

A DSL for Fluorescence Microscopy

Birthe van den Berg

Tom Schrijvers

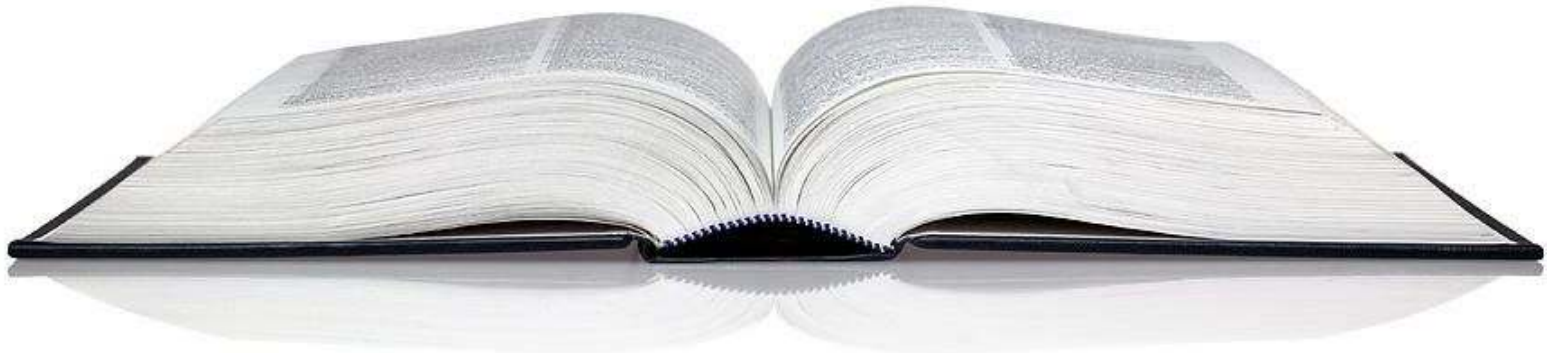
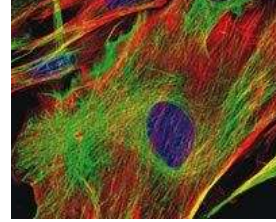
Peter Dedecker

KU LEUVEN

Introduction

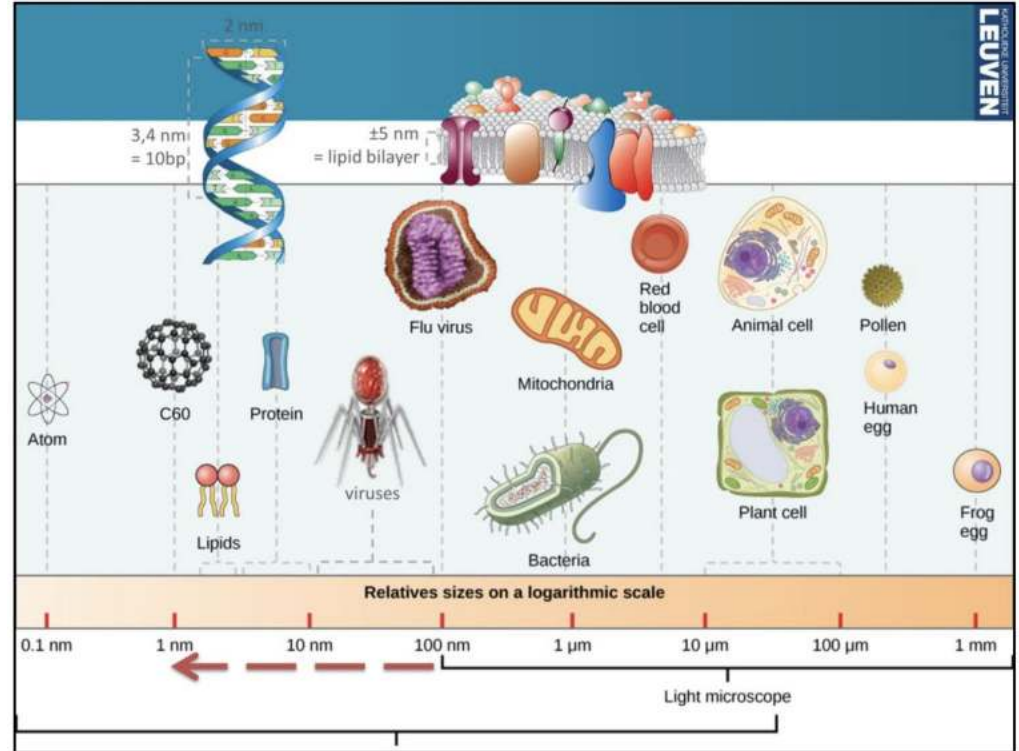
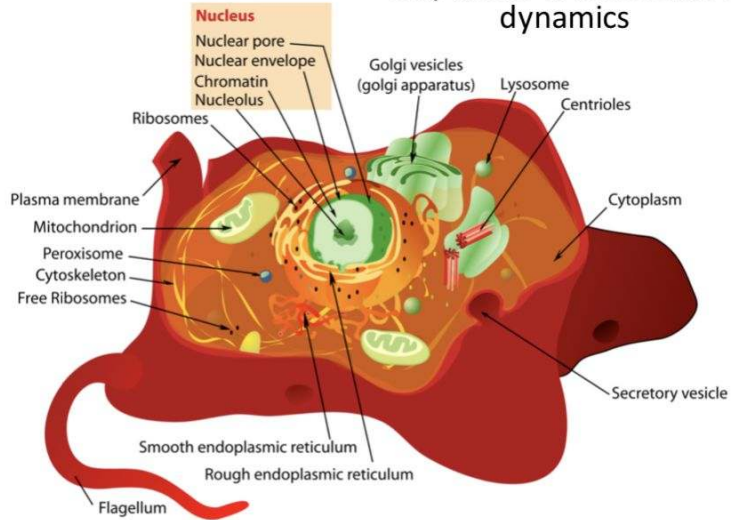
NanoBilogy
01101110 0100001 01101110 01101111 01000010 01101111
01101110 0100001 01101110 01101111 01000010 01101111

