of oxygen. This is the amount of oxygen that the ground tissue of a decent sized tree will produce in a few hours. You have also spent the past 10 minutes sitting on the wood that the vascular tissue of a tree has produced in several decades. Plants, and plant products are everywhere, and mankind strongly depends on this. I hope you will agree with me that it is important to understand these organisms. I certainly am convinced that basic understanding of the plant building plan should help making better use of our natural resources, or to change these in rational ways.

Plant embryos: miniature models of development

I have shown you plants that look more or less familiar to you, and have made a case that we should try to understand how the atoms and molecules inside the plant cell determine development. This brings me back to the invitation you all received. Most of you have been very polite and kind in telling me that the image looks nice. Thank you. I doubt, however, that the appreciation went further than the esthetics. I will not ask how many of you recognized this as a plant, but it is. To be precise, this is a plant embryo. Like most animals, plants also reproduce sexually, by fusing an egg cell and a sperm to form an embryo. What you see in the photo (Figure 3) is an embryo of the plant *Arabidopsis thaliana*, which is found inside the seed that is in turn found within the fruit. On the left of this photo is a hair, which is a tenth of a millimiter wide. As you can see, these embryos are very small, about a hundredth of a millimiter, or 10 micrometer wide.

Why then, would I be interested in these micro plants? And how could the study of these help us forward in understanding plant growth and development?
The answer is very simple: the plant starts as a single cell. Step by step, this cell divides and develops into a larger, multicellular structure, the embryo. This gives rise to the seed, which in turn gives way to the seedling. As we have discussed, the seedling already has the characteristic tissue organization and carries the stem cells

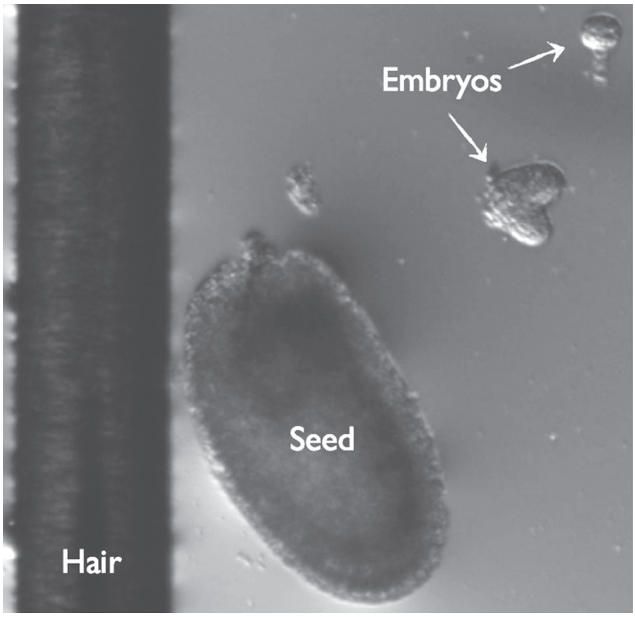

Figure 3. Arabidopsis thaliana seed and embryos.

to make the rest of the plant. In other words, sometime after fertilization, the very first tissue precursors and stem cells must be formed. The embryo model therefore allows the study of the very first formation of tissue and stem cells from scratch (Wendrich and Weijers, 2013). You could now argue that this is not unique to plants…exactly the same is true for any animal that undergoes embryogenesis. Yes, this is true, but there is one thing that is unique to plants, which, as you will see, is a major advantage when studying the control of development. Let me introduce you to an animal embryo, to be precise, the zebrafish.

These embryos grow outside of the mother's body and are transparent, which makes for beautiful microscopy. All the cell nuclei of this fish embryo (movie found at: www.youtube.com/watch?v=vslaD-mWaNA) are labeled, and you can see cells divide as the embryo grows (Keller *et al*., 2008). More and more, you see the shape of a tadpole, or fish arise. It is very obvious that nuclei are very mobile, in fact almost every cell moves through the embryo to end up in a new location. Of course, after playing the movie, we can reconstruct where every nucleus came from, but if I were to stop the movie halfway through, we have no way of telling where every cell came from, nor what it will end up becoming, head, tail or fin. In other words, there is very limited predictability, which is difficult if we want to study what happens in a cell while it changes its properties from non-specialized to for example a fin cell.

