Success with EU Proposals: ERC Grants

(Richard Wheeler)

Please no photos, as presentation contains confidential material.

ERC Grants

- The highest profile award a researcher in the EU can receive.
- Very hard to get, *very hard*, but will make your career if you receive one. Number of ERC ADV ever received in Slovenia: 4.
- Three flavours: ERC *Starting*, *Consolidator*, and *Advanced*.
- *"In particular, proposals of an interdisciplinary nature, which cross the boundaries between different fields of research, pioneering proposals addressing new and emerging fields of research or proposals introducing unconventional, innovative approaches and scientific inventions are encouraged."*

ERC Grants

- Should be curiosity-led; 73% of completed ERC-funded projects produced breakthroughs or major scientific advances
- Likely to become more and more important after Horizon 2020
- If your ERC application is not well evaluated (category B or C at first stage), you may have to wait one or two years to reapply
- *An ERC grant will radically change the course of your career*

Characteristics

ERC is similar to FET-Open in terms of focus, though the instruments are actually very different. ERC is *personal*, FET-Open is *collaborative.*

Long-term vision. If your research doesn't reach far beyond the immediate future, it's not ERC material.

Breakthrough scientific and technological target. If your research idea does not contain a clearly identified breakthrough, it's not ERC material.

Novelty. If your proposal tackles the next logical step of an already existing concept or proposes a continuation of a previous project, it's not ERC material.

Foundational. If it doesn't envisage a new line of investigation leading to a new technology, currently not anticipated, it's not ERC material.

High-risk. If your research methods are not adapted to explore unknown territory with potential high risk but also high gain, it's not ERC material.

Inter-disciplinarity. If you team up only with collaborators from neighbouring disciplines or engage in established collaboration patterns, it's not ERC material.

ERC Grants: Starting (STG)

- *The work that gets you a professorship*
- Five years/€1.5M (plus €500K materials) per project
- The Principal Investigator shall have been awarded his/her first PhD ≥ 2 and ≤ 7 years and at least one important publication as main author or without the participation of their PhD supervisor
- Focus on building a new team around the PI's great ideas
- Next call deadline likely October 2018

ERC Grants: Consolidator (CONS)

- *The work that makes you dominant in the field*
- Five years/€2.0M (plus €750K materials) per project
- The Principal Investigator shall have been awarded his/her first PhD > 7 and ≤ 12 years and have several important publications as main author without the participation of their PhD supervisor
- Focus on consolidating a small team into a world leading one, led by the PI's great ideas
- Next call deadline February 2018

ERC Grants: Advanced (ADV)

- *The work that wins you the Nobel Prize or equivalent.*
- Next deadline August, 2018
- Not the subject of this talk. See me after the lecture. :>)

Getting Started

- This talk is not for reviewing things already found online, in the GFA and call texts, or about good writing techniques
- Read the call materials very thoroughly, and investigate previous ERC awards in your field
- Begin developing your big idea
- Begin making images and graphics illustrating your ideas
- Begin understanding your own career narrative, and making a list of your weaknesses to be addressed
- Think of *who* you want to work with, make a list, and begin contacting people
- Discuss the grant and your idea with your head of department

Why ERC Grants Fail

I have seen at least 30 ERC grant proposal evaluation reports, and *every single one failed for the same reason.*

They were not innovative enough.

Your ERC proposal is going to fail because it is not innovative enough. So we need to discuss new ideas and innovation. Everything else we can probably fix.

Getting Started

Though it varies, it usually helps if you have at least some applied aspect to your research. In this presentation, we will continue with the example from previous lectures.

Example: you work in machine learning and optimization:

> *"Develop quieter turbines…"* + *machine learning* = *work package in modeling and genetic algorithms for turbofan design and optimization…*

…now you need partners in turbine engineering and testing. ERC grants usually have some external partners, but it is not common for them to get much of the budget, as it is a grant focused on the PI.

Ideas…

Is your idea innovative?

If you describe the problem to an expert in your field and ask them to think of five ways to overcome it, they should not be able to describe your method.

My advice: take your good idea to the smartest people you know and discuss it openly and ask for input.

Stand next to geniuses. Seriously, this works. Find a genius you are afraid of, and then bug them constantly over coffee.

Ideas…

Having innovative ideas is usually about *immersion* in your field, and *exposure* to other fields and ideas unrelated to yours.

Even in fundamental science, great ideas are usually rooted in a problem to solve, so investigate problems that seem unrelated to your expertise ("why are turbines noisy? - what makes them inefficient?").

Up your game. Find people much smarter than yourself; find the best people in Europe and visit them. Be passionate, be excited, have high standards. No, *higher* than that.

How Far To Go…

In software engineering and coding, we often think of versioning, Version *1.0, 2.0, 3.0*. Here is a thought experiment using this idea to help you know how to pitch your ideas in an ERC proposal.

Let's return to the jet engine idea.

Version 1.0…

"Develop quieter turbines…" + *machine learning* = *project in modeling and genetic algorithms for turbofan design and optimization…*

Version 1.0: use genetic algorithms and deep learning to interface with existing design tools and methods to optimize existing design parameters and link these with existing modeling and evaluation tools. Test and refine methods and approaches.

New solutions to existing and well understood problems.

Result: more or less known in advance, incremental science, good article in a journal or conference like SGAI or ECML. Low risk, low chances of project failure.

Version 2.0…

"Develop quieter turbines…" + *machine learning* = *project using advanced methods to create new design tools for the design of new engines with advanced properties suggested by new AI and ML approaches…*

Version 2.0: creation of new design and engineering tools at a low level early in the process to create end-to-end optimization and engineering specifications for next generation engines.

New solutions to existing but not well understood problems.

Result: much less known in advance, less incremental science, high risk and possibility of failure throughout the project at various points. Article in best journals or conferences like IJCAI.

Version 3.0…

"Develop quieter turbines…" + *machine learning* = *project investigating the very bases of jet propulsion methods at a low level using tools and methods not yet imagined…*

Version 3.0: investigation of the basic problems with jet engines at the level of physics and materials; imagining of radically new types of AI and ML that might exist only for the realm of creating new types of jet propulsion systems. *(Impossible? SCRAMJET, of course this is already known, but is an example of a radical rethinking typical of v3.0)*

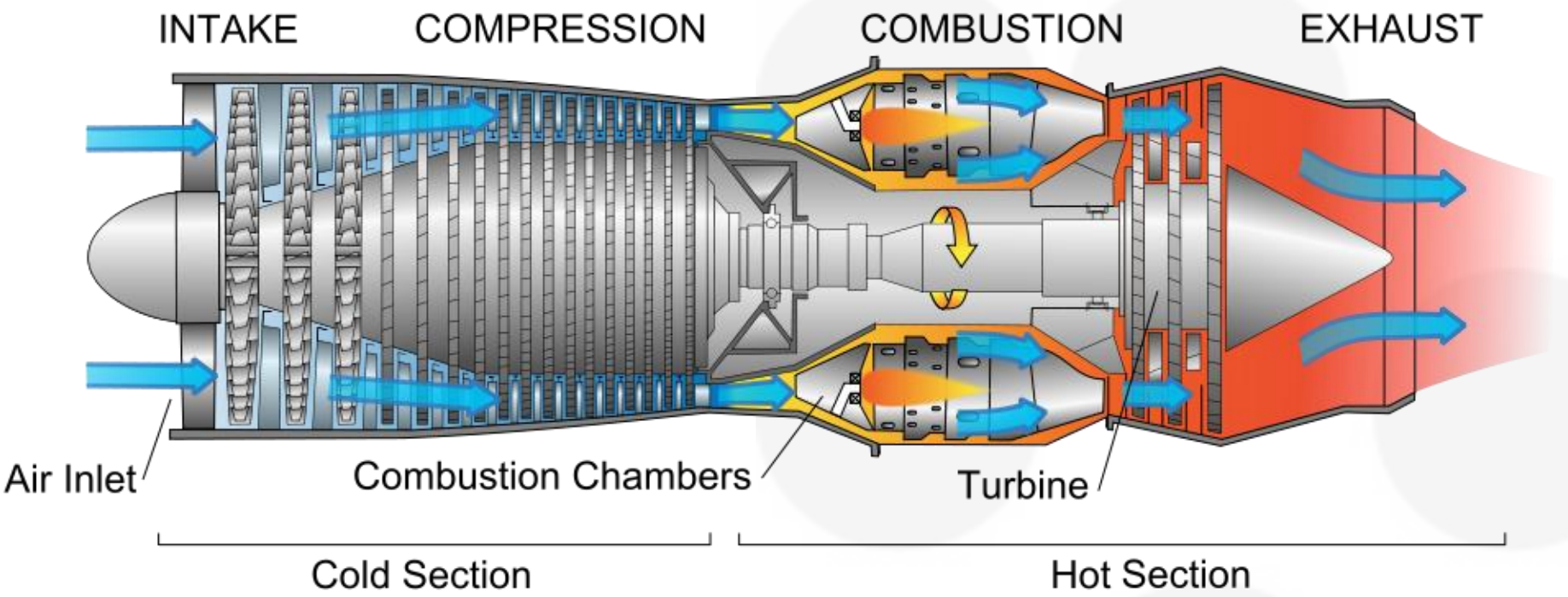
*Proposing and developing **new questions** necessary for the fundamentals of the field to advance.*

Result: not known in advance, fundamental science, high risk but lower probability to fail, as the results will be new questions and ideas. Articles in best journals or conferences like IJCAI, possibility for breakthroughs in other fields of science.

Version 4.0…

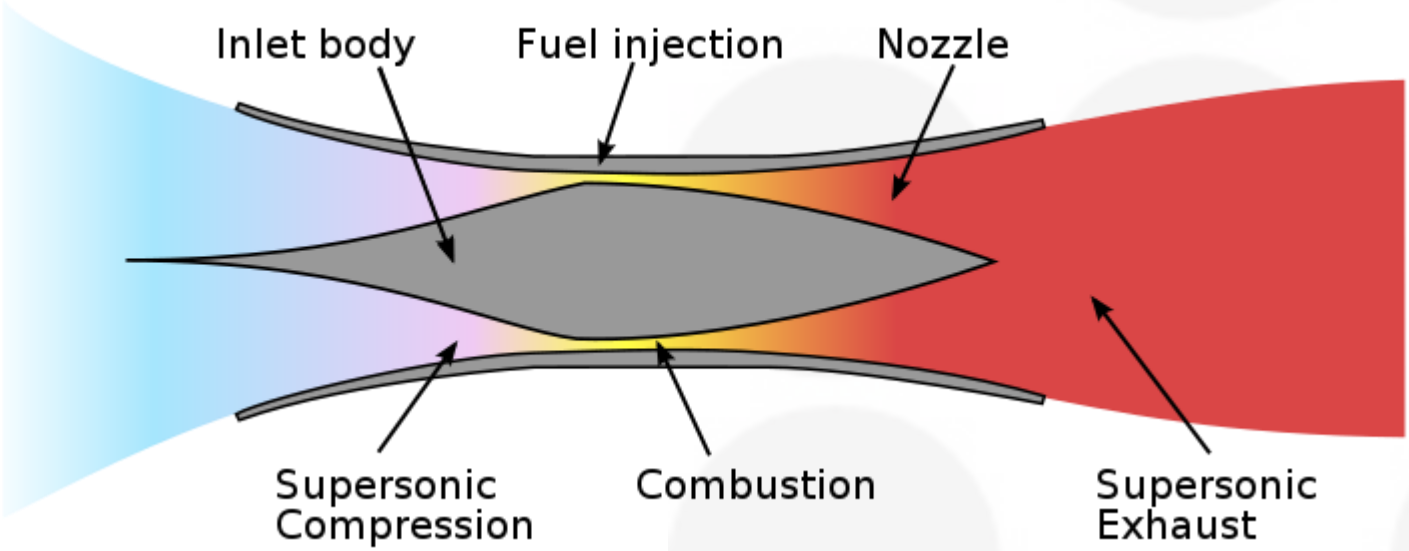
Version 4.0: Prototyping and testing the results of v3.0

