Science Meeting – Scientific Report

The scientific report (WORD or PDF file - maximum of seven A4 pages) should be submitted online within two months of the event. It will be published on the ESF website.

Proposal Title: *Quantitative Biology of Auxin Transport*

Application Reference N°: 5671

1) Summary (up to one page)

Scientific summary

Polar transport of the plant hormone auxin (PAT) directs patterning of embryos and tissues, initiation of new organs, and environmental responses. The topic has received much attention from quantitative biologists, but most mathematical models are of a qualitative nature. This workshop has brought together a team of experts and young researchers to make a start with developing more quantitative modeling-experimental approaches, with a focus on aspects of PAT that are still poorly understood.

This workshop has discussed how to apply a joint modeling-experimental approach to aspects of PAT that are still poorly understood, with the objective to force a breakthrough with this method on the longer term.

In detail, the goals of the workshop were:

(1) To share, discuss and summarize the latest ideas, experimental insights and theories concerning the cellular mechanisms that underlie PAT, where we use mathematical modeling additionally as a method to make explicit all detailed assumptions that are (sometimes implicitly) made in a conceptual model. Thus, clear discussion and identification of fundamental open problems are facilitated.

(2) To adapt existing and develop new mathematical models of proposed mechanisms for PAT and implement versions of these in suitable simulation during the workshop,

(3) To investigate *in silico* emerging properties of the system and some of the issues in the mechanisms of PAT, e.g. how is auxin transported intracellularly, are PIN proteins involved in long-distance PAT, what determines transport velocity? In this way we obtain predictions and get ideas for wet experiments that may validate these predictions.

Specifically, we aim to bring together both junior and senior researchers in mathematical, computational and experimental (plant) biology with research interest in the topic of PAT, in an interdisciplinary setting, and to get them acquainted with each other's approaches and techniques.

The success criteria of the workshop were:

• The discussions in the workshop, supported by the mathematical modeling, lead to new experimentation afterwards.
• Two alternative cellular mechanisms for intracellular auxin transport and intercellular auxin exchange have each been formulated precisely in a mathematical model for PAT.
• At least one of the mathematical models leads to predictions concerning PAT (e.g. the intracellular distribution of auxin) that can be validated experimentally.
• At least one of the teams of modelers and experimental biologists (or part thereof) continues their collaboration after the workshop, as shown e.g. by publishing jointly on the newly developed model(s) for PAT and performed simulations and analysis.
• Junior participants have benefitted from their contact with seniors during the workshop, e.g. by obtaining invitations to pay a research visit afterwards.
The workshop will be a good starting point to come to a grant application for further interdisciplinary research on the topics of the workshop, e.g. in the Horizon 2020 EU framework

2) Description of the scientific content of and discussions at the event (up to four pages)

Workshop, "Quantitative Biology of Auxin Transport", Jan 12-16, 2015.

On Monday, several field leaders presented overviews of recent research on auxin transport biology and open questions. In the evening, during the wine and cheese party, several research topics for the week were proposed and discussed.
On Tuesday morning, participants were presented with four possible research topics and asked to join one. These became four working groups, around which the remainder of the conference was organized.
The Wednesday and Thursday program consisted of team discussion sessions, followed by plenary junior presentations and feedback sessions.
On Friday morning, each working group presented a final summary of their discussions and any new work performed.

Topic 1. Intracellular auxin transport: vesicles vs cytoplasmic streaming.
This group was led by modeler Sander Hille, with additional participation by Kees Boot, Bert van Duijn, Matous Glanc, Genevieve Hines, and Kees Libbenga.
This group considered the possibility that auxin is stored in vesicles within the plant cell, and secreted into the extracellular space during vesicle-fusion events. This hypothesis, initially proposed by Jiri Friml, has been championed by conference participant Franticek Baluska for many years, and it has always been regarded as a controversial alternative to the conventional wisdom that auxin is simply secreted from the cytoplasm across the cell membrane. The possibility that vesicles play a key role in auxin transport has tended to polarize auxin biologists into two camps – for and against.

The working group decided to take a more pragmatic approach. They considered the hypothetical case in which auxin is secreted in both ways - across the cell membrane and via vesicle fusion events. Then they spent several days estimating, semi-quantitatively, the fraction of the observed total transport that could be due to vesicles. This work relied on available estimates for auxin flux, membrane permeability, vesicle pH, etc. By pursuing a mathematical approach, and avoiding any dogmatic assertion about the importance of vesicles, this group made a good start on a project that will likely be publishable on a 12-month time scale.