Enter the plant…unlike animals, plants build a wall around the cell to generate mechanical strength. This wall however, prevents cells from moving. The fact that cells stay in the same place adds predictability to development. In addition, particularly in the small Arabidopsis embryo, it turns out that the divisions are very stereotypical. If we make cross-sections of embryos of the same age, these are almost identical. All will have put their walls in exactly the same place. This combination of stereotyped cell divisions and a lack of migration make the Arabidopsis embryo an almost perfect, predictable model for development. These properties can be exploited to map precisely which cells give rise to what other cells, and where these ultimately end up in the mature embryo. In other words, we can predict the "fates" or "identities" of cells, and mark the trajectories that connect them (Figure 4).

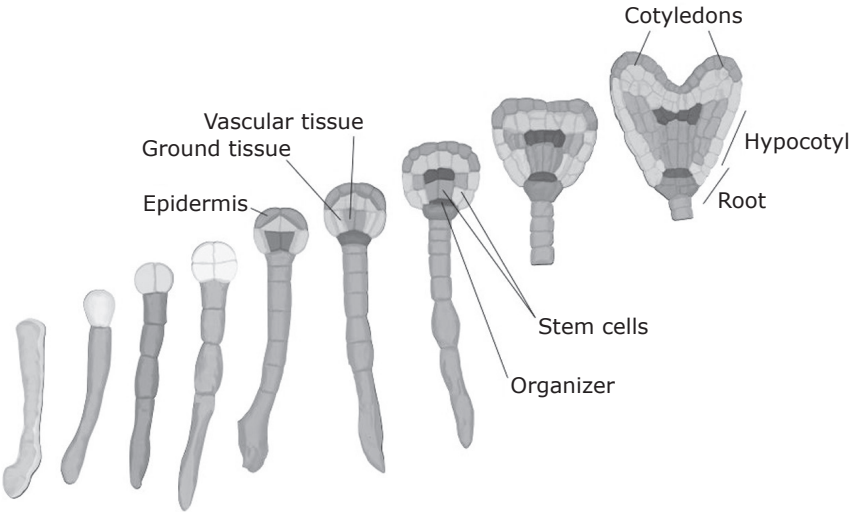

Figure 4. Stages and cell fates in Arabidopsis embryo development.

When we now go back to the original question: how are stem cells and tissues first formed, we can precisely define when and where the first precursors are formed. Quite strikingly, this is at a stage when there are only about 50 cells. My thesis therefore is that, in order to define mechanisms that control the basic recipe of plant development, we should focus our attention on the predictable events that lead up to this stage. Even though we and other groups are trying hard to visualize the living, growing embryo, we have not yet succeeded. However, we can reconstruct the development in a movie. I hope you appreciate that in contrast to the zebrafish case, in this case we actually *do* know at any moment where every cell came from and what it will become, without the need to see the whole movie.

Genes, proteins and development

I have already voiced several times that a major challenge is to understand how the process of tissue and stem cell formation is controlled. A first, very important consideration is that the processes are under genetic control. This means that the different types of cells are different at the level of the activity of their genes. This plant has about 30 thousand genes, and not all genes are active in all types of cells. In this image (Figure 5), the activity of 4 genes is shown. In each case, the cells in which the gene is active light up in green. From this analysis we can conclude that already at this early stage of plant development, the cells in the center are marked by the activity of a gene that is specific to vascular tissue. The same is true for ground tissue, for stem cells and for the organizer cell. This is an important observation, as it means that gene activity and therefore gene functions differ in each of the cell types.

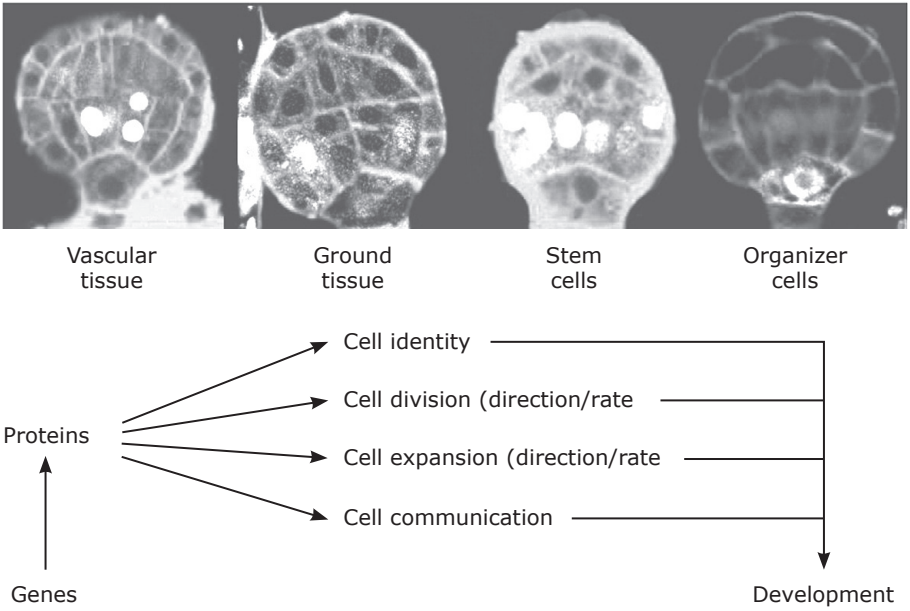

Figure 5. Genetic control of development.