DSL



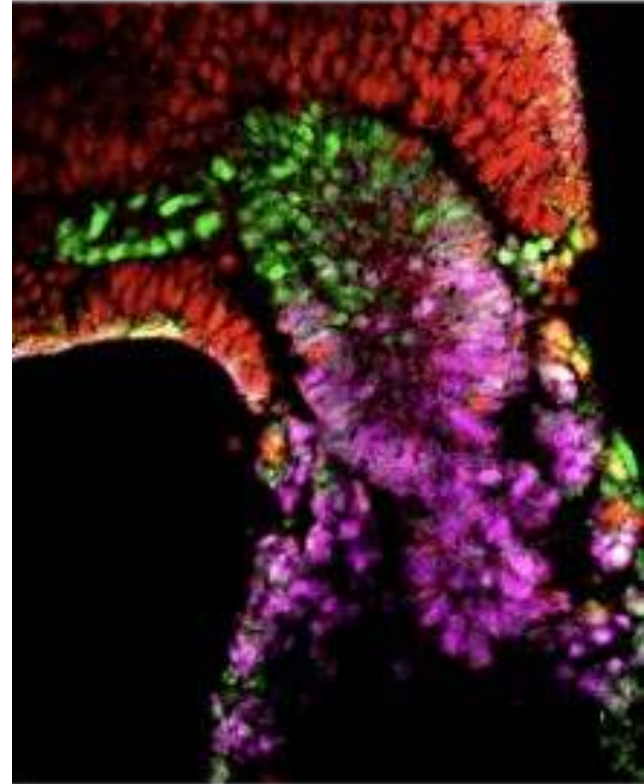
Why fluorescence?

Cell/Tissue architecture & dynamics



Why fluorescence?

- **non-invasive**
 - in situ
 - in vivo
- **selective**
- sample preparation
 - **simple**
 - **wide range** of fluorescent probes

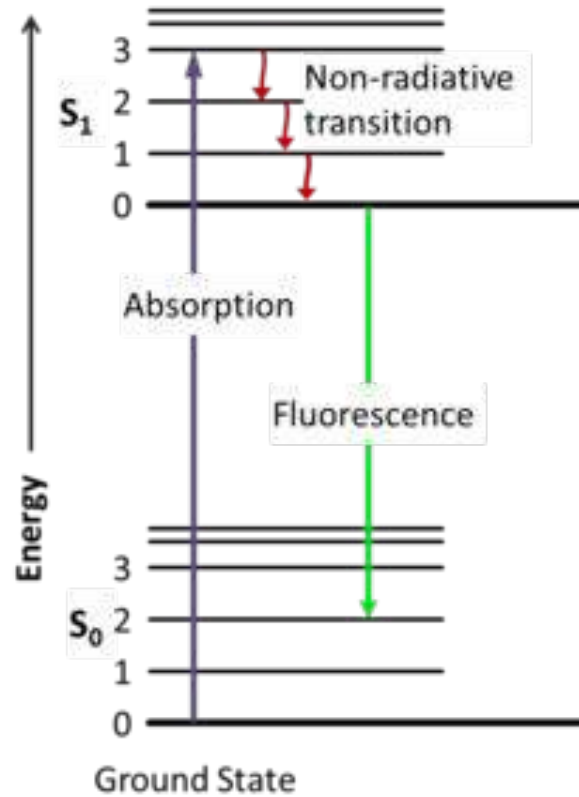




What is fluorescence?