Topic 2. Auxin and coordinated cell polarization.

This group included Claudiu Antonovici, Laura Braun, Ross Carter, Mik Cieslak, Pau Formosa-Joran, Jiri Friml, Christophe Godin, Henrik Jonsson, Jürgen Kleine-Vehn, Roeland Merks, Wojcieck Palubicki, Richard Smith, and Kirsten ten Tuscher.

The group was committed to reviewing the wide range of different models already in the published literature to explain auxin-mediated pattern formation. Auxin plays a key role in the regulation of cell polarity, as shown in the dynamic patterns of polar localization of auxin efflux carriers (the PIN protein family) on the cell membrane. This regulation is key to auxin action, and the mechanism has been the subject of perhaps a dozen different hypotheses during the last decade.

A large part of the first discussion session was used to compare different and models and modeling programs on the role of auxin in coordinated polarization of PIN auxin transporters in plant tissues. After that, the group was split up in smaller groups that considered three different models (the Wabnik model, the Jonnson up-the-gradient model, and the Ableу model) and different modelling programs (Virtual leaf, morphograhX, ….). An attempt to compare the models led to recognition that a greater uniformity was needed in the mathematical description of the models. Since many of the speakers at the workshop had covered some models of pattern formation, these models as well were brought into the discussion as well. One of the conclusions was that more reliable methods need to be established to quantify some of the parameters that are used in the models.

Topic 3. Long-distance polar auxin transport.

This group included experimental biologists Ottoline Leyser, Remko Offringa, Angus Murphy, and Eva Zazimalova, with Veronica Grieneisen, and Stan Maree as modelers. Drs. Leyser, Murphy and Offringa are all conducting research on auxin transport through stem segments of *Arabidopsis thaliana*. The projects of Leyser and Offringa involve measurements through basal stem segments, and include respectively a cell-based or a mesoscopic model of auxin transport that provide a foundation for interpreting the experimental data.

In contrast, the Murphy group is measuring transport in the upper portion of stems, and therefore the question arose how to explain observed differences based on differences in anatomy and gene expression between stem apex and stem base. During the week, a new, draft computer model was constructed describing transport through both stem apex and base. This model opens the door to a more far-ranging analysis of auxin transport throughout the entire stem – a project that may be pursued further by the group participants. Recently, a manuscript describing the mesoscopic model for auxin transport through stem segments from the Offringa/Hille group was accepted for publication in Journal of Experimental Biology. One option will be to use this mesoscopic model a basis for the cellular model.

Topic 4. Subcellular PIN polarity establishment and maintenance.

This group was led by Eric Kramer, with additional participation by Remko Offringa. On the first day of the workshop, Jiri Friml pointed out that the molecular determinants of PIN polarity are still largely unknown. One key player is the PINOID (PID) gene family, studied by Remko Offringa. Dr. Kramer worked with Dr. Offringa to use publically available genomics databases to search for additional candidate genes and gene families.

A search on PID revealed a strong correlation (correlation coefficient R = 0.92) between PID and the gene ERECTA (ER). A correlation this high suggests that the two

genes may be part of a functional module. ER is known to play a role in cell-to-cell signaling.

This collaboration will continue beyond the workshop. Dr. Kramer will continue to search for candidate genes. Dr. Offringa will pursue experimentally the possible role of ER and other gene candidates in his lab.

3) Assessment of the results and impact of the event on the future directions of the field (up to two pages)

As spin-off of the discussions in the group that discussed Topic 1, a set of experiments was conducted by Matous Glanc as member of the research group of Jiri Friml and in collaboration with Eva Zazamilova as follow-up to the workshop. These experiments were designed to put some of the model predictions that were found during the workshops to the test. At the time of writing of this report the experimental data are being assessed in order to draw conclusions on the possible contribution of vesicles to the overall cell-to-cell transport of auxin.

The discussion among members of the topic 2 group has led to the recognition that a greater uniformity is needed in the mathematical description of the models, and that quantification of some of the parameters in these models requires more emphasis. As such the workshop has been successful in bringing together modelers and to stimulate their collaboration, and the unifications of their models.

Along the same lines, Dr. Hille will visit Drs.Greiniesen and Maree in Norwich to present details of the mesoscopic model and discuss the possibility that this model is used as a basis for the more detailed cellular model they are generating as a spin-off from Topic 3.