Which brings me to a central dogma in biology: Genes determine development. An example: all plants in your garden grow in the same environment, all the plants of the same species look similar, yet plants with different genes, belonging to different species, look very different. Therefore: genes control development. However, by and large genes are nothing more than instructions for when and where to build what proteins. Therefore, it would be more accurate to say that proteins control

development. Development, in turn, is a rather vague term, as the ultimate growth depends on a few components: cells are uniquely defined, or specified by which of the genes are active. Next, cells can either expand or divide in a particular direction, and with a certain rate. Finally, cells can communicate, by sending signals back and forth. The sum of these processes is "development". Yet, to understand development will require dissection into these components. Before we can dissect these processes, we will however first need to identify the major components that control embryogenesis., a starting point This has traditionally always been done by genetics, which I will explain next.

Flying on one wing to understand plant embryogenesis

After I had studied how plant hormones control embryogenesis during my PhD in Leiden, in 2002 I moved to Tübingen in Germany to join Gerd Jürgens, who had studied the genetic control of plant embryogenesis for 15 years. No better place to study genetics than Tübingen, where in the castle, Friedrich Miescher had discovered nucleic acids a few centruries earlier. The principle of genetics is very simple: to find the genes required for a process, you randomly make genetic variation, or mutations, and search for individuals in which the process is disturbed. By definition, the mutated gene is required for the process, and by identifying the mutated gene one can connect gene function to a process. When Gerd did this many years ago, he identified the *monopteros* mutant (Greek: one wing), in which no root develops (Mayer et al., 1991; Berleth and Jürgens, 1993). Thus, the *MONOPTEROS* gene is required for root formation When we now look at the early embryo of a *monopteros* mutant, it actually turns out that the ground tissue, vascular tissue, stem cells and organizer cell all have a serious problem. None of these cells are correctly specified, nor do they expand or divide correctly (Figure 6). Therefore, MONOPTEROS is required for all these ingredients of tissue and stem cell development. Both during my post-doctoral work in Tübingen, and later, after starting a group in the Laboratory of Biochemistry at this university, I used the critical requirement for MONOPTEROS as a starting point to dissect the formation of tissues and stem cells in the embryo.

When studying *where* the MONOPTEROS protein acts, we made a surprising discovery. Even though the gene is required for the specification, elongation and division of the organizer cell, the MONOPTEROS protein is only present in the future stem cells (Weijers *et al*., 2006). This means that MONOPTEROS is required for the normal development of the cell *next to* the ones it acts in. This means that MONOPTEROS must activate some form of cell to cell signaling, or cell communication. When the *MONOPTEROS* gene was identified in 1998 (Hardtke and Betrleth, 1998), it was shown to be a protein that binds to the DNA, and activates other genes.

This type of protein is also called a transcription factor. By identifying which of the 30 thousand genes are activated by MONOPTEROS, we recently identified the *TMO7* gene. This gene is activated by MONOPTEROS, and the protein it encodes is then transported to the organizer cell to control the development of this cell (Schlereth *et al*., 2010). This protein is therefore a communication signal, and its transport ensures that the organizer cell is positioned right next to the stem cells.

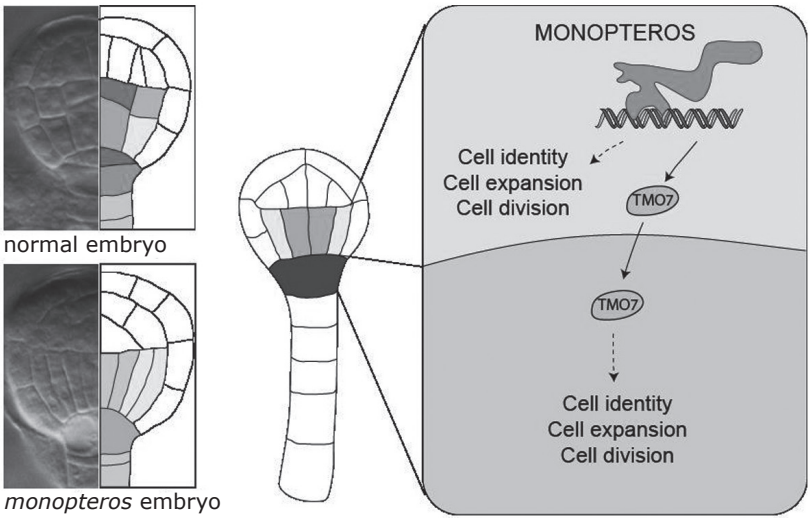

Figure 6. MONOPTEROS as a key regulator of stem cell and tissue development.