Fluorescence

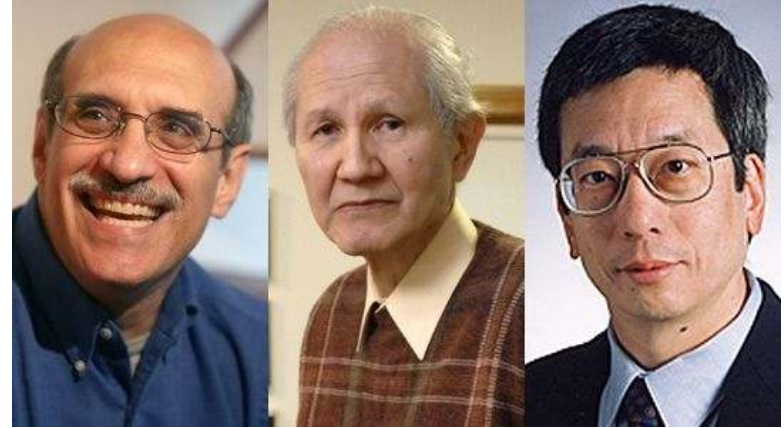
Jablonski diagram



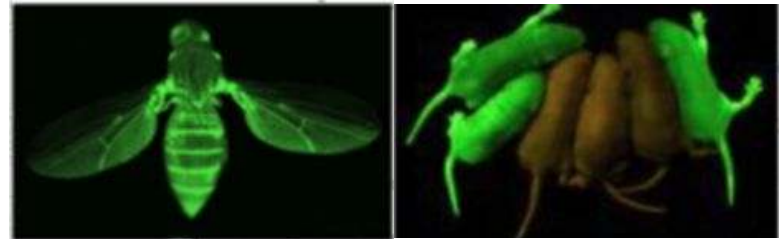
Fluorescence



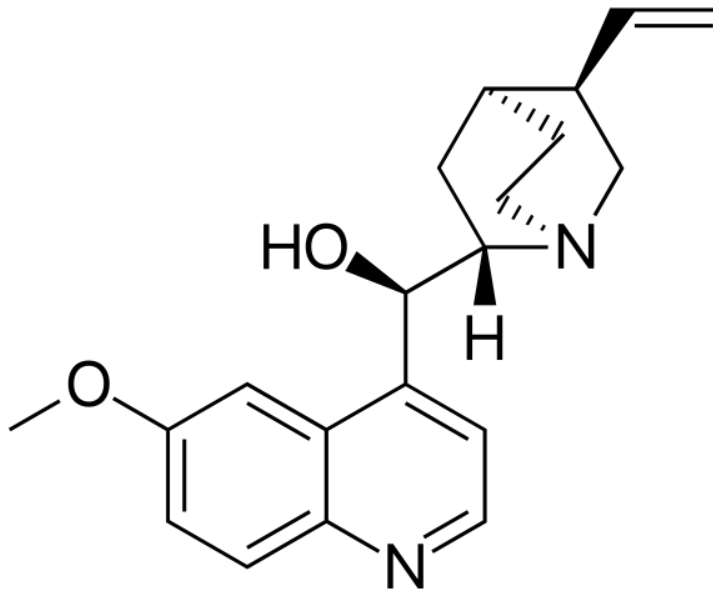
Green
Fluorescent