4) Annexes 4a) and 4b): Programme of the meeting and full list of speakers and participants

Annex 4a: Programme of the meeting

Monday 12 January 2015

09.30-10.00 Arrival, registration and coffee
10.00-10.15 Welcome by Henriette Jensenius (Lorentz Center)
10.15-10.45 Explanation of format and goals of the workshop: propose topics (Roeland Merks)
11.00-11.45 Overview of main theories (Kirsten ten Tusscher, review).
11.45-12.00 Define topics
12.00 Lunch@Snellius Cafeteria
14.00-14.30 Discussion/presentation Topic 1: *'Intracellular auxin transport'* (Frantisek Baluska)
14.30-15.00 Discussion/presentation Topic 2: *'Involved membrane transporters'* (Angus Murphy)
15.00 Tea
15.30-16.00 Discussion/presentation Topic 3: *'Feedback and polarity'* (Jiri Friml)
16.30 Wine & Cheese Party

Tuesday 13 January 2015

('Hands-on': topics, registration on topics, start modelling)
10.00-10.30 Note (presentation) on Topic 1: *'Balancing auxin metabolism and transport'* (Eric Kramer)
10.30-12.00 Work & team discussion session: Organisation of teams per topic, start modelling
12.00 Lunch@Snellius Cafeteria
14.00-15.30 Work & team discussion session
15.30-17.00 Plenary feedback (3x 30 min): Presentation of initial approach per topic, Discussion/suggestions

Wednesday 14 January 2015

10.00-10.30 Note (presentation) on Topic 2: ?
10.30-12.00 Work & team discussion session
12.00 Lunch@Snellius Cafeteria
14.00-15.00 Feedback(3x 20 min): provide update of approach
15.15-15.35 *'The importance of auxin influx transporters in the leaf margin'* (Ross Carter)
15.35-15.55 *'Formation of leaf vascular networks by auxin transport and signalling'* (Laura Brown)
15.55-16.15 *'Agent-based auxin transport modelling'* (Wojciech Palubicki)
16.30 Bus leaves for workshop diner
17.00-21.00 Workshop Diner and Boat Trip
21.00 Return by bus

Thursday 15 January 2015

10.00-10.30 Note (presentation) on Topic 3:
10.30-12.00 Work & team discussion session.

12.00 Lunch@Snellius Cafeteria
14.00-15.30 Work & team discussion session
15.30-15.50 '*Auxin influx modulates periodic vascular patterning*' (Pau Formosa-Jordan)
15.50-16.10 '*ER and its role in auxin biology*' (Matouš Glanc)
16.15-17.15 Plenary feedback (3x 20 min): further update on progress

Friday 16 January 2015

10.00-10.45 Final presentation & Discussion progress Topic 1
11.00-11.45 Final presentation & Discussion progress Topic 2
11.45-12.30 Final presentation & Discussion progress Topic 3
12.30-13.00 Closure of workshop (by organizers): Get overview, how the work will be completed / published
13.00 Lunch@Snellius Cafeteria
(Participants may still use the Lorentz Center facilities after lunch)

Annex 4b: Full list of speakers and participants

Organizers:
Bert van Duijn (Leiden, Netherlands)
Sander Hille (Leiden, Netherlands)
Eric Kramer (Great Barrington, United States)
Roeland Merks (Amsterdam, Netherlands)
Remko Offringa (Leiden, Netherlands)

Participants
Claudiu Antonovici (Leiden, Netherlands)
Frantisek Baluska (Bonn, Germany)
Kees Boot (Leiden, Netherlands)
Laura Brown (Cambridge , United Kingdom)
Ross Carter (Norwich, United Kingdom)
Mik Cieslak (Calgary, Canada)
Pau Formosa-Jordan (Cambridge, United Kingdom)
Jiri Friml (Klosterneuburng, Austria)
Matouš Glanc (Praha 6, Czech Republic)
Christophe Godin (Montpellier, France)
Verônica Grieneisen (Norwich, United Kingdom)
Genevieve Hines (Cambridge, United Kingdom)
Henrik Jönsson (Cambridge, United Kingdom)
Jürgen Kleine-Vehn (Vienna, Austria)
Ottoline Leyser (Cambridge, United Kingdom)
Kees Libbenga (Leiden, Netherlands)
Stan Marée (Norwich, United Kingdom)
Angus Murphy (College Park, United States)
Wojciech Palubicki (Cambridge, United Kingdom)
Bert Peletier (Leiden, Netherlands)
Richard Smith (Cologne, Germany)
Kirsten ten Tusscher (Utrecht, Netherlands)
Eva Zazimalova (Prague 6, Czech Republic)