To briefly summarize: MONOPTEROS is a critical regulator of all ingredients of tissue and stem cell formation, and it does so by activating other genes. One of these genes, TMO7, encodes a communication protein. In our current research, we use MONOPTEROS as a stepping-stone to identify the genes, proteins and mechanisms that regulate each of these developmental ingredients. As I pointed out, a key challenge is to connect the different levels along the chain. In the following, I will give a few recent examples that highlight how we approach these problems, and with this I also hope to outline the types of questions and strategies that my group will be employing in the years to come.

On soap bubbles…

The first example is one in which we would like to understand the mechanisms underlying how cells decide where to build a wall during division. This is an important process, because as anyone who has done this at home will agree, placing a wall is a laborious process, and cannot be changed without serious damage. Even though orienting cell division plane is very important in plant growth, surprisingly

little is known about how this is controlled. The problem of cell wall positioning is best captured by a film of soap bubbles. This is because there is an old theory, postulated by Leo Errera in 1888 (Errera, 1888) that plant cells divide just as soap bubbles would. In his essay named "Ueber Zellformen und Seifenblasen", Errera demonstrated that many cell divisions in plants follow simple geometric rules. New walls are often the shortest path through the middle of the cell which essentially says that cell shape decides division plane. Many variations of this rule have been tested, but importantly, so far only in 2D.

After developing a method to visualize and recognize cell shapes and volumes in the Arabidopsis embryo in 3D, and by computationally analyzing all possible cell walls, our team, together with collaborators, has recently shown that quite strikingly, the real division of many cells in the embryo does not at all follow the shortest wall. Instead, a much longer wall is chosen. Several years ago, we noticed that in *monopteros* mutant embryos, cell divisions were often very strange (Rademacher *et al*., 2012), and even when we analyzed this in 3D, the divisions did not really make sense. However, when we simulated cell division planes in the *monopteros* mutant, it turned out that these division planes were actually the shortest (Figure 7). So, in the absence of MONOPTEROS, cells do divide like soap bubbles! What this tells us is

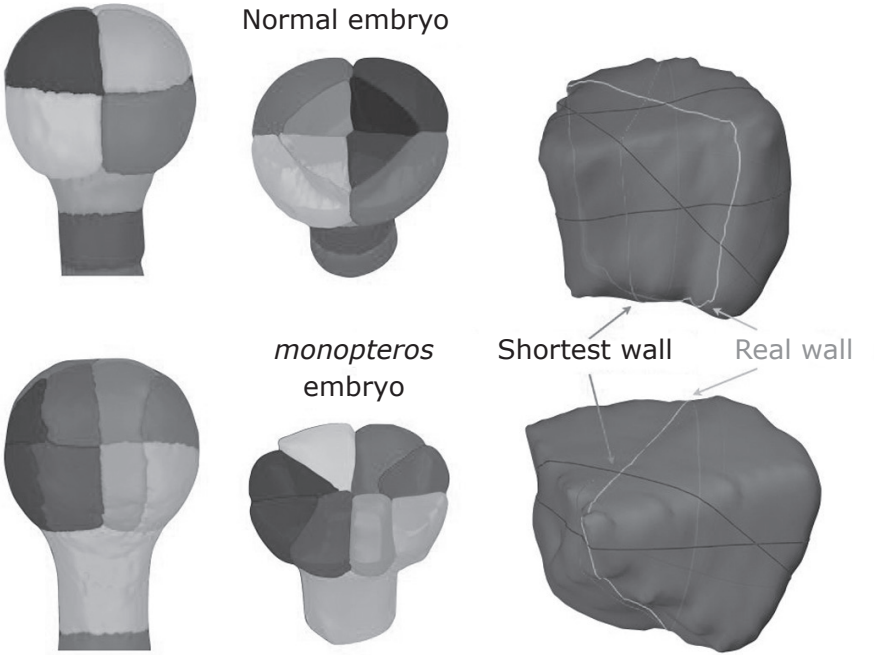

Figure 7. Embryo cells divide by a default rule, unless there is regulation.

that there is a default rule by which cell shape determines the division plane. Factors such as MONOPTEROS control cell division plane by preventing this simple, geometrically controlled division plane. This finding tells us something about the cellular mechanisms underlying oriented division, but of course it does not inform about the molecular mechanisms involved. To illustrate how we may learn about those molecular players, I will show you another recent example. An example that also highlights why it is important to study this process at the level of proteins.