Protein



M.Chalfie - O.Shimomura - R. Tsien
Nobel Prize in Chemistry 2008



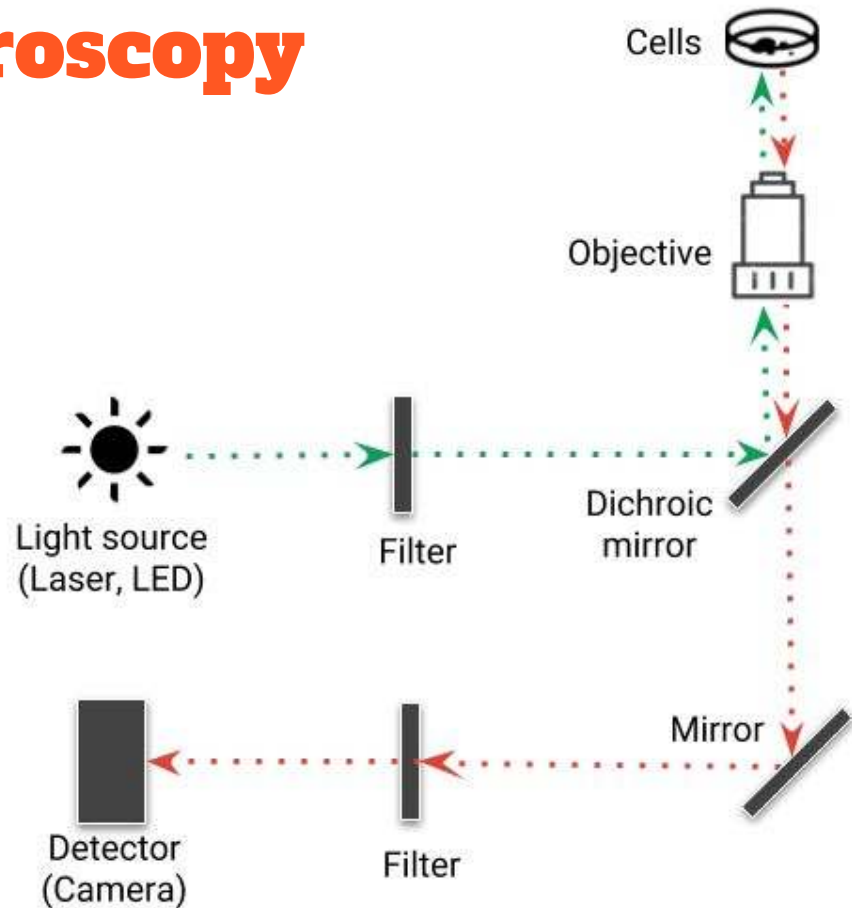
Fluorescence



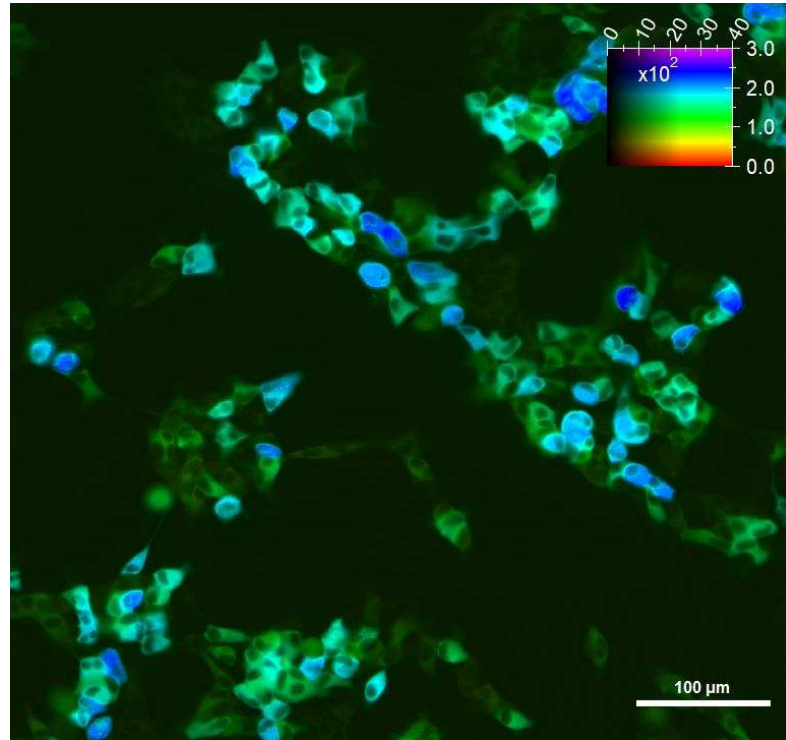
Quinine