Jet Engine Turbine v1.0



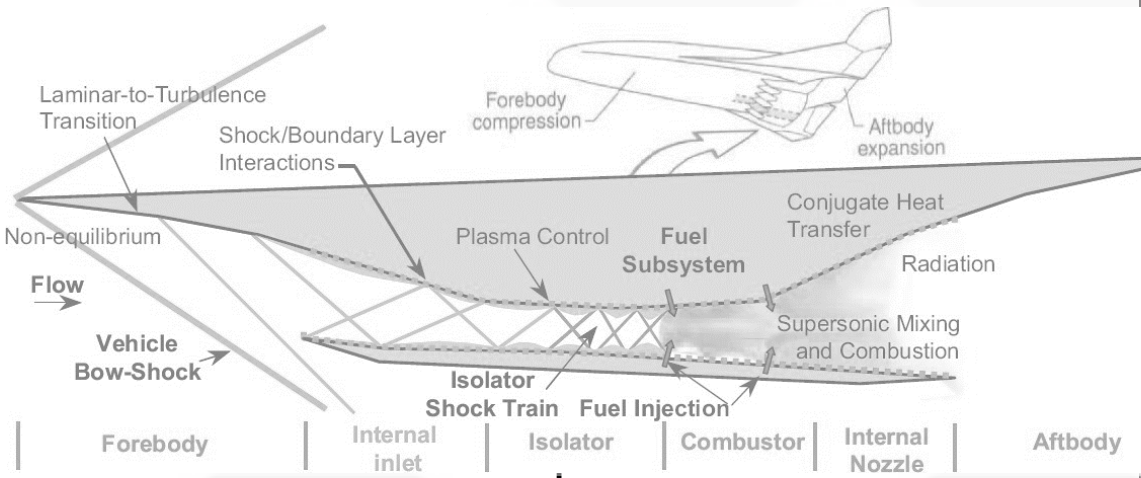
Complex, turbojet/turbofan compression

SCRAMJET v3.0



(From Wikipedia) *A scramjet (supersonic combusting ramjet) is a variant of a ramjet airbreathing jet engine in which combustion takes place in supersonic airflow. As in ramjets, a scramjet relies on high vehicle speed to compress the incoming air forcefully before combustion, but whilst a ramjet decelerates the air to subsonic velocities before combustion, the airflow in a scramjet is supersonic throughout the entire engine. That allows the scramjet to operate efficiently at extremely high speeds.* ***No turbofan.***

Version 3.0…



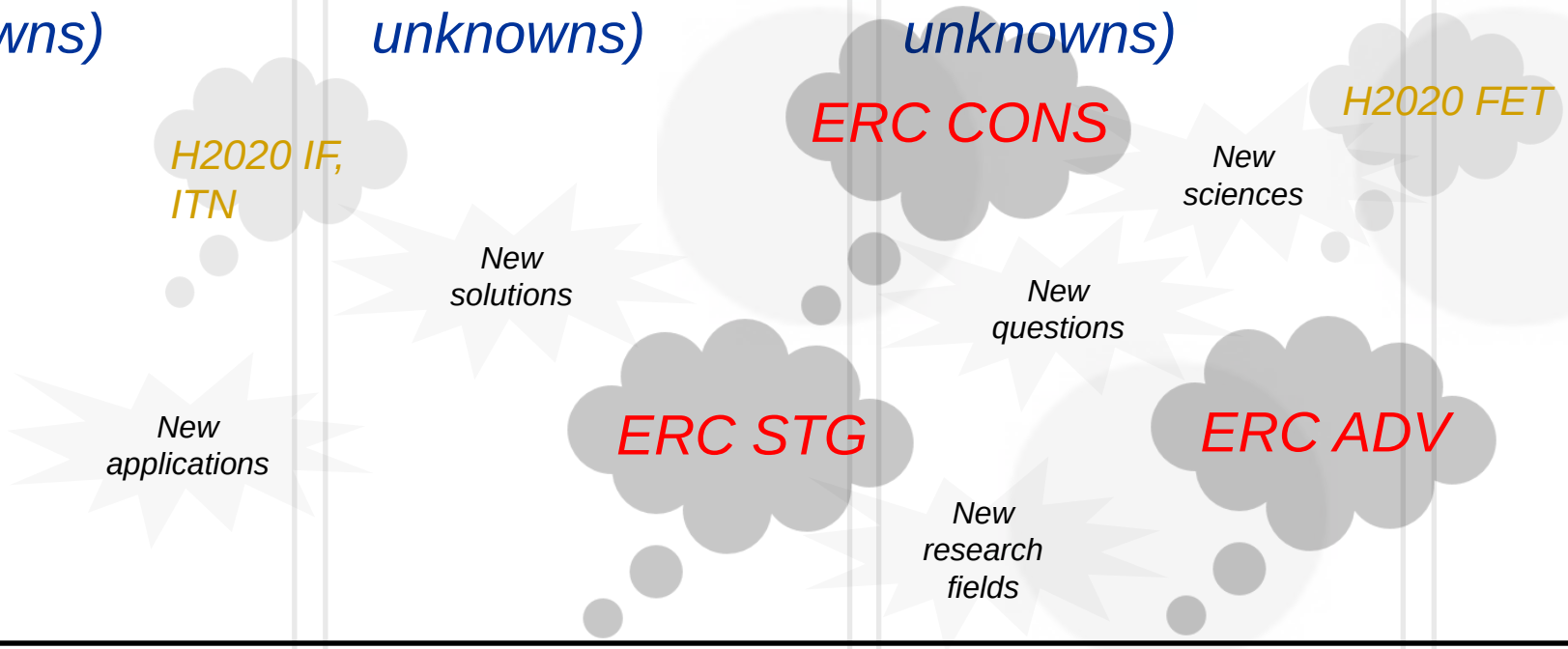
Version 1.0 | **Version 2.0** | **Version 3.0** | **Version 4.0**

Version 3.0…

Known systems, known likely improvements *(known unknowns)*

Known systems, unknown likely improvements *(partially known unknowns)*

Partially unknown systems, unknown likely improvements *(unknown unknowns)*



Version 1.0 | **Version 2.0** | **Version 3.0** | V4.0

Version 3.0…

Known systems, known likely improvements *(known unknowns)*

Known systems, unknown likely improvements *(partially known unknowns)*

Partially unknown systems, unknown likely improvements *(unknown unknowns)*

Where you are now

Where you need to be

Geniuses in the field

Version 1.0 | **Version 2.0** | **Version 3.0** | V4.0

ERC and Innovation

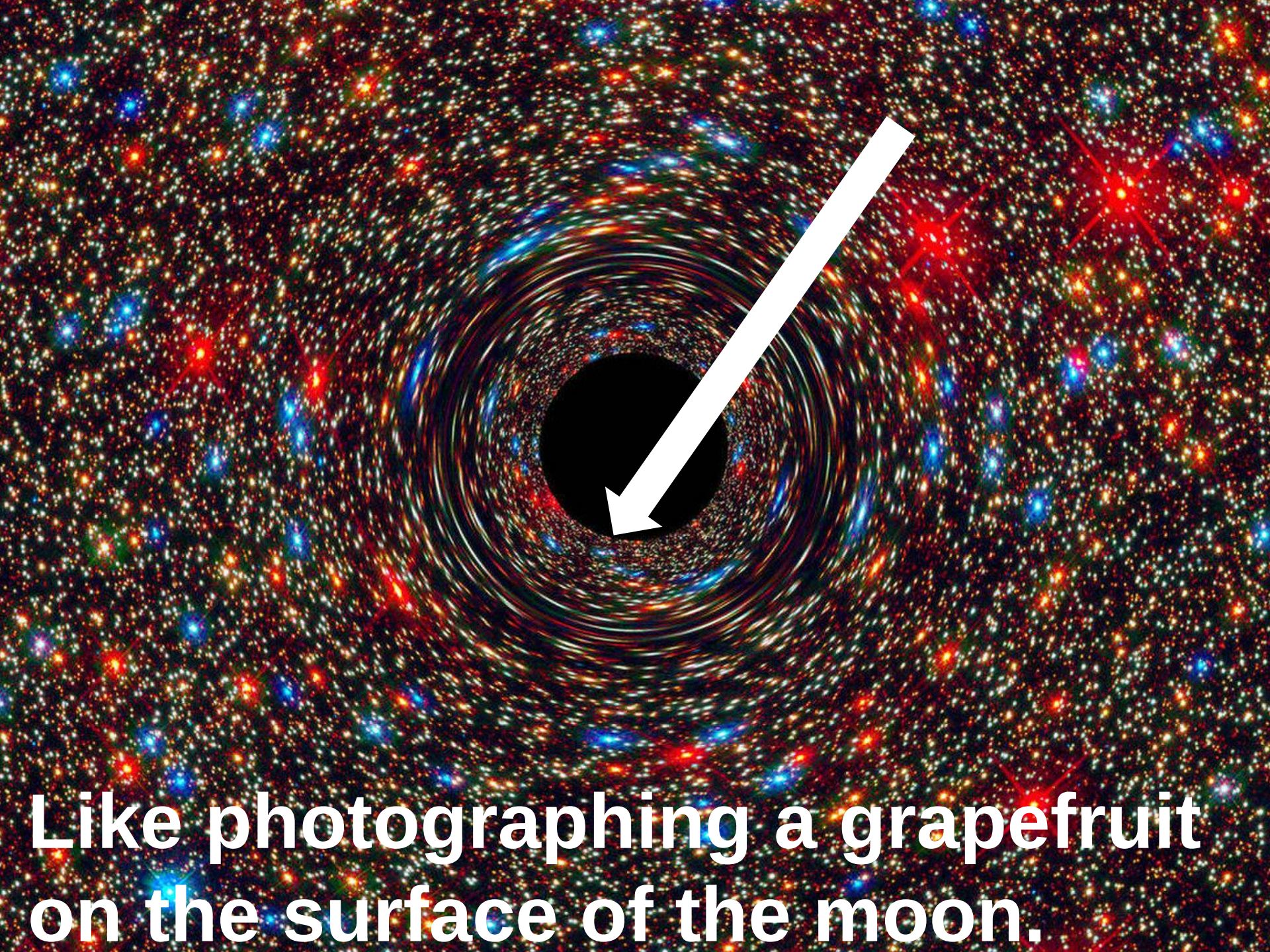
Your ERC proposal failed because it was not innovative enough.

To succeed your proposal must go beyond the realm of existing research ideas and end in a *new scientific field.*

A good research project suitable for ERC raises more new questions than it answers.

These new questions seed the creation of new fields in research and science.

ERC innovation example: Photographing a black hole raises…
lots of new questions.


Like photographing a grapefruit
on the surface of the moon.

Unfolding a Black Hole

But also, light will be severely bent around the event horizon; in fact, you will be seeing light that had come from many directions before skipping around the black hole's edge. You are seeing multiple viewpoints at once and will need to *unfold* the image.

How do you see things from multiple viewpoints at once

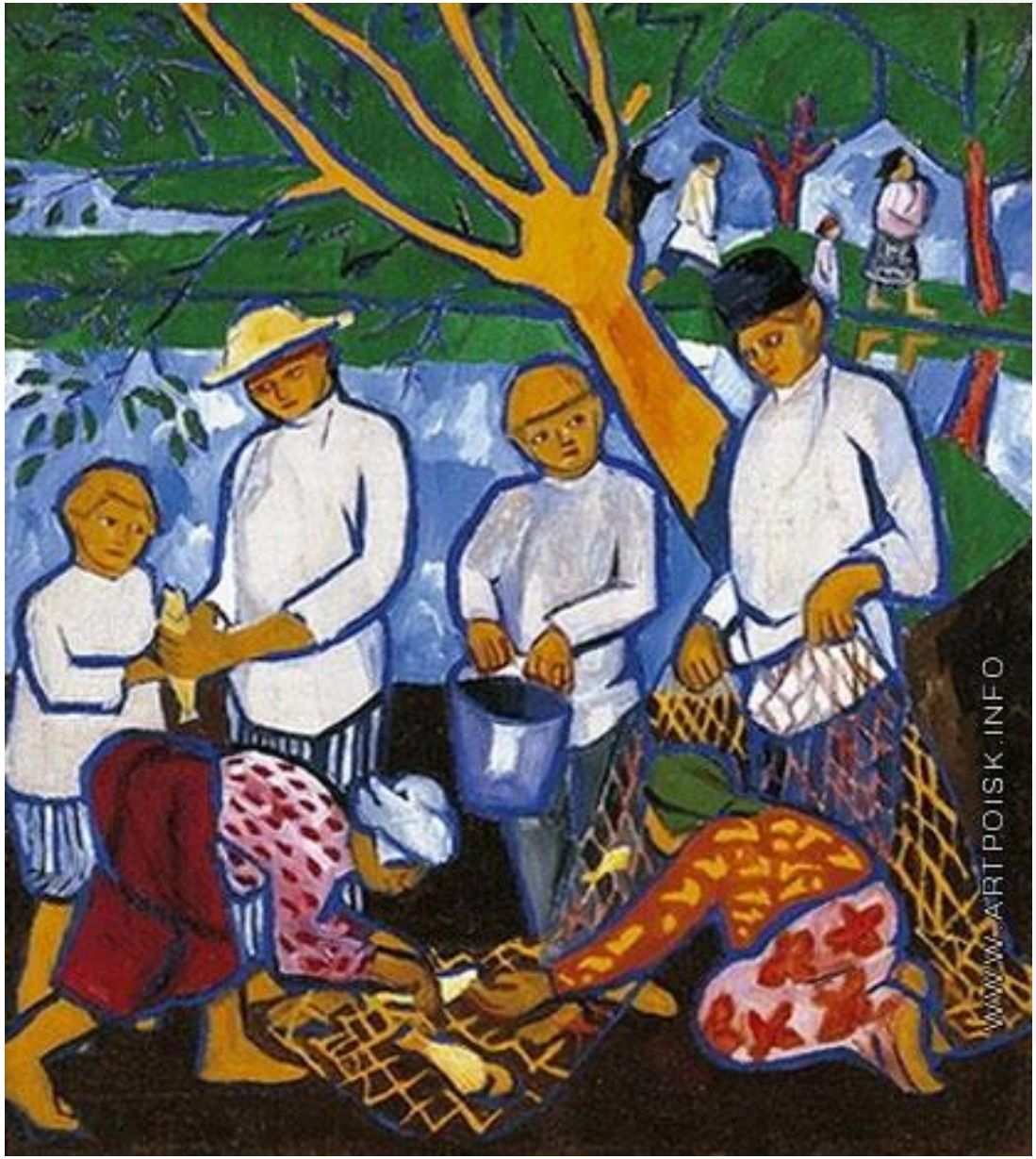
Unfolding a Black Hole; Cubism?