Joining forces

I mentioned that MONOPTEROS is a transcription factor, a protein that activates other genes. I also showed you that one of these genes is TMO7, which encodes a communication protein. We also identified another gene that is activated by MONOPTEROS. This gene is called TMO5, and is active only in the vascular tissue precursors. Normally, the four vascular tissue cells all divide along the long axis of the embryo to generate two rings of cells. When we remove TMO5 gene function by a mutation, this highly controlled, oriented division does not occur as it should, and therefore vascular tissue formation is disturbed (Figure 8). TMO5 encodes a protein

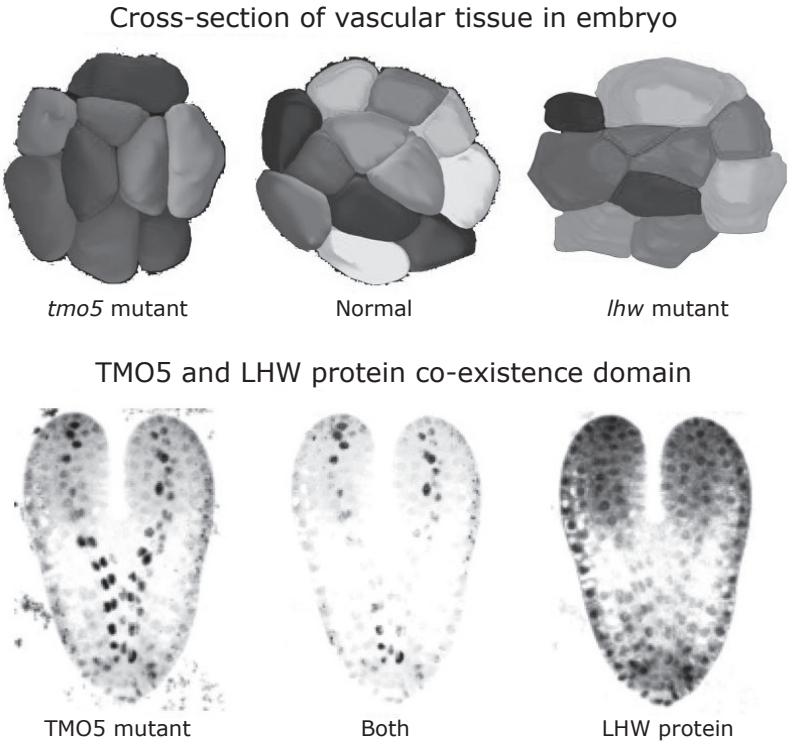

Figure 8. Control of cell division by a protein complex.

that locates to the nucleus, and an important question is how this protein controls cell division orientation. As I mentioned earlier, proteins can bind to one another to form complexes, and the identification of such protein complexes can help to understand how proteins work. A central methodology in Biochemistry is the isolation and identification of such complexes. When we performed complex identification for the TMO5 protein, we find that it does not act alone, but it binds to another protein, named LHW (De Rybel et al., 2013). Importantly, like TMO5, also LHW is required for normal divisions in the vascular cells, since when we mutate *LHW*, the same division defects occur (Figure 8). Therefore, the TMO5 and LHW proteins not only bind to each other, but they are also both required for the same process. This is an important finding, because we can use this information to define exactly where these proteins control oriented cell division. Common sense tells that the proteins can only bind and act together where they co-exist. Let me show you why this is important. The TMO5 protein is found in all cells in the vascular tissue, while the LHW protein is almost everywhere, only the levels are much higher near the tips of the embryo. The overlap of these two patterns marks only a very small domain in the vascular tissue near the tips of the embryo (Figure 8). Here, biochemistry, microscopy and genetics tell us that the two proteins act together to control cell division orientation.

With this example, I have shown you how the combination of these approaches, grounded in understanding of the key proteins and the context in which they act have helped to define how a very small population of cells is selected for a particular, oriented division. As you will understand, a major future goal will be to dissect what cellular processes need to be changed in order to prevent the shortest wall, and to orient the division plane. The examples I have given you now are aimed at understanding how cell division plane is oriented. Since development comprises all these other ingredients, a goal for the future is to systematically identify the key regulators of these ingredients, and the mechanisms by which such proteins act, very similar to what I have outlined so far.