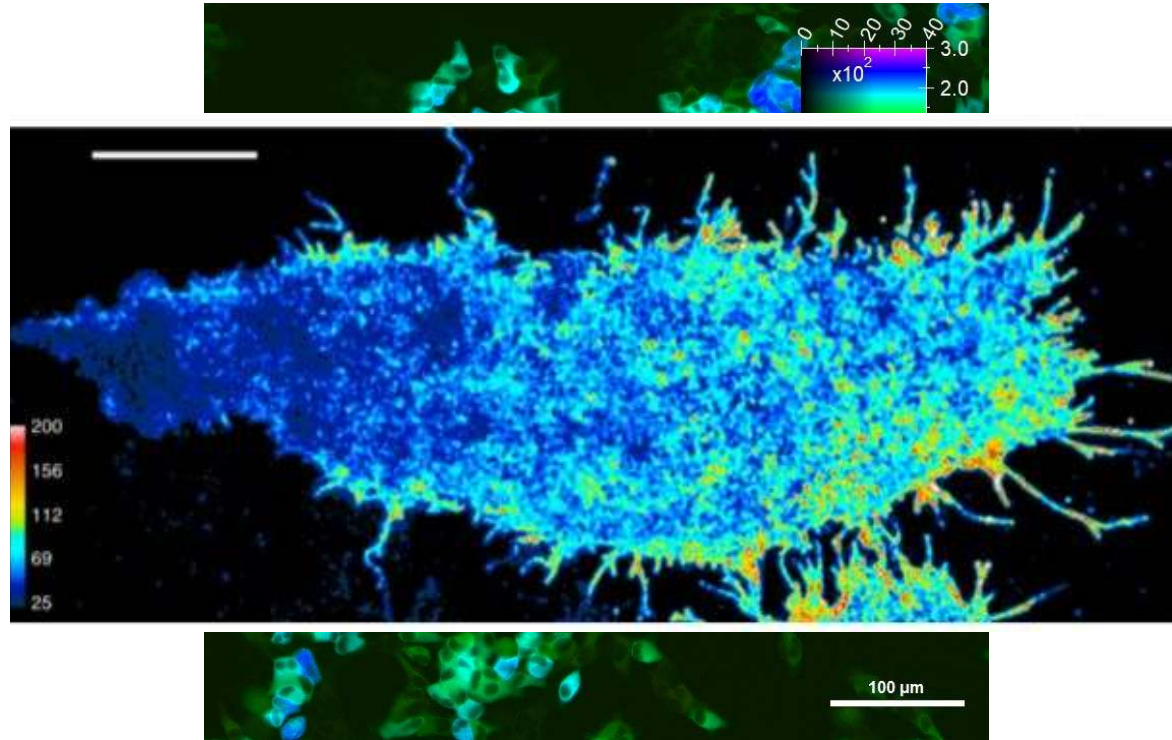
Fluorescence Microscopy



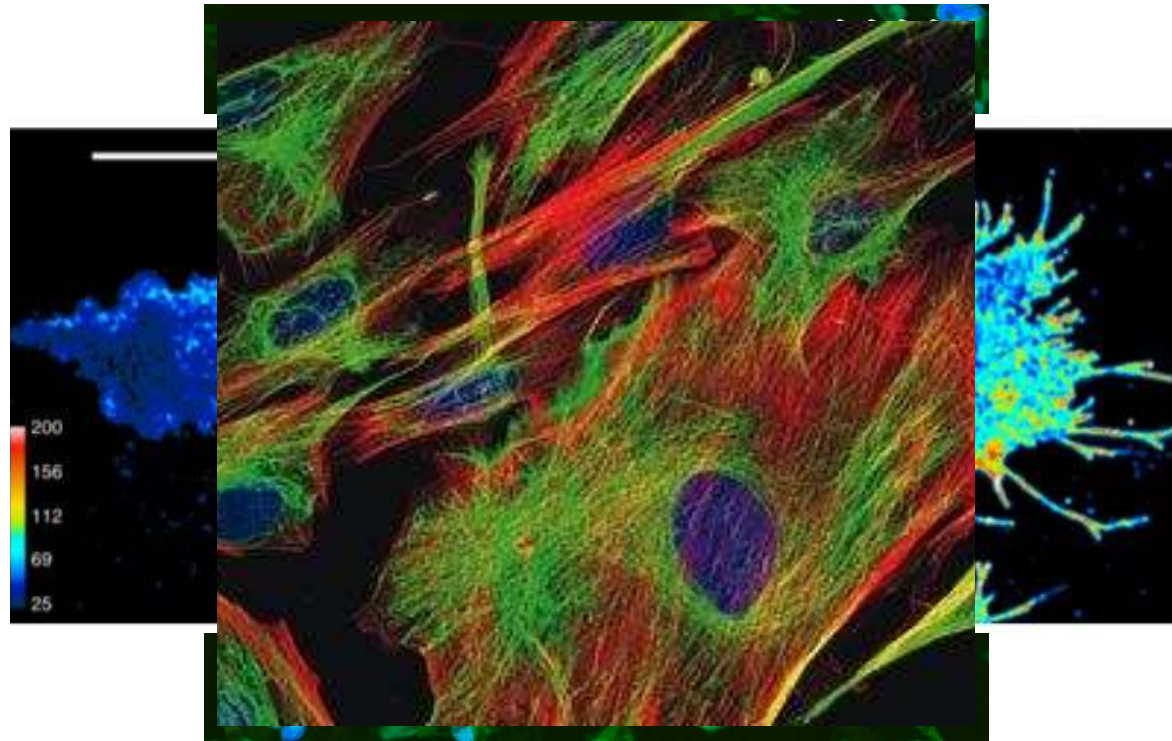
Fluorescence Microscopy



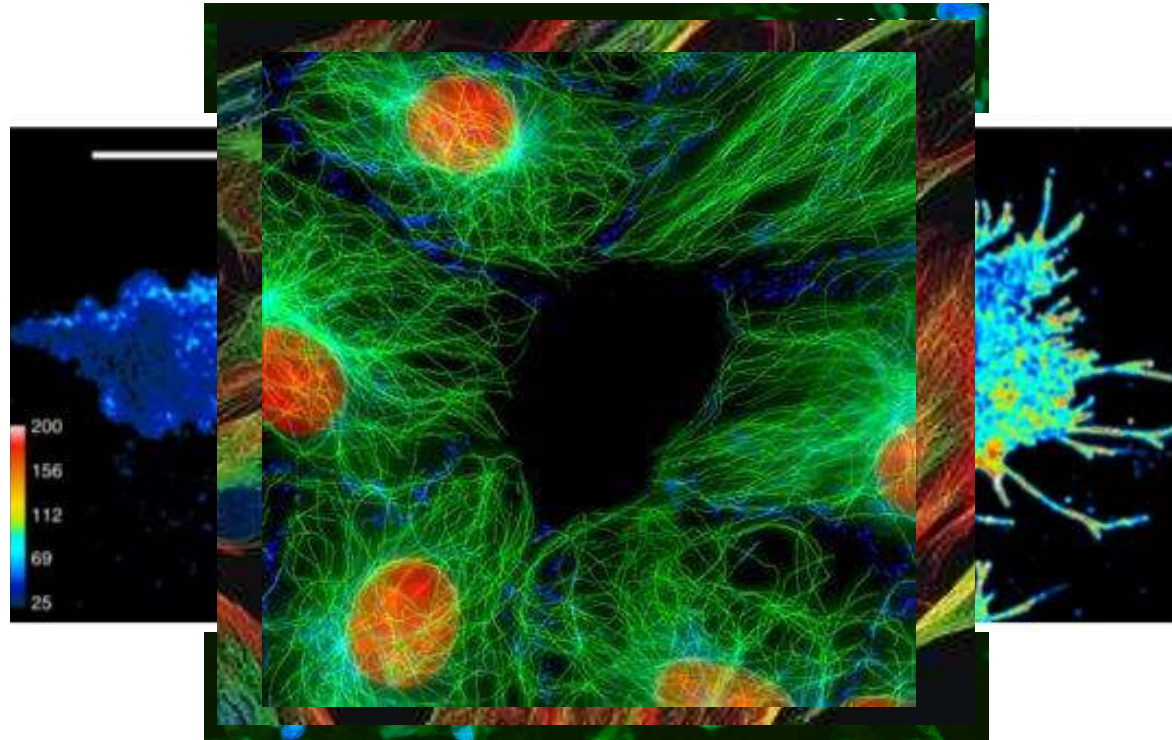
Fluorescence Microscopy