Brother Picasso

Unfolding a Black Hole; Rayism?

Ivan Kliun

Unfolding a Black Hole; Gone Flat



Natalia Goncharova

Unfolding a Black Hole; Collapsed to Idea

John Dodgson

Unfolding a Black Hole; Complex Topologies

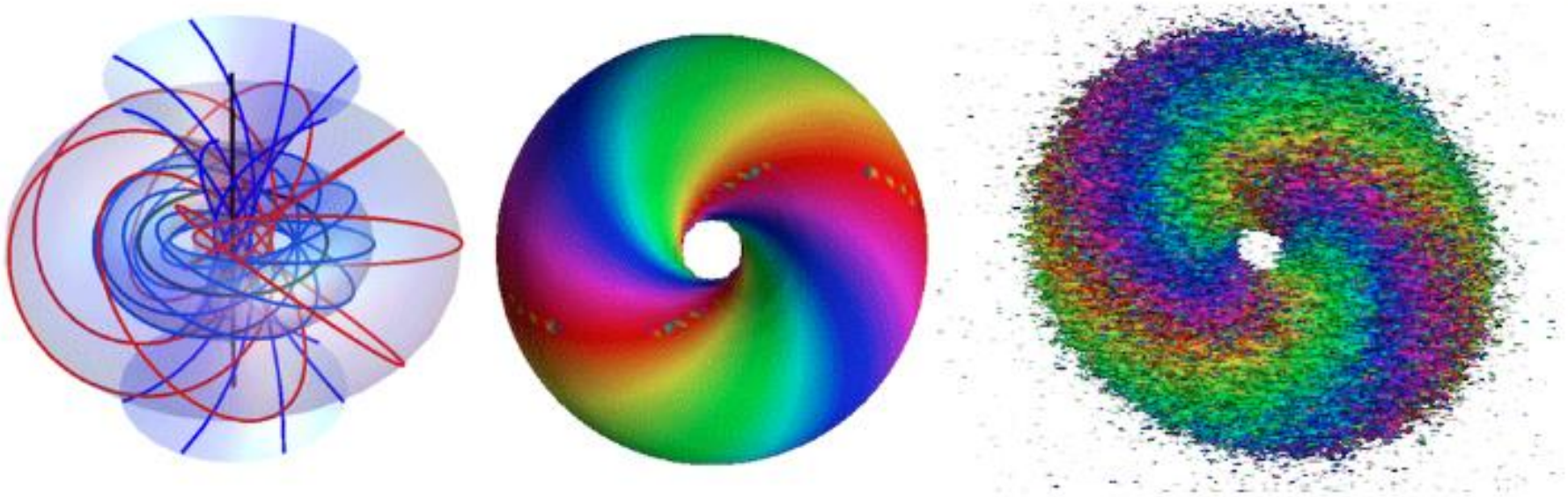
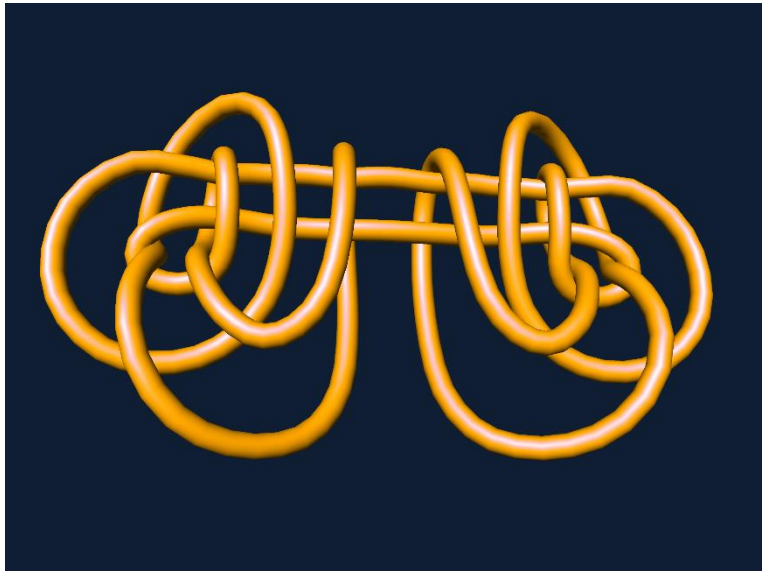
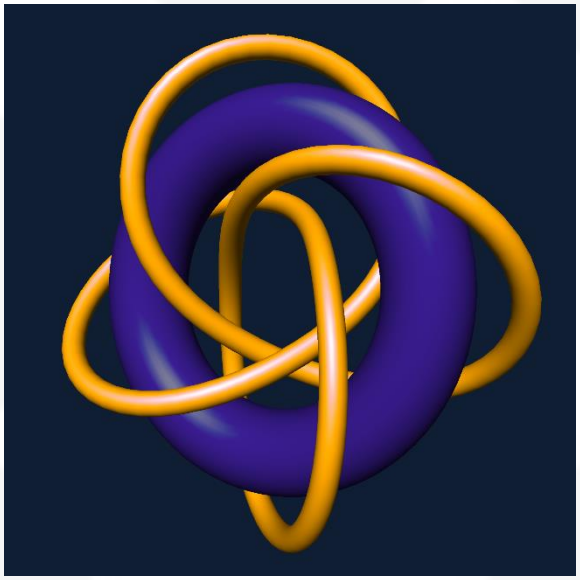


Figure 1: The Hopf fibration (left) is a complex shape discovered in the field of topology that resembles a series of linked rings wrapped into a torus. Experimentalists used a laser beam to reorient the molecules in liquid crystals such that their molecular field—represented by lines that correspond to one specific orientation of the molecules in space—formed the same shape. (Center) A simulation of what the Hopf fibration should look like using the authors' technique for mapping the liquid-crystal director field to a color map. To read the visualization, note that every point on the surface of the torus lies in the xy plane, while the colors correspond to points on a color wheel and define the polar angle of the director field in the xy plane. (Right) The winding of the actual field lines, as measured with fluorescence microscopy. [Credit: B. G. Chen *et al.* [1]]

Unfolding a Black Hole; Minimal Knot Energy





Is there an optimal way to tie a knot in space, or to embed a more general submanifold? And is there a natural way to evolve any knot to an optimal equivalent one, so that we could detect whether two knots are really the same?

One approach to such questions is to associate to any geometric knot an energy, and look for minimizers or critical points of this energy. If the energy is infinite for immersions which are not embeddings, then presumably its gradient flow will prevent self-crossings and preserve knot type. One way to get an energy with such an infinite barrier against self-crossings is to think of spreading charge along the knot and then consider the electrostatic potential. Such an energy for knots was introduced by Ohara and studied by Freedman, He and Wang, who proved it was invariant under conformal (Möbius) transformations of the ambient space.

Photographing a Black Hole

Should we be looking to art, or mathematics, or engineering, physics, chemistry, information theory?

So many new questions, many of which may trigger advances
across many fields of human understanding.

The result is not just new answers, but new questions, suggestions
for new methods, tools, and ways of thinking that may have to be taken up by other fields and future generations.

Photographing a Black Hole

An aside: this illustration is at least partially dependent upon the assumption that information cannot escape the black hole, but this may not be true; since making these slides, a new way of photographing a black hole may have emerged: imaging the Hawking radiation emitted from black holes coupled through arrays of traversable wormholes (example https://goo.gl/uWDLME).

How to Innovate and Have Good Ideas

- Now that we know what the goals are, *how innovative you need to be*, the questions remains *how to get good ideas.*
- I have asked a number of well known scientists, and compiled their responses.
- First, what the experts say…

How to Innovate and Have Good Ideas

James Webb Young, from *A Technique for Producing Ideas:*

1. Gather raw material, and don't shy away from any subject field.
2. Digest the material, looking at it in every possible way.
3. Step away from the task at hand. Here, he stresses the importance of making "no effort of a direct nature."
4. Let your idea return to you organically. "Out of nowhere the Idea will appear," he writes.
5. Bring your idea into the real world, and develop it based on feedback. Young calls this stage "the cold, gray dawn of the morning after."

How to Innovate and Have Good Ideas

It seems likely that different people have different natural processes for being creative and thinking of great new ideas.

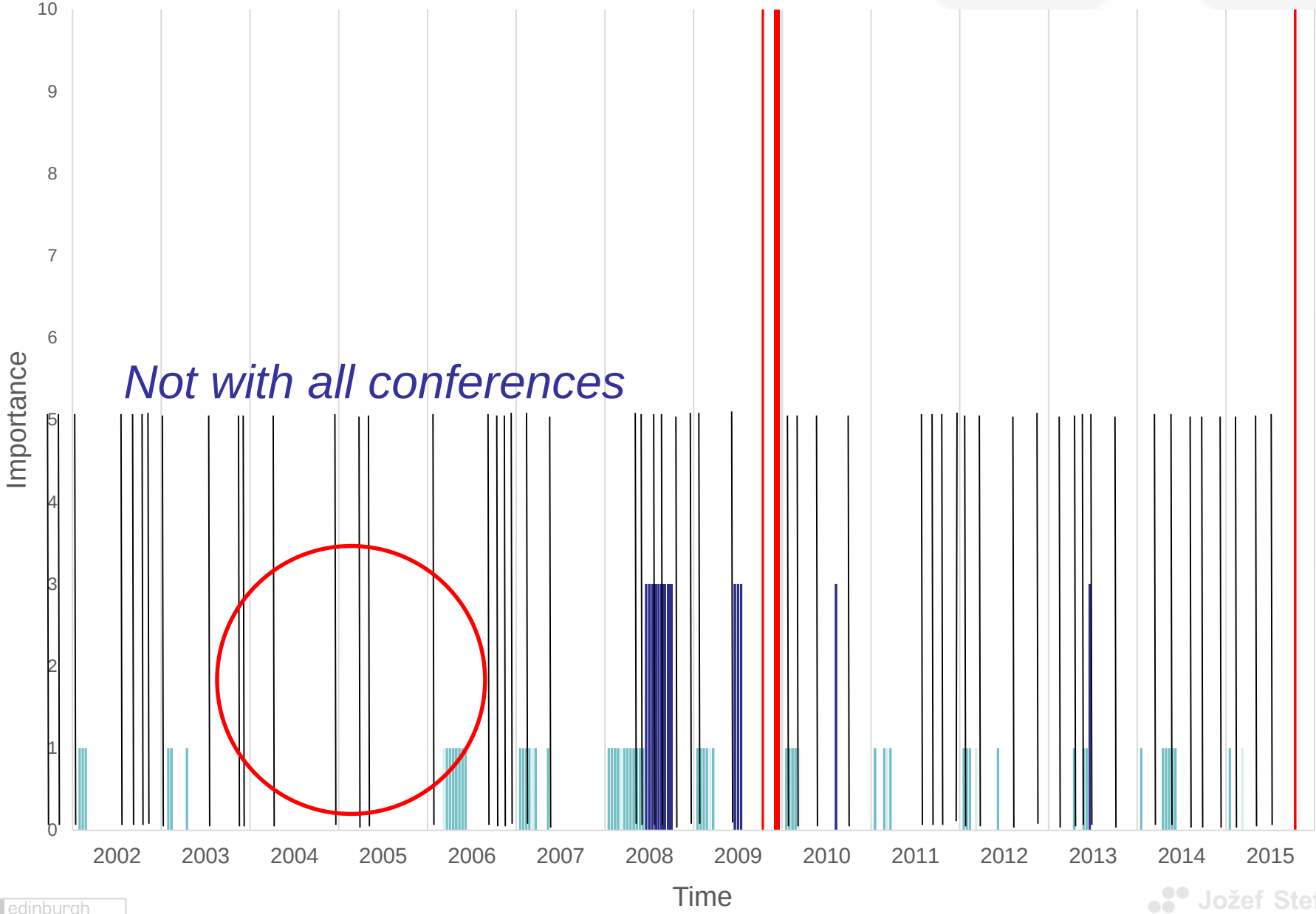
An example, courtesy of Igor Musevic.