From atoms to cells

I have started this lecture by impressing upon you how important it is to link the different scales in biology. So far, we have seen examples of how the organism, organ and cell are connected, and we have identified genes and proteins, as well as protein complexes that control this. The deepest level however, that of molecules and atoms, has been notoriously absent up to this point, even though I tried to convince you that this is the deepest level that we need to understand. In the final example, I would like to give you an impression of the type of approaches I feel can help to connect this final, deepest level to the higher levels.

This example brings me to a very basic and fundamental question in biology. Most biological processes, be it cell type specification, cell division and so forth, are regulated at the level of gene activity. You have seen that for example, ground tissue cells have a different set of active genes than vascular tissue cells. The genes that are active in each of these cell types determine the properties of that cell, as we have seen with for example *TMO5* in the vascular tissue. But how does a cell know which of the 30 thousand genes should be active? This involves DNA-binding proteins, transcription factors, such as MONOPTEROS, that recognize genes and switch these on. The central question is therefore: how does the MONOPTEROS protein determine which genes to activate? DNA is a long string of letters: A, C, G and T, and it is the order of these letters that determines whether a gene is switched on or off. If we want to understand how MONOPTEROS selects which genes are active in what cells, we should try to define how the protein recognizes the letters in the DNA. To define this, we will need to visualize the exact 3-dimensional structure of the MONOPTEROS protein, and determine where and how it binds the DNA letters.

I was very fortunate to meet Roeland Boer several years ago. Roeland is a structural biologist and works in Barcelona. In a close collaboration with our team, Roeland has been able to crystallize the MONOPTEROS protein and collect X-ray diffraction data. Quite miraculously the pattern of diffraction can then be used to calculate the shape of the protein. Using this approach, we have now solved the 3-dimensional structure of the MONOPTEROS protein, which you see here (Figure 9). As you can see, the double helix of the DNA sits on top of the protein, and recognizes the letters TGTCTC.

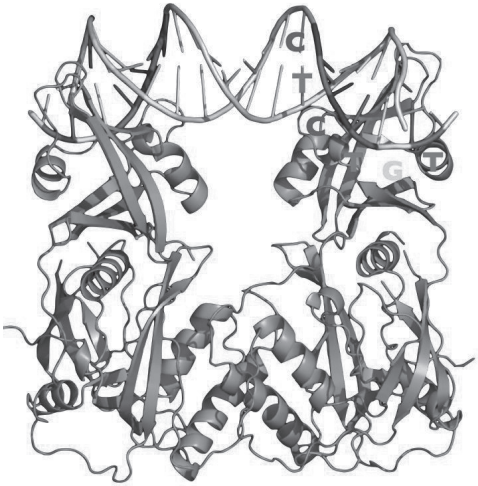

Figure 9. Atomic structure of a protein-DNA complex.

Of course, this makes for pretty pictures, but the important message is that we now know for every single building block, or amino acid in the MONOPTEROS protein, exactly where it sits in the protein and what its likely function is: whether it is required for folding the correct structure of the protein, or if it binds the DNA. As I hope you will appreciate, the reason why the MONOPTEROS protein binds this particular set of DNA letters is hidden in this structure. When we now zoom in on the interface between the MONOPTEROS protein and the DNA, we can see the individual letters in the DNA as different ring shapes, and we can see amino acids of the protein sticking towards or in between these rings (Figure 9). What you are now watching is the atomic interactions between a protein and a DNA molecule, and it is these atomic interactions that define which series of DNA letters is bound by MONOPTEROS. This directly follows from which amino acids are positioned in this DNA-binding surface.

The next step is that we can use these structures to test which of the amino acids, and therefore which atomic interactions, are important for binding of MONOPTEROS protein to the DNA. We can even go one step further: I have told you that when the MONOPTEROS protein is missing, many things go wrong, and embryos are not able to make a root. If we now bring MONOPTEROS protein back into the mutant, this defect is repaired, and plants are normal again. If we want to test the importance of individual amino acids, for example those that contact the DNA letters, we can replace that amino acid in the MONOPTEROS protein, and introduce the engineered version of the protein into the mutant. If the amino acid *is* important for biological function, we would expect that the engineered protein is *not* able to repair the mutant. If the amino acid is *not* important, the engineered protein should be able to repair the mutant.