Fluorescence Microscopy



Fluorescence Microscopy

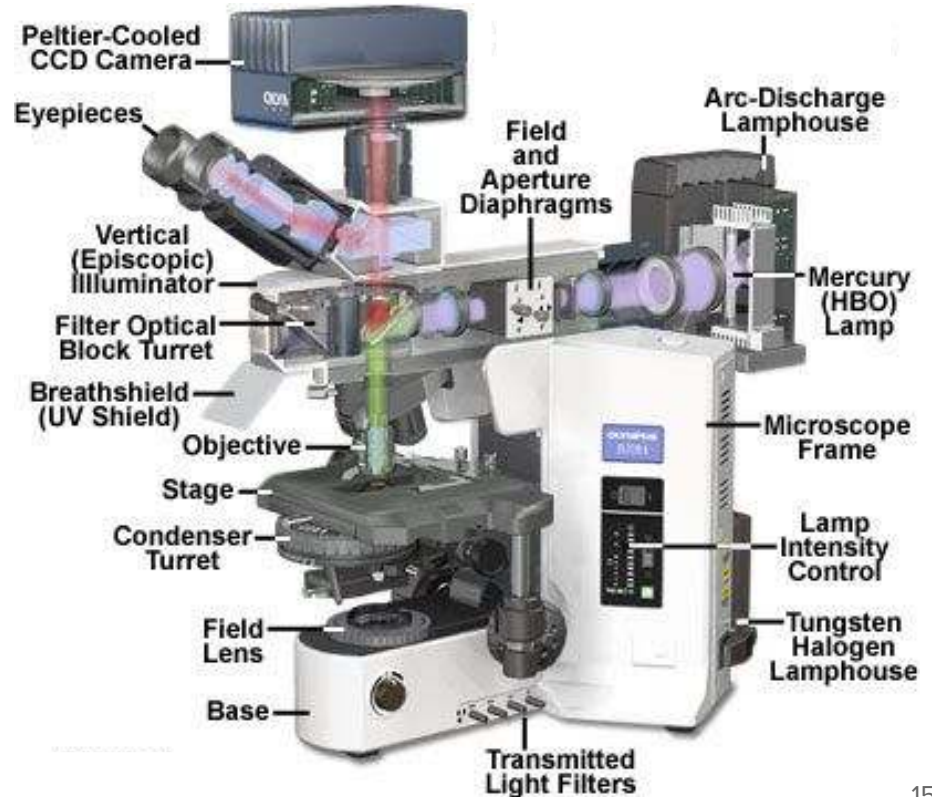




So, what's the problem?

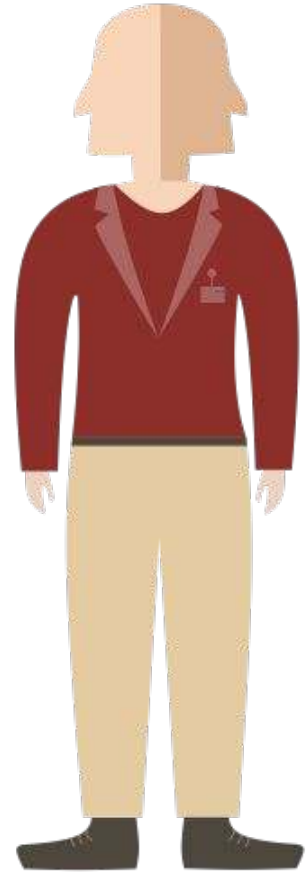
So, what's the problem?