How to Innovate and Have Good Ideas

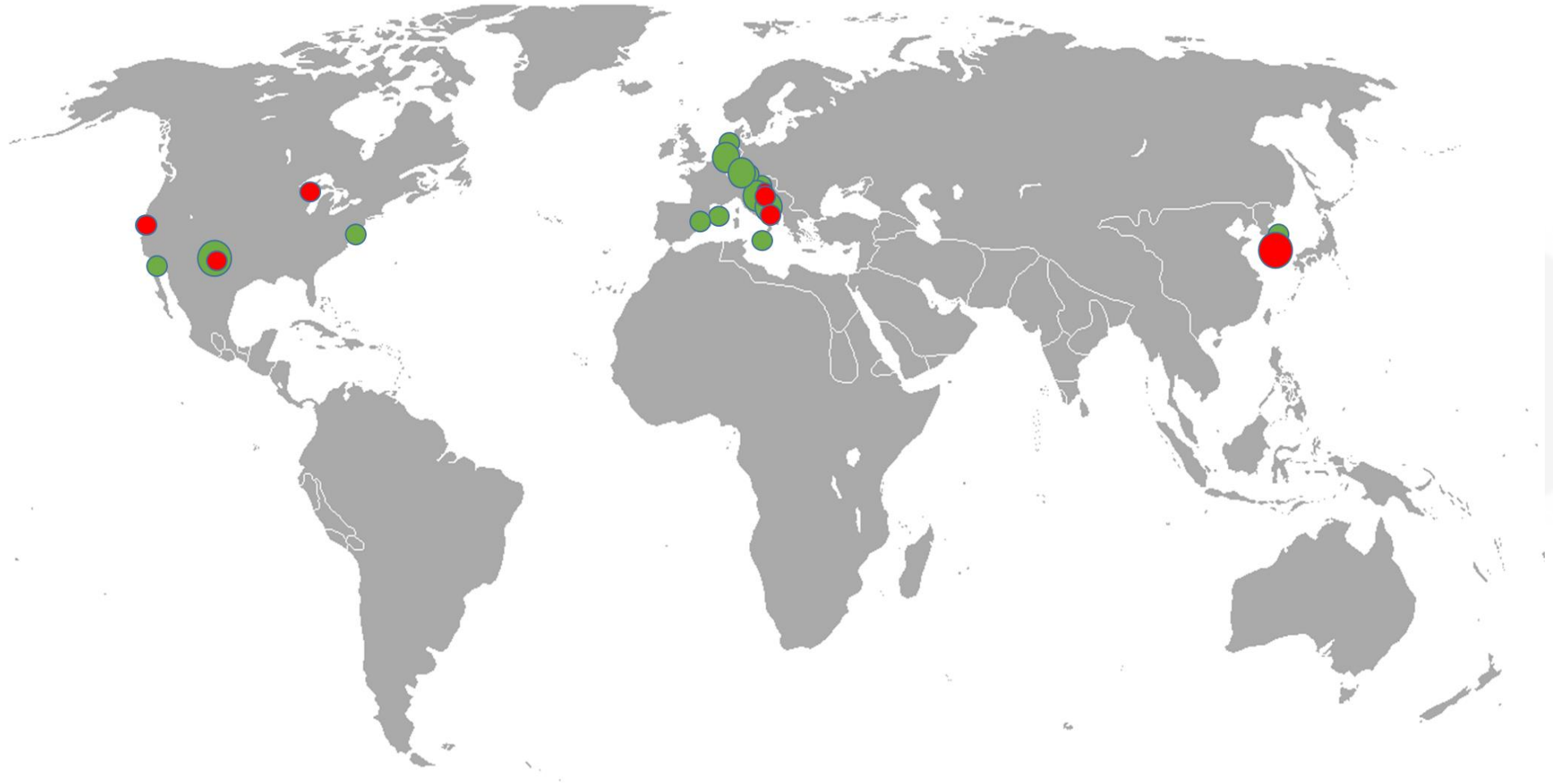
Igor kept records of each idea he got, so has records of his own good ideas since 2004. Being an experimental physicist, he made an analysis of these records to identify what might trigger good ideas. *A summary…*

- There is a certain period in a lifetime when there is strong creativity.
- Most of the good ideas happened at conferences (10 times more), especially the “wrong” conferences, that were outside of his field.
- “Wrong” experiments and thinking perpendicularly often helped.
- There are good *places* in the world where his creativity was enhanced: San Francisco, and Jeju island in South Korea.
- Science fiction movies notably enhanced his creativity. Also shaving.
- Similar good ideas tend to emerge simultaneously across the population.

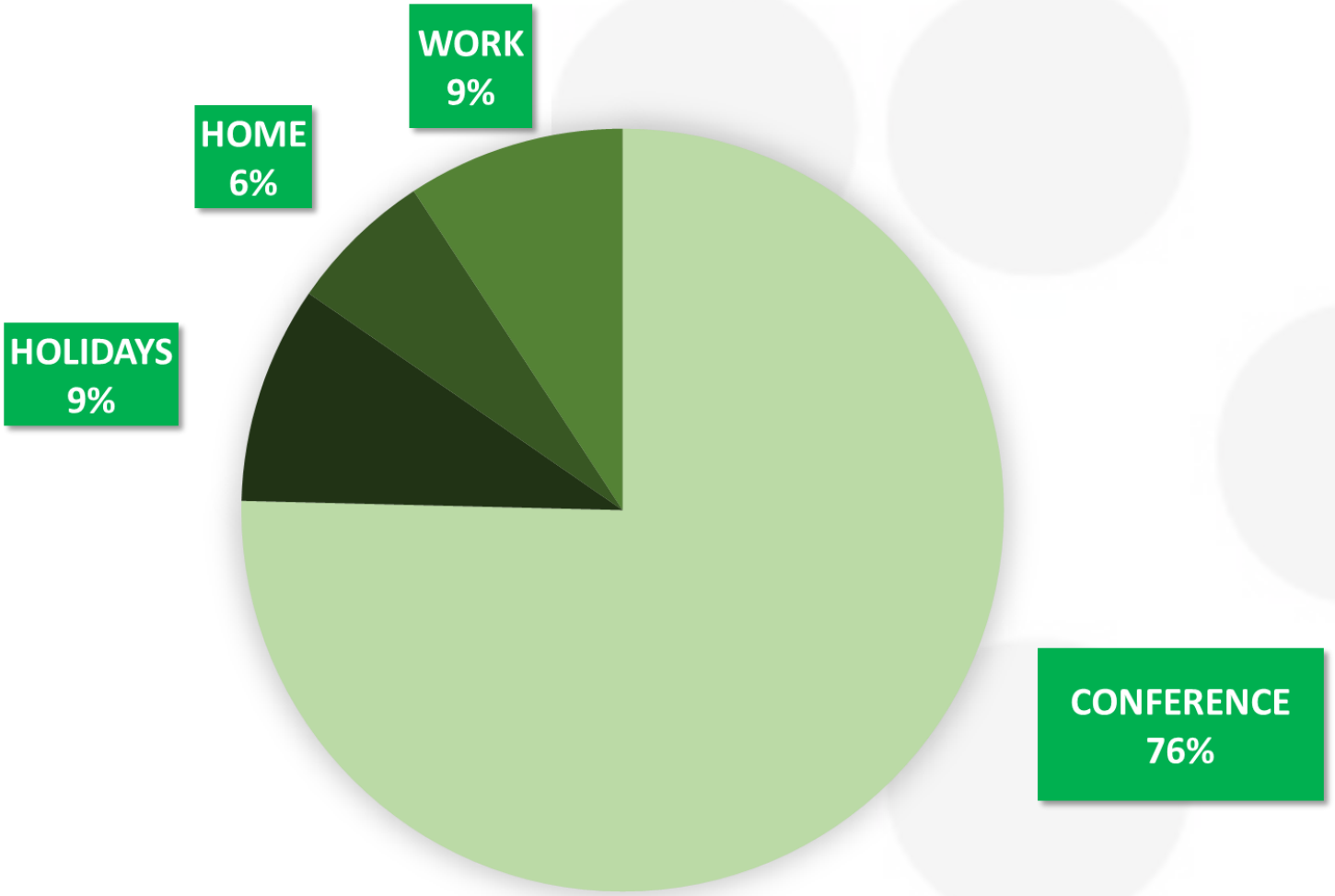
Is there a coincidence with conferences?