Let me show you two examples: when one amino acid, a proline, is replaced by another amino acid, an alanine, the engineered protein can repair the *monopteros* mutant defect, and mutants now make a root. If however, another amino acid, an arginine, is replaced by an alanine, the engineered protein is no longer capable of repairing the mutant. The conclusion is that even though both amino acids touch the DNA letters, only one of the two is essential for function in the biological context.

This is a study we recently completed, but as you can imagine, it is a very powerful approach to connect atomic scale properties with cellular and organismal scale functions. As such, I believe that studies of this kind are going to be an important strategy towards understanding the biochemical basis of plant development.

The biochemical basis of plant development
Ladies and gentlemen, I have started by telling you that life can be observed at many scales, and that these scales are intimately linked. I have also told you that connecting these scales will be crucial if we want to understand living systems.
I have given you arguments why the plant embryo is a very interesting model to study the mechanisms that control development, and I have shown several examples of the approach that we take to investigate and eventually link the different scales.

It is my conviction that protein-centered biochemistry is a central, and if you will fundamental element in this chain. However, while biochemistry can identify properties and interactions of molecules, its power also ends there. Cell biology is crucial to define where and when proteins act, while genetics offers a superb and perhaps the only available tool to assign biological functions and relevance to proteins. Finally, computational biology allows to explore limitless scenarios, and to validate intuition. I believe that we have to step out of the boundaries of traditional disciplines or domains, and embrace complementary approaches to place protein-centered biochemistry in a biological context.

In other words: To define the biochemical basis of plant development

"de Nederlandse Top-40"
I have been able to develop my research subject, and am standing before you today despite my tender age because of several reasons. One of these reasons is that throughout the last years, I have been well supported by several funding agencies. Each of these has put their trust in me, for which I am very thankful. To be honest, the main driver behind my motivation to focus on this problem, is that I believe it is of fundamental importance to understand biology if we want to use resources efficiently, and modify them rationally. These agencies agreed that this is a good starting point for research projects.

Recently, the Dutch government has implemented new policy that should promote the economic valorization of research in the Netherlands. This has led to the definition of 9 priority areas, so-called topsectoren, in which academia and industry should collaborate to tackle problems of economic relevance. Much has already been said about the topsectoren, and I do not think this is the appropriate place to reiterate all concerns. What makes the discussion particularly difficult is that this incentive, which is in itself a very good idea, is actually not an impulse, but is accompanied by budget cuts. Even though I would wish scientists that start their careers today the same type of freedom that I enjoyed, I fear this policy will set serious constraints on such freedom.

Back to the 9 topsectoren. One can of course debate about the choice of the priority areas, which were all chosen based on proven success in the past. However, there is a more fundamental consideration, which is best illustrated by the music charts. I am sure many of you are familiar with "de Nederlandse Top-40". Based on proven success, the 40 best-selling songs are ranked every week. Every body of the right age will recognize these 40 songs as being popular. But how to predict the hits of the future? To spur recognition of potential hit songs before their success is obvious, decades ago the Tipparade was started, a list of potential hitsongs. As it turns out, most songs that enter the Top-40 have been in the tipparade for at least one week. Along the same lines, I would like to make a plea for maintaining and extending support for the less obvious, but promising areas, also in science funding.

…on the shoulders of giants

Money is important, but a much more important reason I am here today is that I have been very lucky with the people I had the privilege working with.

After finishing a HBO, professional college, I felt strongly about starting a PhD, even if I did not have the regular qualifications. I am strongly indebted to Remko Offringa and Paul Hooykaas for seeing potential and offering me a PhD position. The freedom that Remko gave me in my project was fantastic, and helped me to take responsibility and make decisions from early in my career.

My years in Tübingen were no less than formative. Gerd Jürgens is one of those rare individuals who can profoundly influence peoples careers by bringing together a group of ambitious people, facilitating their development and helping to ask the right questions. I am proud to be one of the members of the Jürgens school.

After an initial hiccup imposed by a crack in a bicycle path, Sacco de Vries spent several months on a sabbatical in Gerd Jürgens' lab. This was shortly before Sacco became the new chairholder of the Laboratory of Biochemistry. I fondly remember discussing how biochemical approaches could be the next step forward in plant biology. Inspired by the successes in Sacco's group, I became convinced that my developmental biology needed a solid biochemical basis, and I am grateful that Sacco supported my transfer to Wageningen. This support has been continuous for the last 7,5 years, and it has been a pleasure working together. Your advice that a good proposal or presentation should be like a good suspense novel, was invaluable, and will be passed on to generations to come.