- Growing **technical complexity**
- **Expensive** instrumentation



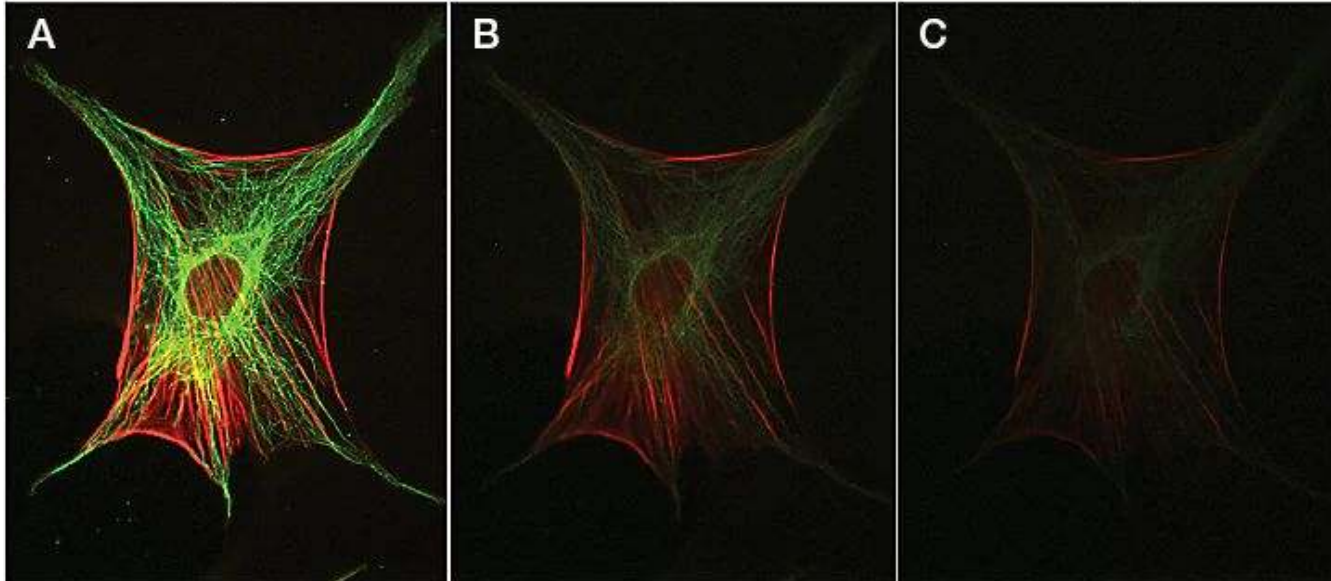
So, what's the problem?

- Growing **technical complexity**
- **Expensive** instrumentation
- **Dedicated staff members** (researchers + technicians)

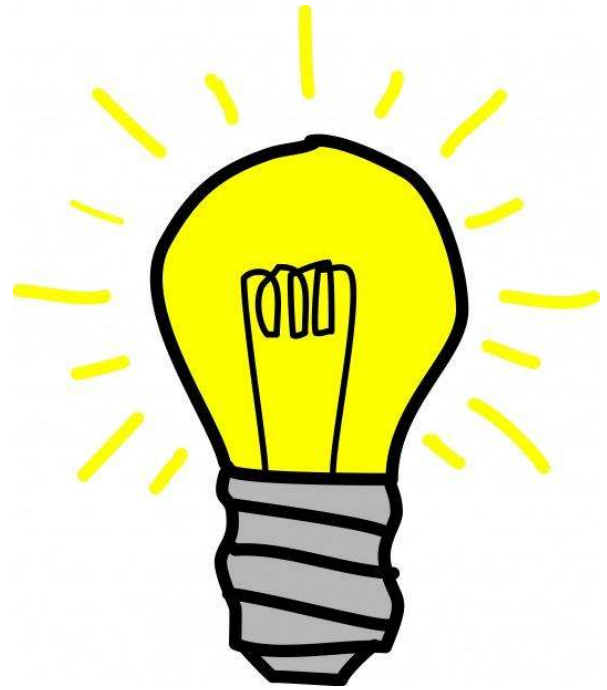


So, what's the problem?

- Adapting the **experimental strategy**, setting **many parameters**
- No or little **safety** controls



So, what's the clue?

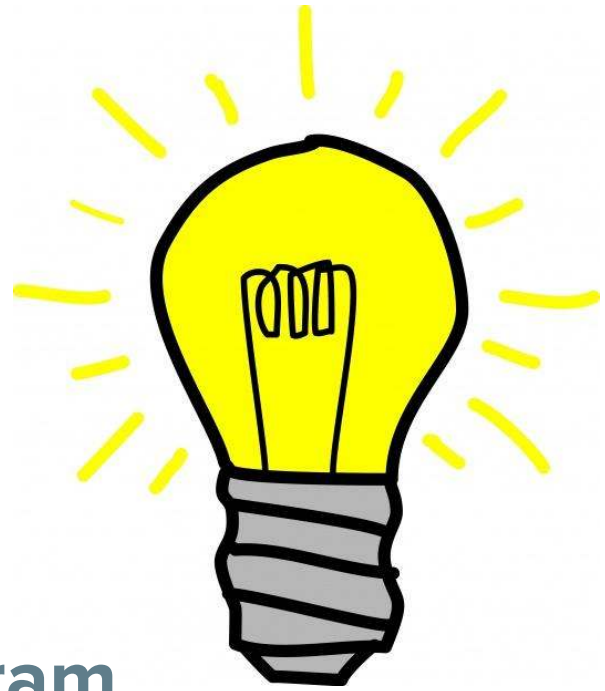


So, what's the clue?