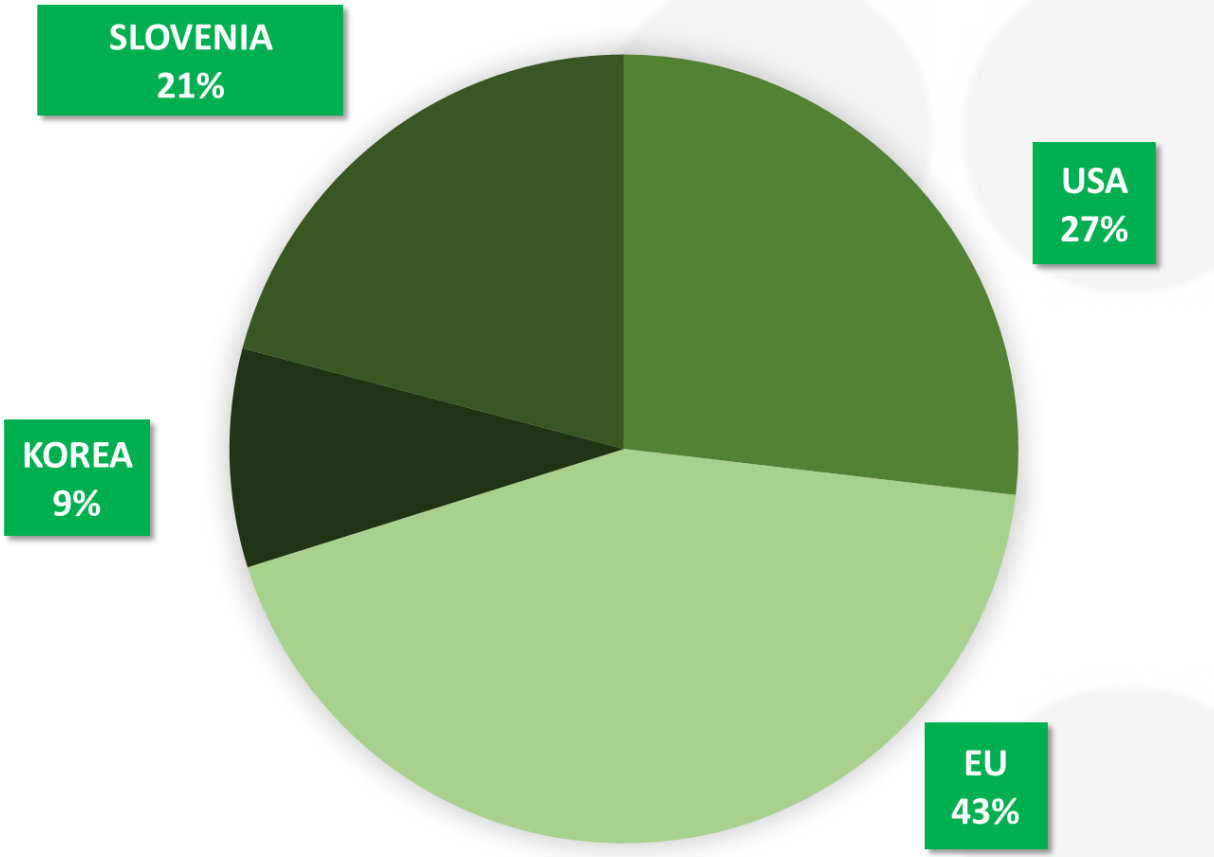
IDEAS BY PLACE OF ORIGIN



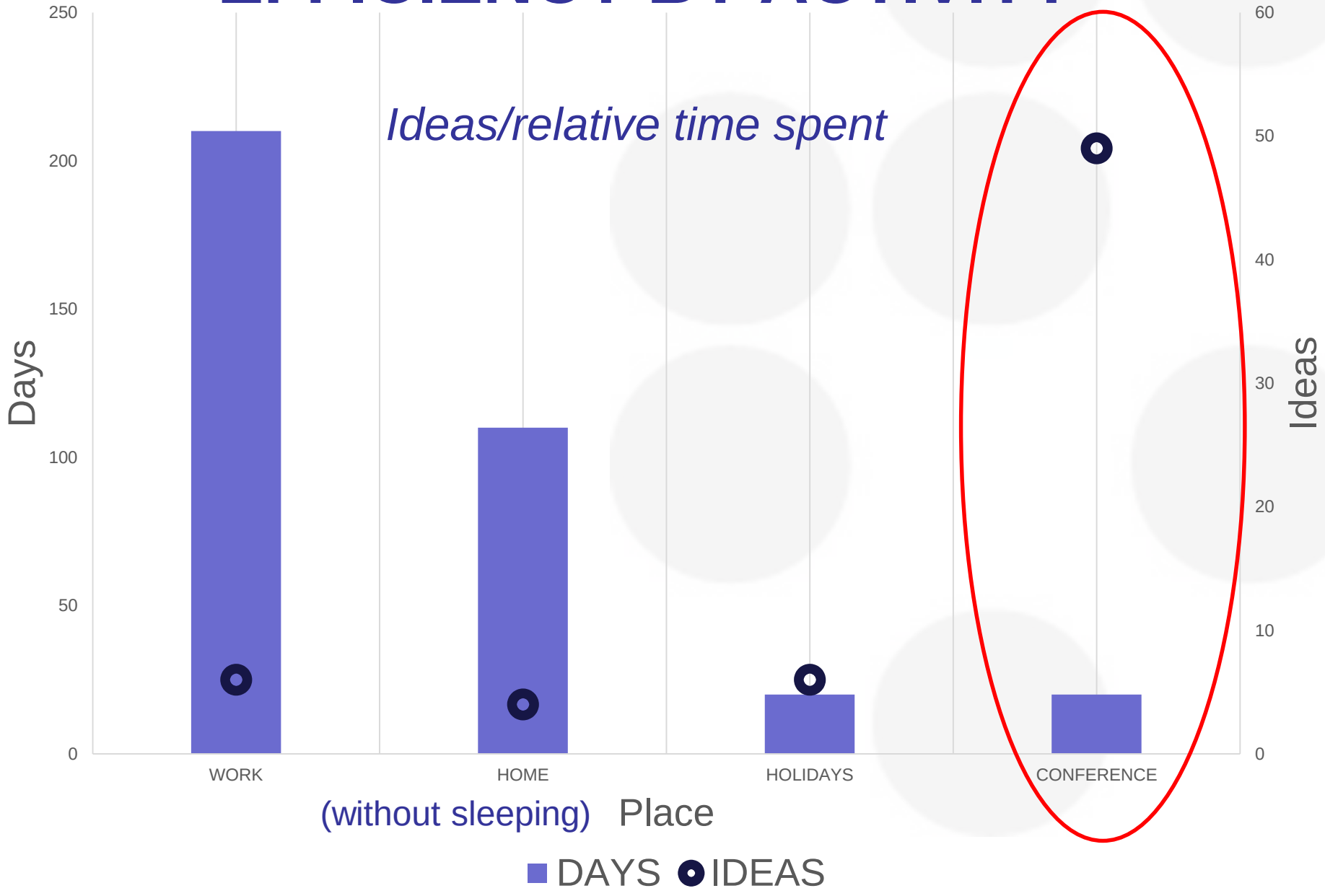
IDEAS BY PLACE OF ORIGIN



IDEAS BY PLACE OF ORIGIN



EFFICIENCY BY ACTIVITY



What Works: Find Your Space…

On the importance of **place.**

Inspiration will not come to you, you must go to it. Where is your inspiration?

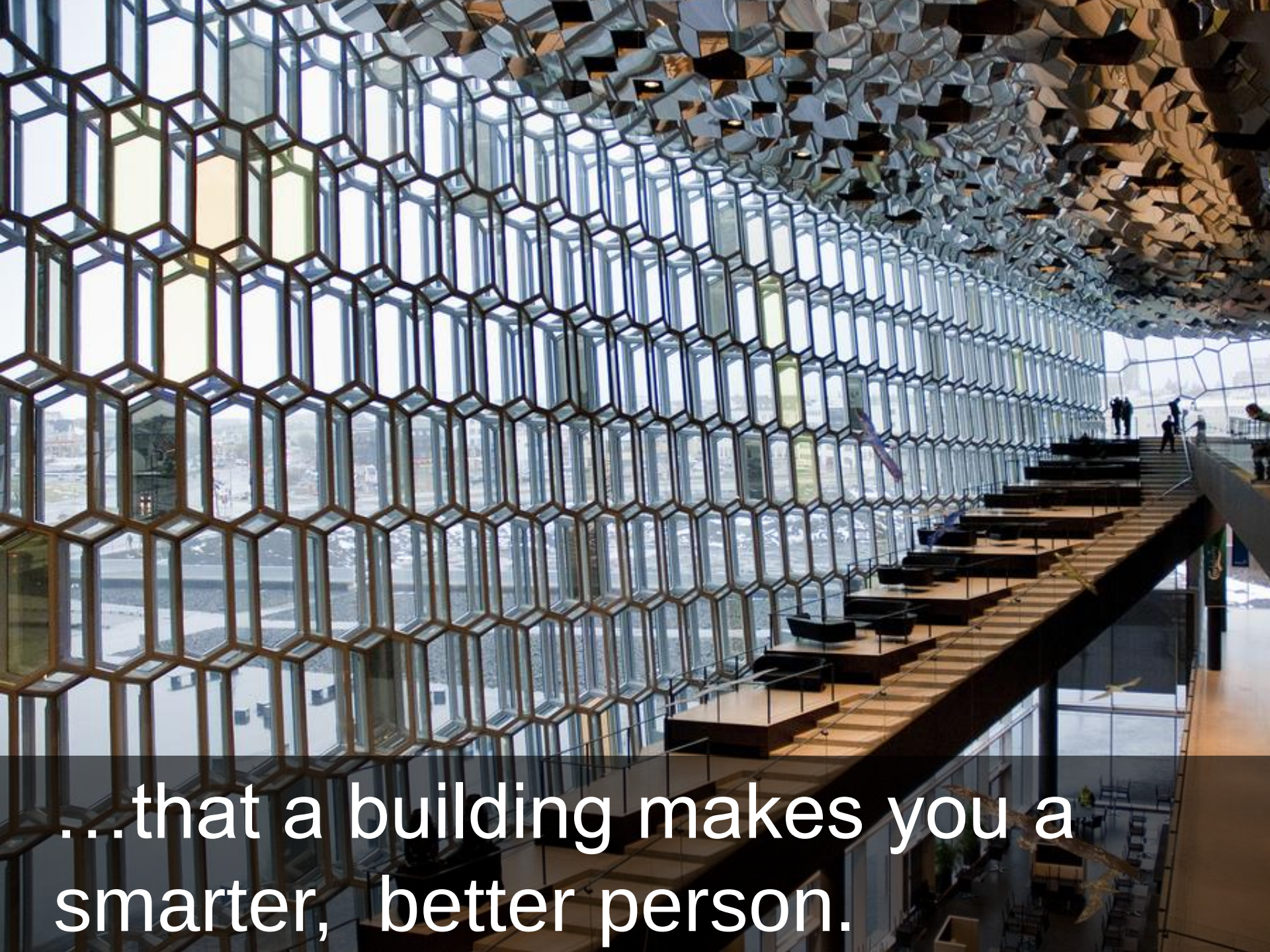
Story: Ásmundur Sveinsson Museum in Reykjavik, Iceland

“I love my job and love coming here to work…”

“…because this building makes me smarter…”

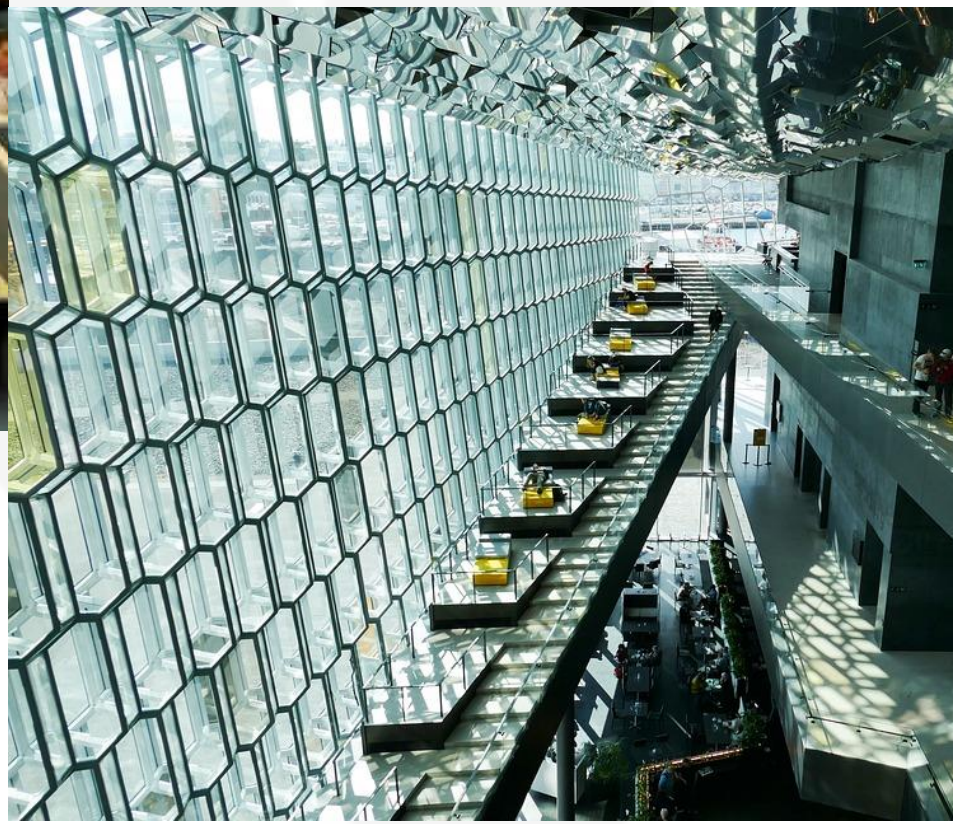

“…this building makes me a better person.”


Think about what it means…



…that a building makes you a smarter, better person.

Bad ideas.



Good ideas.

Find your space that makes you a smarter, better person, and good ideas may find you.

How to Innovate and Have Good Ideas

What also works?

What Works: Mentors…

- I cannot stress this enough: working with clever people will make you clever. *Working with stupid people will make you stupid.*
- Find great people and stand next to them. Literally. Find someone you respect, someone you want to impress, someone you are scared of.
- Mentors can be younger or older.
- *As in jazz, always work with people much better than yourself.*

What Works: Opinions…

- Meet new people and find people you want to work with. Be enthusiastic, find things you are positive about.
- Think big.
- Never stop learning. Have high standards. Be uncompromising. Demand to do what you really love.
- *Sleep.* Sleep whenever you want as much as you want, but work whenever you are awake. :>)

What Works: Opinions…

- History is made by those who turn up and are in the right place at the right time. This is usually called *luck.* Figure that out.

- *Have a go.* The more you try, and the diversity of things you try, the more you will succeed. Combine things. Story: *WHO, EU Working Group on Teledemocracy.*

What Works: Opinions…

- Explore the **edges of fields** through studying, visiting new places and labs.

- Immerse yourself across fields: every day I get newsfeeds on AI and ML, new businesses, politics, architecture and design, mathematics, physics and materials, *Nature*, art and literature, logistics, literature, philosophy and theology…

- Identify your creative activities (might be reading, art, swimming, good wine…)

What Works: Opinions…

Find things that are likely to make you a better *thinker*.

Example for me – literature. Literature makes you more *literate* and a better, more creative, more agile thinker (for example: Nabakov, Camus, Canetti, Dostoyevsky, Genet, St. Exupery, Wells, Orwell, Vonnegut, Huysmans, PK Dick, Grass, Hesse, Levy, Angelou, …)

What Works: Opinions…

From Peter Ross:

"I don't think there are universally applicable tips; what works for one person doesn't necessarily work for another. Some thrive on stress and hard work; others don't. Klaus Roth (a Fields medallist) told me that he was convinced that a person could do no more than four hours of really good mathematical work per day, and advised spending the rest of the day doing other things: music, admin, non-creative parts of teaching, reading, etc. I also think that if you want to be creative, you can actually learn it by studying, especially in areas such as maths where there is so much creativity and so enormously many varied techniques and methods. Being creative: does it help to have a sense of humour? Think of the people you know who you regard as notably creative: what characteristics do they have?"