I believe I have been, and still am, exceptionally lucky that very talented, but importantly, very nice people agreed to join me. The feeling that we are all on a quest together is very exciting, and motivates me every day. It is because of your hard work, good ideas and perseverance that our group is successful, and that I stand here today. Because her efforts are largely invisible, it would be easy to forget the exceptional importance of Laura van Egmond. You have made my life at the department so much easier…

Context is everything

One of the aspects that make life at a university very exciting is the abundance of young, ambitious and energetic students, and over the past years, many have performed Bachelor or Master thesis projects in our group. These students have made invaluable contributions to the research projects, but also to the great atmosphere. In essence, your presence makes our group a learning environment, which is what a university should be.

A challenge I see is how to translate the concept of biologically embedded biochemistry to our teaching curriculum. What I personally remember from my biochemistry courses is summarized in the "Biochemical Pathways". I would not dare to state that it is not important to know and understand the reactions happening in cells, the risk of our discipline is that it can tend towards cartography if the activities and behavior of for example protein molecules is not presented in the context of their biological role. To turn this around, when the biological context is clear, the importance of the biochemical details can become much more vivid. With this idea in mind, it is in fact very well possible to make students aware of the essential nature of understanding biochemical principles, and I am happy that this philosophy is appreciated by students in my courses.

Because, when considering the context, scientific details are simply more exciting. The power of context is very evident from the success of Science Café Wageningen, that Pim Zabel and I founded a few years ago. Here, 6 times per year, many interested students, employees and laypeople gather to discuss frontiers of science with experts. Importantly, with live music and with a beer. As scientists, we are often encouraged to "bring our science to society". This is nonsense…science *is* part of society, that is a fact. It is our task to show why science is so important, and how interesting it is.

And fortunately, we are not alone in our conviction that science, to be precise the science I have discussed with you today, is exciting. Over the years, I have been able to develop fantastic collaborations both within our laboratory, with Jan Willem Borst and Sjef Boeren, but also with other chair groups in Wageningen, and with many colleagues all over the world. It is truly remarkable to be focusing on such a specific scientific problem, and yet to have so many like-minded friends and companions. Having one's research embedded in a larger community is absolutely critical if we want to introduce other approaches and technologies. But since words, opinions and facts are our commodity, being part of a network is also critical to develop new ideas. Such new ideas are much more likely to come from discussions with researchers that work on entirely different problems I have been fortunate to become member of the Young Academy of our Royal Netherlands Academy of Sciences and meet scientist from all fields imaginable to exchange ideas and develop views on matters related to science, policy and society. The national young academy has only 50 members, and David Lentink and I both felt that the inspiring meetings with ambitious young scientists should not be limited to these few. With support from our rector Martin Kropff and many others, we have been able to start a local, Wageningen Young Academy. 27 bright minds, with which I am looking forward to share ideas and experiences.

This brings me to the end of my lecture. I thank the board of the University and the Appointment committee for granting me the honor to serve as professor at Wageningen University. In passing, I have already mentioned several people that have had important impact on my career and development. I reserve the final words for those closest to me. If you allow me, I will switch to Dutch for this.

Allereerst wil ik mijn ouders bedanken voor het feit dat ze, ondanks een LTS-advies voor een drukke jongen, altijd hebben geloofd in mijn kunnen. Waarschijnlijk zijn jullie van iedereen hier het minst verrast dat ik hier sta. Daarnaast wil ik mijn schoonouders bedanken voor het verlichten van de last die de echtgenote van een drukke wetenschapper ervaart. Ik ben mijn zussen, zwagers en natuurlijk mijn vrienden dankbaar voor hun steun en interesse, Heel fijn dat jullie er vandaag allemaal zijn. Ik wil in het bijzonder Haico noemen. Wij hebben samen onze eerste stappen in de wetenschap gezet en zijn sindsdien elkaars steun en toeverlaat.

Maar de allerlaatste woorden gaan naar degene die de allereerste plaats verdient. Marieke, het is dat je niet van lange zwarte jurken houdt, maar op basis van de inzet en offers die gemaakt zijn, had jij hier moeten staan. Jouw rol is vaak onzichtbaar, maar is de motor achter het mooie leven dat we met onze prachtige dochters Puk en Sam hebben.

Ik dank u voor uw aandacht.

Ik heb gezegd

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Prof. dr Dolf Weijers

'Plants develop highly elaborate structures, ranging from small mosses to large trees. All these structures are made by stem cells and consist of a few basic types of tissue. The field of Biochemistry of Plant Development studies the mechanisms by which regulatory proteins control the formation of stem cells and tissues. The young embryo, developing within the seed, is the simplest model to study these fundamental processes, and to gain understanding of the basis for plant development at cellular, molecular and atomic scale.'

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