What Works: Opinions…

From Jean-Marie Dubois:

"It is difficult for me to answer such a profound question. Why this idea, and not this one? First, because few people have ideas of their own, and second, because as Louis Pasteur used to say, chance favours only prepared minds. And for me, to prepare his mind is a question of culture and therefore curiosity. Einstein said that he had no talent, except that he was curious of everything. Science nowadays is organised in such a way that there is no time for curiosity. Young scientists have to add one or two points to an already existing curve, and they like to show off like a chicken when they find a small polished stone in the stream of their predecessors.

Time should be given to young scientists, especially to young lecturers, to think and look at few stupid ideas. Shechtman, Nobel prize winner, says that in his country, Israel, it is admitted that one needs 1000 ideas, to have a brilliant one."

What Works: Opinions…

From Jean-Marie Dubois:

“This brings us a bit far from your question, but since it is a personal question, I had 1.5 years in Cambridge to do nothing except my commitment to dine once a week at the high table. Therefore, I could read quite a few books on topology, catastrophe theory, differential equations, etc. which were of no value for my job, but relaxed my mind. And with this I got some preparation to understand theoreticians who blossomed when quasicrystals were discovered few years later. As an indirect consequence, I was the first who published an experimental verification of the six dimensional crystallography of a quasicrystal.

In brief to answer your question: read, listen, visit, go to museums, chat with colleagues, in and outside your field, and never confine yourself to one single special field. And of course, teach to answer the nasty questions of your students, and sometimes, of your friends. This also helps to refresh one's mind.”

What Works: Opinions…

From Jean-Marie Dubois:

“Great ideas are mandatory, but they must be conveyed to one's contemporaries' minds. Something that is too early, or too complicated because people cannot understand (either due to their lack of knowledge or because it is not clear enough) is useless. Georges Brassens, the most famous contemporary French singer (according to my taste) says in one of his songs: "Un don sans technique n'est rien qu'une sale manie" (a gift without technique is nothing else than a bad habit). It is important to stress how much the presentation and its clarity matter on top of the genius ideas.”

What Works: Opinions…

From Jean-Paul Brasselet:

"Of course it is necessary to be curious, open-minded, ready to see and consider "out of the ordinary" things which are inside "ordinary". Maybe, for some people, inspiration comes with an overworked brain. However, I think that new ideas, inspiration comes in a quiet, peaceful state of mind.

Here, in Japan, I got new, original ideas… in onsens. To be in hurry is not good for inspiration, and onsens are excellent for that: being relax, not as in zen, but another way. I have to recognize that I had also some (few) "zen" experiences and that these were not immediately fruitful. But zen helps to put ideas in good place and opens the door for discovery of new theories, for example. Ideas do not come alone, they are fruit of the brain produced by comparison, by analogy of different inputs. The magic sentence (at least in maths) is "That makes me think about….". The most the inputs are different, nicer is the idea. Of course that does not work each time, you need to be patient to catch a fish and to let the fish coming to you, no hurry…"

What Works: Opinions…

From Jean-Paul Brasselet:

"I do not say that the brain should be "well ordered" in a too much tidy way. If too much ordered, you cannot see analogies and you miss inspiration. Disorder is good!

Inspiration comes in visiting museums, attending a lecture, a conference, reading books, discussing with colleagues, with people in general. Always being curious. One of the reasons I am reluctant to new ways of publications (internet articles) and I enjoy written journals is that many times searching for a paper in a scientific journal in a library, I was attracted by another paper before or after the one I wanted to see. Several times such "non searched paper" gave me new ideas, in particular one of them was one of my most famous discovery.

Yesterday I was in onsen in Kirishima, near Kagoshima, that time, no new inspiration, no new discovery but peaceful and relax."

An *Onsen*…

What Works: Assumptions…

- Sometimes you need to make a leap of faith or realization about your *assumptions.* Example: the age of *artificial intelligence* is actually coming to an *end,* while the age of *machine intelligence,* which we know almost nothing about, is just about to *begin*. What would my work look like in this new age and paradigm? What can we know about it that is likely – what *assumptions*?

- Radically altering assumptions leads to good *thought experiments*.

What Works: Thought Experiments

- Try to formulate thought experiments that carry your field and its assumptions to the edges of rationality. Try to think in metaphors and comparisons. Follow trends to their natural end points and look for intersections with other trends and ideas.

- An example: *the end of AI.* Most artificial intelligence is based on biomimetics, getting machines to do what humans do. Many people say this is the only way possible because it is the only intelligence we know, and nature evolved neural networks and CNSs for sensing, and it is all we can reason from. But is that true?

Create Thought Experiments

As a metaphor, let's think not of *reasoning,* but of locomotion – of *going really fast.*

Create Thought Experiments

Inspiration from nature.

Create Thought Experiments

Resulting machine.

Create Thought Experiments

Why wasn't biomimetics enough? Because we learned early on that *go-fast* machines want *wheels*, it's their *natural preference.*

The machines are not like us.

Create Thought Experiments

So one thought experiment might be about wheels versus legs.

Animals have legs, and we have no natural examples of wheels. But we discovered that machines do not want legs, they want wheels. We abandoned biomimetics because machines prefer wheels even if nature does not.

Now, applying this metaphor to artificial intelligence: **what is the *wheel of reasoning* for machines?** Probably not neural networks.

What might it be made of, based on what principles? Wheels want roads. What does the *wheel of reasoning* **want**?

Questions?

Sections of the Proposal

Let's look at an ERC proposal that is well formed and identify some of the things that were done right.

Thanks to our guest for allowing her ERC STG to go under the, *ahem*, *microscope.*

Abstract

The *abstract* needs to clearly draw the reviewer in and create a narrative that shows why the project is useful, innovative, and makes

The inability for existing methods to accurately model and predict spatial distribution of elements in plants at the tissue level has critical consequences for nutritional quality and safety of edible plants. A major obstacle is the lack of sequential sample sectioning method in cryo, which would combine speed, low costs and reproducibility, whilst avoiding chemical fixation and ice-crystal formation. The *SPADE* project will develop a high-throughput sample preparation method satisfying all these requirements and standardise a user-friendly workflow for the prediction of spatial distribution of elements in plants. Sections will be analysed using micro-proton induced X-ray emission, a multi-elemental and fully quantitative technique with resolution <1 µm. Quantitative 2D element distribution maps will be used to construct 3D distributions providing unprecedented knowledge useful for increasing concentrations of elements often lacking in human diets and restricting accumulation of potentially harmful elements in edible plant tissues. In addition, representative cross-section(s) that will suffice for predicting 3D element distribution maps, avoiding the need to analyse large numbers of sections from a whole organ, will be identified. This will increase the value of 2D distribution maps, providing that cross-sections are taken in designated regions, and will enable us to move closer to reaching consensus on tissue-specific element distribution in plants. The workflow and quantitative 3D distribution maps will be available open-access allowing retrieval of tissue-specific element concentration profiles and investigation of element interactions in tissues. Deposition of data, obtained following the standardised workflow by plant biologists, agronomists and food technologists, will enable initiation of a global data depository valuable across fields for the development of a more nutritious and safer food chain.

The *SPADE* project is interdisciplinary. Research combines life sciences with physics and engineering. It is suggested that the project is reviewed across panels:

Panel 1: LS9 Applied Life Sciences, Biotechnology and Molecular and Biosystems Engineering

Panel 2: PE4 Physical and Analytical Chemical Sciences

Section B1

B1 Section A - Extended Synopsis is limited to five pages; this is where you hook the reviewer on the idea, and offer just enough details to prove its usefulness and plausibility. Describe WHY, WHAT, and a very small bit of HOW, WHEN, and WHO.

Section a: Extended Synopsis of the scientific proposal (max. 5 pages)

State of the Art

Spatial visualisation of biomolecules has revolutionised biochemistry (and the development of the technology was awarded the Nobel Prize in Chemistry this year). Having in mind that all biomolecules are built from elements and interactions between them enable life, we are ready for the next step: visualising spatial distributions of elements in cells, tissues and organs of different organisms. At present, elements are too small to be directly visualised microscopically; we can detect and visualise most of them indirectly using X-ray fluorescence (XRF) or mass spectrometry (MS) techniques. However, we are significantly limited by challenges connected with sample preparation that would preserve both structure and element distribution at all levels (Vogel-Mikuš et al. 2014). Furthermore, while the instrumentation for element imaging is developing very quickly, already reaching nanometre lateral resolution, sample preparation has been significantly neglected (Castillo-Michel et al. 2017), raising doubts about the reliability and replicability of conclusions. The overall aim of the *SPADE* project is to overcome the challenges of sample preparation and spatial visualisation, and standardise workflow for the fast and cheap acquisition of tissue-specific element distribution maps crucial for the development of more nutritious and safer food products.

***SPADE* will focus on spatial distribution of elements in plants as their element composition is critical for quality and safety of human diets.** Most essential elements in human diets are provided either directly or indirectly by edible plants, therefore variation in the element compositions of edible produce is of considerable importance for human nutrition (White et al. 2013). Seven elements (iron, zinc, magnesium, copper, calcium, selenium and iodine) are often lacking in human diets with resulting negative impacts on health and wellbeing of more than two billion people worldwide (White and Broadley 2009). Substantial progress has been made in increasing concentrations of these elements in edible plant tissues to reduce malnutrition (http://www.harvestplus.org/) on one side, and in limiting allocation of potentially harmful elements to edible plant tissues (Norton et al. 2014, Duan et al. 2017, Punshon et al. 2017) on the other, and both challenges have generated extensive public and political interest. Nevertheless, further actions are required to expand our understanding of uptake, transport and final deposition of essential elements and potentially harmful elements in edible plant tissues. To date, we have compiled large data sets on element composition of plants at organ levels (roots, shoots, leaves and grain; Salt et al. 2007, Blamey et al. 2015, Sugita et al. 2016) and have made significant advancements at the cellular level (e.g. Zhao et al. 2014, Hare et al. 2015). However, our understanding of element distributions at tissue level is lagging behind (Conn and Gillham 2010), and requires focused efforts to bridge the gap between these two scales.

The project will address the grand challenge of obtaining crucial, quantitative information on the spatial distribution of elements in biological samples, so far limited by the limited efficacy of the data acquisition. There are several working methodologies used for visualising spatial element distribution in plants at the tissue level, however these methods usually disclose the location but not the concentration of an element. Quantification of data corrects for multiple

Section B1

Identify possible weaknesses that a reviewer might find, and address these directly throughout the proposal's sections. Remember, these are not necessarily *actual weaknesses*, they only need to be *possibly perceived weaknesses* by the reviewers.

Weaknesses, Strengths

How to turn weaknesses into strengths?

- EU projects fund *overcoming limitations*, both in the SOTA of a field and in its personnel, teams, and research landscape.
- Identify weaknesses and have a clear plan for each.
- Weakness = lack of management experience; Strength = clear, comprehensive plan to learn and apply management skills through courses, mentoring, regular meetings and feedback, and complementary training.
- Weakness = ***x.*** Strength = clear, ambitious plan to *overcome* ***x***.

Section B1

Link *challenges* in the field to limitations in the SOTA, and then formulate these directly as project innovations and objectives.

Weakness: possible perception of low innovation

The *SPADE* project will innovate beyond the state-of-the-art and address key challenges in the field:

- New workflows based on standardised high-throughput cryo-sequential sample preparation useful for structural visualisation of tissues in 3D and tissue-specific metabolite analyses.
- Identification of representative sections, whose analysis suffices to describe tissue-specific analysis of the whole organ, reducing the amount of resources and time previously required for element distribution analysis.
- Algorithms developed to predict quantitative 3D element distribution from representative sections enabling evaluation of environmental and genotypic effects at the tissue level greatly increasing the information available from current bulk analyses.
- An open-access website providing access to results and models that will enable best practice and knowledge exchange for all levels of education.

These innovations will bring real benefits to industry and help introduce new tools and standards:

- The new workflow will enable faster, more robust informative acquisition of relevant quantitative tissue-specific elemental composition.
- The ability to impact human diets with the aim to decrease element deficiencies.
- The reduction and prevention of intake of potentially harmful elements.

Section B1

Link *challenges* in the field to limitations in the SOTA, and then formulate these directly as project innovations and

Main Objectives and Innovations

The aim of the *SPADE* project is to create a fast and flexible workflow for modelling, predicting and applying spatial distribution of elements in plants. The workflow will comprise six steps (Figure 2), sufficing to model 3D element distribution maps, after key research challenges have been overcome. The workflow will be used by plant biologists, agronomists, and food technologists to address basic and applicable questions (as in two case studies detailed later on).

The *SPADE* project will innovative through a series of linked core objectives, all of which have measurable outcomes and targets for results:

- **Objective 1: development of an innovative sample preparation method combining speed, simplicity and reproducibility**. This sample preparation will replace laborious freezing of small pieces of organs individually and sectioning them piece by piece, which results in weeks of sample preparation for determination of element distribution.

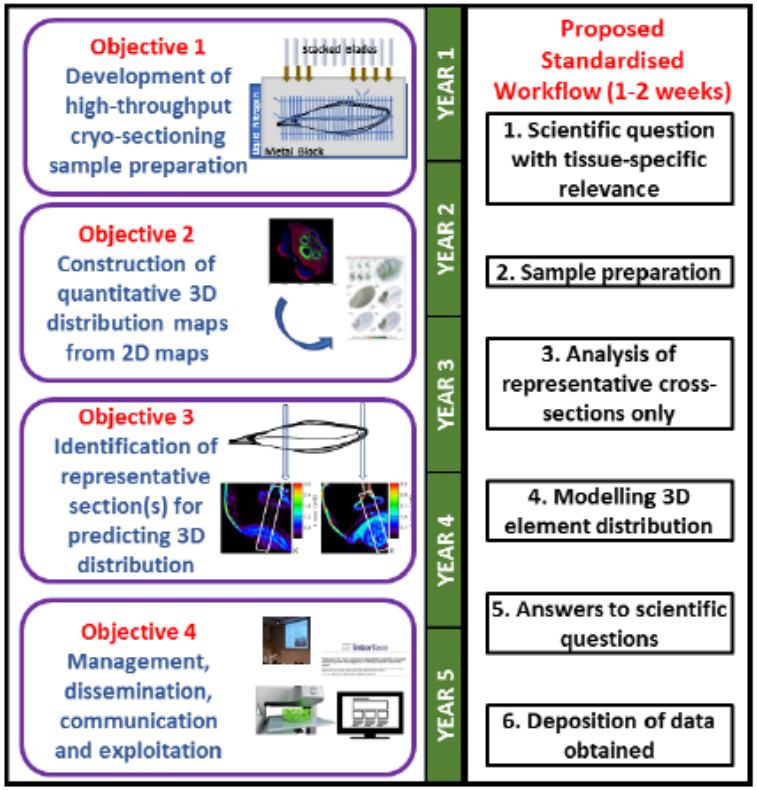


Figure 2: *The objectives and the proposed workflow, which will be standardised and optimised within the SPADE project.*

- **Objective 2: construction of quantitative 3D element distribution maps from 2D distribution maps.** The 2D distribution maps will be obtained using quantitative micro-PIXE set-up, which will be upgraded

Section B1

Objectives specify *what you will do*, methodology explains *how*. In B1 keep the methodology focused and short, and linked directly to the outcomes/objectives. Case studies *illustra*

Methodology

High-throughput sample preparation method for tissue-specific multi-element distribution analyses must avoid chemical fixation and ice crystal formation, whilst combining speed, simplicity, reproducibility and low costs. Tissue hydration and the dynamic nature of cells and tissues make water management during sample sectioning of paramount importance (Dubochet et al. 1988). Therefore, water in the samples needs to be replaced or frozen. Replacement or substitution with organic solvent is a basis for well-established chemical fixation protocols (Davies 1999), but it is a slow method and can result in solute displacement, including leakage of mobile elements (e.g. potassium and magnesium; Perrin et al. 2015). This makes it unacceptable for element distribution analyses. The success of freezing or cryofixation depends on the freezing speed, which prevents the formation of damaging ice crystals. Four different cryofixation approaches have been used: high-pressure, plunge, jet and metal mirror freezing and when performed properly, they can result in water vitrification (Dubochet et al. 1988, Morgan et al. 1999). Cryofixation approaches offer differing levels of simplicity, freezing depths, and costs, and these need to be considered. *SPADE* will make use of metal mirror freezing, performed by pressing the sample on metal pre-cooled with liquid nitrogen, as the most efficient for freezing of larger, soft samples (Morgan et al. 1999).

CASE STUDY 1: A plant physiologist is interested in increasing calcium, magnesium, iron and zinc concentrations in flour. To this end, different soil and foliar fertilisers are being tested to achieve the greatest increase in the endosperm, central part of the grain, predominant component of the flour. Using *SPADE*'s workflow and by analysing only representative section(s), identified within *SPADE*, 3D distribution maps are generated and tissue-specific element concentrations in different grain tissues are determined. Fertiliser effects for optimal increase in calcium, magnesium, iron and zinc concentration in the endosperm are evaluated and decided upon.

Weakness: use cases

To achieve the required speed, reproducibility, and low costs of the proposed innovative high-throughput sample preparation, we propose to combine cryofixation with cryo-sectioning. The metal mirror freezing approach also permits sufficient manipulation space around the sample to allow for simultaneous cryo-sectioning. For analyses of element distribution at tissue level the section will ideally be of a single cell layer to avoid overlapping of cells, which results in blurred distribution maps. Plant cells are of various thicknesses depending on their function; therefore, sectioning tools need to be flexible in

Weakness: too much equipment

Section B1

Methodology should end with a section about verification and measurement of results; *quantify*. Provide key performance indicators and desired outputs/level of innovation.

Weakness: too narrow application – how will it expand its reach and impact?

representative sections. Algorithms for structural whole-plant phenotyping will be adopted and adapted (e.g. Chéné et al. 2012) for use in element distribution analyses.

Verification and validation of results and new methods will be critical to refining the new methods to their most useful outcomes as compared to declared objectives and defined key performance indicators. After analysis of statistically important number of samples, the proposed workflow will be tested with unknown samples. If the standards set will not be achieved, step by step troubleshooting to recognise and act upon weaknesses in the mode will take place. Data, new workflows and standards will be published regularly on the project's website and knowledge repository, and web interfaces and exploratory tools will be assembled according to established practice for bulk element composition data on many thousands of plant samples curated by ionomics HUB (iHUB; http://www.ionomicshub.org/home/PiiMS).

Section B1

End with a presentation of the practical details: *who* and *when*. Show a strong command of the planning and impacts.

Weakness: international engagement

Weakness: not enough managemen t experience

Section B1: CV

Identify weaknesses and develop a strategy for compensating for them. Remove anything in the CV that makes you look “small”. Remove all negative words and phrases, do not highlight weak spots unless you can turn them into strengths.

Section B1: CV

Create a *career narrative* and structure the whole CV to tell only that story.

Combine weak sections to project them as strengths.

Weakness: collaborations, position in field

Section B1: CV

Always simplify negatives or anything that may raise negative associations

- Weakness: career progression

Career development plan is where you create the narrative, and stick to it. Everything points to the project; no distractions. If smart, you can use this section to address weaknesses very well!

Section B1: CV

CDP ends with weaknesses/ knowledge gaps to be addressed, and how the project fulfils the PI's career development needs.

Weakness: vision for field

CV section ends with a vision for the field at five and ten years!

Section B1: CV

Above: establishing authority in the field; all are directly related to the proposal. Create new CV sections as needed.

Section B1: CV

Above: establishing authority, leadership, engagement with the community, dedication to the topic of the proposal.

No distractions, common narrative.

Section B1: CV

Wow. This CV makes it seem like the researcher only has one love in their life, and it is exactly the topic of this proposal. Everything they have done in their career has been leading to only this one great work.

:>)

Section B1 and B2

Section B1: *inspire, communicate, project positivity, show awareness of the field and community needs, be ambitious, open, and excited about your great ideas.*

Section B2: *be **scientifically hard-core.** Explain why what you propose is **difficult.*** B2 is for experts in your field, do not speak down to them; put them in awe of your scientific ambition and thoroughness.

Part B2: *The scientific proposal* (max. 15 pages, references do not count towards the page limits)

Section a. State-of-the-art and objectives

In *B1* an overview of the *SPADE* project was provided, and in *B2* expansion upon ideas is given and the project's methodology is explained in detail.

Optimal development of all organisms depends upon proper provision of sufficient amounts of essential mineral elements, and the exclusion of those that are potentially harmful. The continuous cycling of elements in the food chain begins in the soil solution, where plants acquire elements with roots and transport them across their tissues, ending up, directly or indirectly, on our plates. The final loop of the cycle is in the elements being excreted, ending up in the waters and returning to the soil. Variation in the element compositions of edible plant-based produce is therefore of considerable importance for human nutrition (White et al. 2013); particularly, seven elements (iron, zinc, magnesium, copper, calcium, selenium and iodine) are often lacking in human diets with the resulting negative impacts on health and wellbeing of more than two billion people worldwide (White and Broadley 2009, FAO et al. 2015). Substantial progress has been made in increasing concentrations of these elements in edible plant tissues to reduce

Section B2

Situate the methodology or use cases.

requires focused efforts to bridge the gap between these two scales. *SPADE* will overcome the challenge of time-consuming sample preparation, increase the efficacy of the element visualisation technique micro-proton induced X-ray emission (micro-PIXE), and propose standardised workflow for fast and cheap acquisition of quantitative spatial element distribution maps. **The knowledge obtained will be required by plant biologists, agronomists, food technologists, nutritionists, and quality control and food safety officials, as it is crucial for the development and standardisation of more nutritious and safer food products. Two case studies will illustrate the applicability of the workflow developed within the *SPADE*.**

CASE STUDY 1: A plant physiologist is interested in increasing calcium, magnesium, iron and zinc concentrations in flour. To this end, different soil and foliar fertilisers are being tested to achieve the greatest increase in the endosperm, the central part of the grain, and the predominant component of flour. Using *SPADE*'s workflow and by analysing only representative section(s) identified within *SPADE*, 3D distribution maps are generated and tissue-specific element concentrations in different grain tissues are determined. Fertiliser effects for optimal increase in calcium, magnesium, iron and zinc concentration in the endosperm are evaluated and decided upon.

Section B2

Be *specific.*

Development of fast, cheap and reproducible sample preparation will facilitate the advancement of element distribution studies and computational modelling in plants. Ideally, there would be no sample preparation required and XRF tomography enables just that, however there are stringent limitations to the sample size (around 50 µm; Hare et al. 2015). This makes the technique useful for analysis of single cell algae (de Jonge and Vogt 2010, de Jonge et al. 2010), root tips (Lombi et al. 2011) or minute-sized seeds (Kim et al. 2006) only. Moving towards larger samples, we need to introduce sectioning to reveal internal structures. Tissue hydration and the dynamic nature of cells and tissues make water management during sample sectioning of paramount importance (Dubochet et al. 1988). Therefore, water in the samples needs to be replaced or frozen. Replacement or substitution with organic solvent is a basis for well-established chemical fixation protocols (Davies 1999), but it is a slow method and can result in solute displacement, including leakage of mobile elements (e.g. potassium and magnesium; Perrin et al. 2015). This makes it unacceptable for element distribution analyses. The success of freezing or cryofixation depends on the freezing speed, which prevents the formation of damaging ice crystals. Four different cryofixation approaches have been used: high-pressure, plunge, jet and metal mirror freezing and when performed properly, they can result in water vitrification (Dubochet et al. 1988, Morgan et al. 1999). Cryofixation approaches offer differing levels of simplicity, freezing depths, and costs, and these all need to be considered. In element visualisation techniques, good results have been obtained using liquid propane or isopentane as cryogen (Vogel-Mikuš et al. 2014, Castillo-Michel et al. 2017). Typically, plant material is cut into 2 x 5 mm small pieces using a razor blade. These small pieces are immersed in an optimal cutting temperature medium, individually frozen in cryogen, cut to 20 - 60 µm thick sections in a

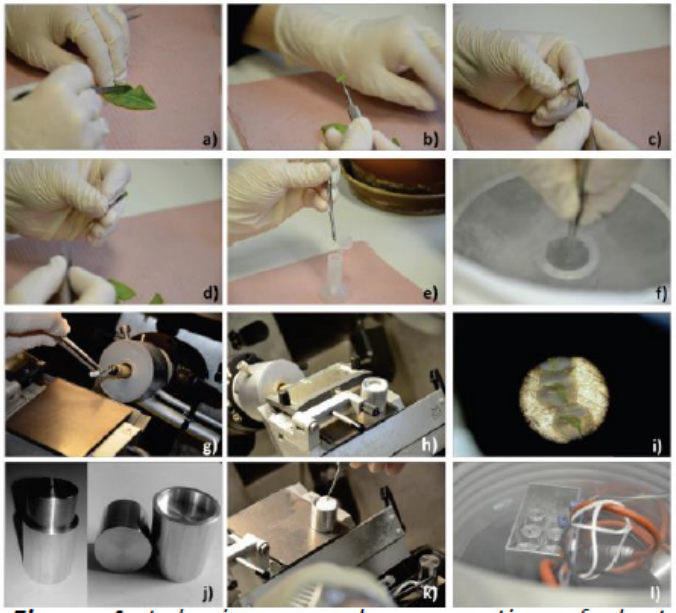


Figure 4: *Laborious sample preparation of plant samples entails excision of small e.g. leaf piece (a-c), immersing in the optimal cutting temperature (d-e), cryo-fixation (f), cryo-sectioning (g-k) and freeze drying (l) (Vogel-Mikuš et al. 2014).*

Section B2

Use images to convey things that cannot be easily described

By creating simple and user-friendly workflows for obtaining quantitative spatial element distribution maps, the project will contribute to providing unprecedented knowledge in the fields of plant physiology, agronomy and food technology. The current understanding of tissue-specific element distribution and interactions between elements in tissues has been assembled from single and often randomly selected cross sections from an organ (Conn and Gillham 2010, White and Pongrac 2017), predominantly acquired in a qualitative manner only, not considering gradients in element concentrations as the tissue arrangement changes along the plant organ. Therefore, it has been impossible to argue that the selected cross-section is representative of the whole organ making conclusions difficult and in need of further validation. The first attempts to create 3D distribution maps have been done (e.g. wheat grain in Figure 6), but the resulting qualitative 3D distribution specify location without fully quantitative information. It is therefore crucial and an objective of *SPADE* to revolutionise this procedure by first creating quantitative 3D element distribution maps, identifying representative cross-sections, and standardising operational guidelines and workflows to acquire interpretable and meaningful data.

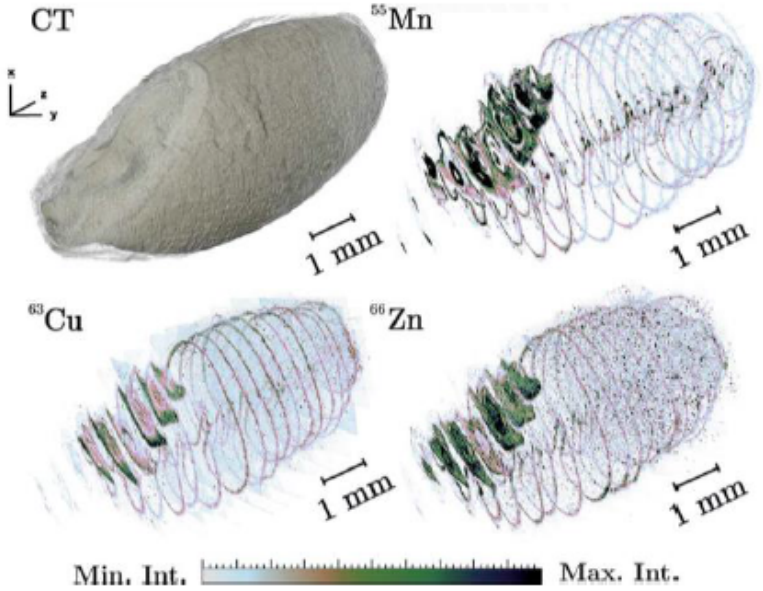


Figure 6: *An example of the proposed stacking of 2D distribution maps to construct qualitative 3D distribution maps of wheat grain (LA-ICP-MS; van Malderen et al. 2017).*

Section B2

Identify and clearly state your breakthroughs. This is usually not done correctly!

The *SPADE* project will innovative well beyond the state of the art and address some key challenges in the field including:

- New workflows based on standardised high-throughput cryo-sequential sample preparation useful for structural visualisation of tissues in 3D and tissue-specific metabolite analyses.
- Identification of representative sections, whose analysis suffices to describe tissue-specific analysis of the whole organ, reducing the amount of resources and time previously required for element distribution analysis.
- Algorithms developed to predict quantitative 3D element distribution from representative sections enabling evaluation of environmental and genotypic effects at the tissue level greatly increasing the information available from current bulk analyses.
- An open-access website providing access to results and models that will enable best practice and knowledge exchange for all levels of education.

The aim of the *SPADE* project is to create a fast and flexible workflow for modelling, predicting and applying spatial distribution of elements in plants. The workflow will comprise six steps (Figure 8), sufficing to model 3D element distribution maps, after key research challenges have been overcome. The workflow will be used by plant biologists, agronomists, and food technologists to address basic and applied questions (as in our two sample two case studies). **The *SPADE* project will innovative through a series of linked core objectives, all of which have measurable outcomes and targets for results (Figure 8).**

Section B2

Methodology should be so clear and detailed someone else could then do your project.

B2: be *hard-core* on the science

Explicit innovations, risks, and KPIs for each task!

T1.1 Upgrade of current micro-PIXE setup with annular SDD to achieve more efficacious data acquisition. Currently, one hour per section is required on average to achieve satisfactory signal to noise ratio. From an e.g. edible grain of approximate 1×0.5×0.2 cm (length × width × height) volume, one hundred 100 µm thick sections in transverse orientation would require analysis. Due to the size of the scanning frame (2.2×2.2 mm), each section will have to be analysed twice. In total this will yield 200 frames to be analysed resulting in approximately 100 hours of data acquisition. However, the number of sections will increase substantially when analysing e.g. young plant leaf of approximate 3×0.2-2×0.01-0.05 cm (length × width × height) volume. Therefore, we need to further increase efficacy of data acquisition. We will do so by purchasing and installing an annular silicon drift detector (SDD) to increase the solid angle (Demers et al. 2013, Zaluzec 2014) thereby achieving fivefold decrease in data acquisition time. The selected SDD, Rococo 2 (PNDetector, Germany), is compatible with the current micro-PIXE configuration (Figure 10) and provides a solid angle of 2 steradian, a fivefold improvement from current germanium detector (only 0.4 steradian). Therefore, a complete data acquisition now taking e.g. 100 hours would only take 20. Once installed, the detector will be calibrated and tested with thin foil standards and with standard plant samples. This will elevate the micro-PIXE station to become one of the most advanced in the EU, similar to synchrotrons, e.g. MAIA detector (Ryan et al. 2014). **Research innovations:** upgrade of the micro-PIXE set-up to decrease time in data acquisition, which has been so far been seen primarily in synchrotron facilities. **Risks:** minimal possibility that the installation and calibration would take longer than anticipated, to be remedied by planning extra time for this task (already included in the Gantt chart). **Key performance indicators:** annular SDD detector installed and calibrated, resulting in decrease time of data acquisition by five times.

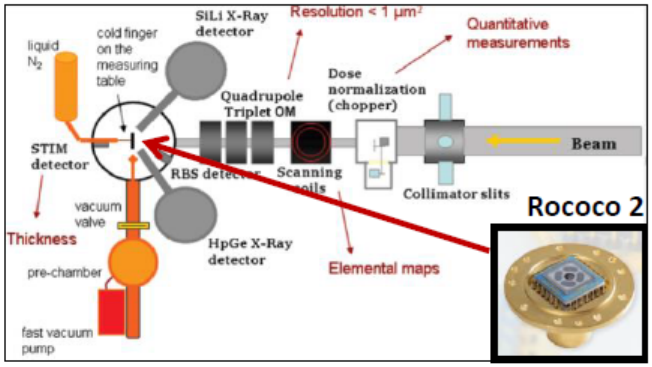


Figure 10: *Nuclear microprobe set-up at Jožef Stefan Institute. The speciality of this nuclear microprobe is a dose normalization chopper and cold finger which enables scanning of biological samples in frozen-hydrated state (in cryo; Vogel-Mikuš et al. 2014). The suggested upgrade entails the purchase and installation of annular silicon drift detector (Rococo 2, PNDetector, Germany), which will enable fivefold decrease in data acquisition time.*

Section B2

Weakness: collaborations, international presence

Don’t forget management, dissemination, team building, planning, outreach, knowledge transfer, especially if these might be seen as weaknesses

Section B2

Be organized, clear, direct, and thorough. Never prove anything more than once.

Table 1: Gantt chart of the proposed work packages (WP), tasks (T) and milestones (M).

	Months																		
	3	6	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60
WP 1: Development of high-throughput cryo-sectioning sample preparation.																			
T1.1																			
T1.2						M1													
WP2: Construction of quantitative 3D element distribution maps from 2D distribution maps																			
T2.1																			
T2.2																			
T2.3												M2							
WP 3: Identification of representative cross-sections for predicting 3D element distributions.																			
T3.1																			
T3.2																		M3	
WP 4: Management, dissemination and communication, exploitation and web-page.																			
T4.1																			
T4.2																			
T4.3																			
T4.4																			

The *SPADE* project will entail several difficult and critical tasks, where new solutions and ideas need to be implemented to overcome bottlenecks in the time and resources required for reliable and meaningful data acquisition. Among the most critical are: a) the ability to satisfactorily freeze larger samples (e.g. plant organs: roots, leaves, grain), b) development of the sequential sectioning tool, c) reaching minimal time for data acquisition. These tasks will be addressed with a working team with interdisciplinary expertise, by exchanging and implementing their ideas, and through intense communication with the research community working on these problems, including within international projects. When these challenges will be overcome, two very exciting pay-backs are foreseen. *The first* is the adoption of the high-throughput cryo-sequential sample preparation for the fast, cheap and reliable use in visualising element and metabolic distributions, determining speciation of elements in connection to their chemical environment, defining structural make-up, and for sample preparation for tissue-specific gene expression studies. *The second* is so-far unseen 3D quantitative visualisations of element distributions, enabling standardisation of sections needed for analytical comparisons in the future, confirmation or rejection of the existing models of element distributions, and interactions between elements. **By making direct comparison of tissue-specific distribution possible, we will be able to evaluate plant breeding, transgenic techniques and agronomic practices of biofortification for the best nutritional and safety outcome.**

Section c. Resources (including project costs)

As a very ambitious and challenging research project, SPADE will be managed in collaboration with the head of department, Primož Pelicon who has years of experience in managing national and international

Section B2

Say specifically *who*, and explain how you will build and manage the team and the project. Name names, and say who is being paid by the project and who not.

Section B2

Say specifically *who*, and explain how you will build and manage the team and the project. Name names, and say who is being paid by the project and who not.

Getting Started: Checklist

What you need to prepare:

1. Read everything online about ERC STG or CONS
2. Name and create an acronym for your project
3. Start an entry in the online submission system and download the templates
4. Write a one page abstract that is perfect
5. Write half a page about you and your career, including where you are now, where you want to be, what skills are strongest, what weakest, and how the project will help you progress from where you are to the position and abilities you need
6. Write exactly one perfect page about the research you propose
7. Now, assume that the research in (6) succeeded; write another page for a new project proposing advanced research building on (6)
8. Write half a page on how you would want your field to develop in the long term, five years, 15 years
9. Combine the last half of (6) above, all of (7), and most of (8) into a one page research plan
10. Make a Gantt chart or other image showing the phases of your proposed project
11. Start a folder of images that make your research ambitions clearer
12. Make a list of four or five people you will need to work with
13. Make a list of three or four external people you would like to visit abroad and work with for a short period like a week or a month
14. Prepare your CV into the template provided, find a photograph or yourself looking like the person you want to be after the ERC is completed
15. Make a list of complementary skills you lack and need to develop
16. Make a list of all of the activities you have done that can be named (“worked at a horse farm”, “gave a talk to children about nature at a local church”) whether directly related to your work or not; include anything that shows ambition, compassion, involvement, awareness, leadership, self-reliance
17. Meet with your supervisor and other senior academics and discuss your ideas and ask them what might you be missing, what might come afterwards, what might be more exciting, useful, innovative, advanced, original

Tips, For What They are Worth

- **Write your ERC as the *person you want to be*, not *the person you are now.*** Assume the voice of the person you will become.
- Use the proposal to describe *transitions*: toward radical innovations in your field, toward your own personal career development, towards the EU developing leadership through your group.
- Make your research seem vitally important and utterly inevitable.
- **Innovation is where you will fail.** Wait until you have a great idea that cannot wait to tell itself, and then find great, inspiring people to work with.
- **Identify why your proposed research is *hard* and *risky.***
- Spend six months on ideas, and a month on writing.
- Always ask for the maximum amount of funding.

Tips, For What They are Worth.

- Use work packages and other formalisms if you think your profile as a manager or leader might be weak. Show *process.*
- Have colleagues read the proposal and get as much input as possible. *Find critical people.* There aren't many, actually.
- Make lists of your strengths and more importantly, your weaknesses. Turn weaknesses into strengths, and show the process by which the project will help fill expertise and career development gaps. Remember that like H2020 Individual Fellowships, the ERC grant, partially, is not for you as you are now, but for the scientist you will become.

Questions?

Conclusion

Thanks to JSI!

Contact: Richard Wheeler
rw@edinburghscientific.com