Setting up an experiment

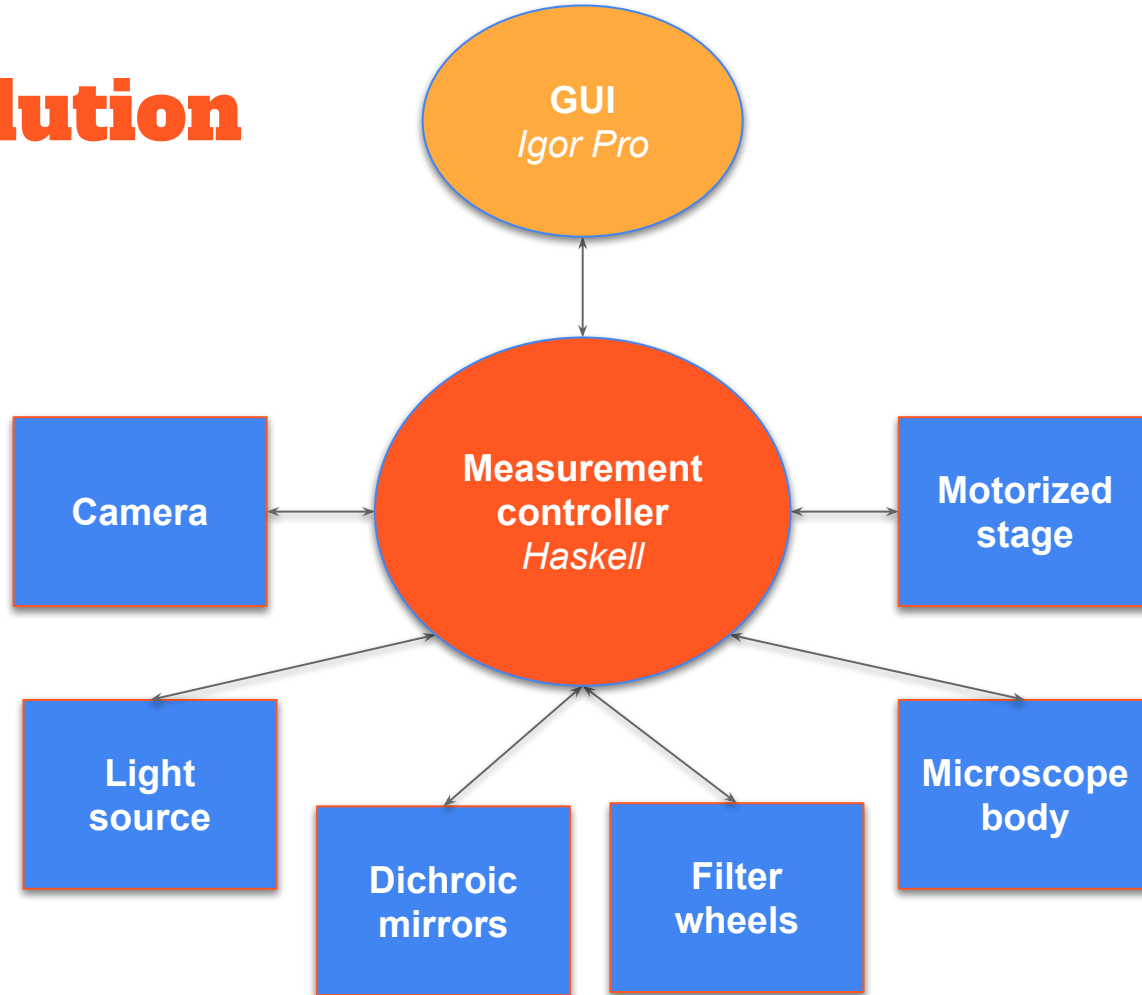
=

Constructing a computer program



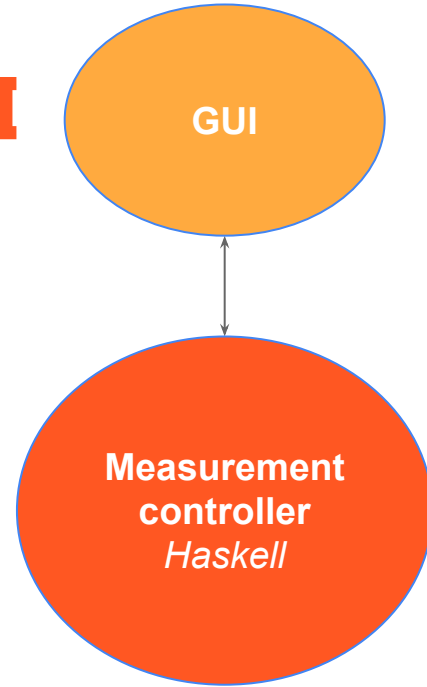
Our Solution

Our Solution



Solution: Controller vs GUI

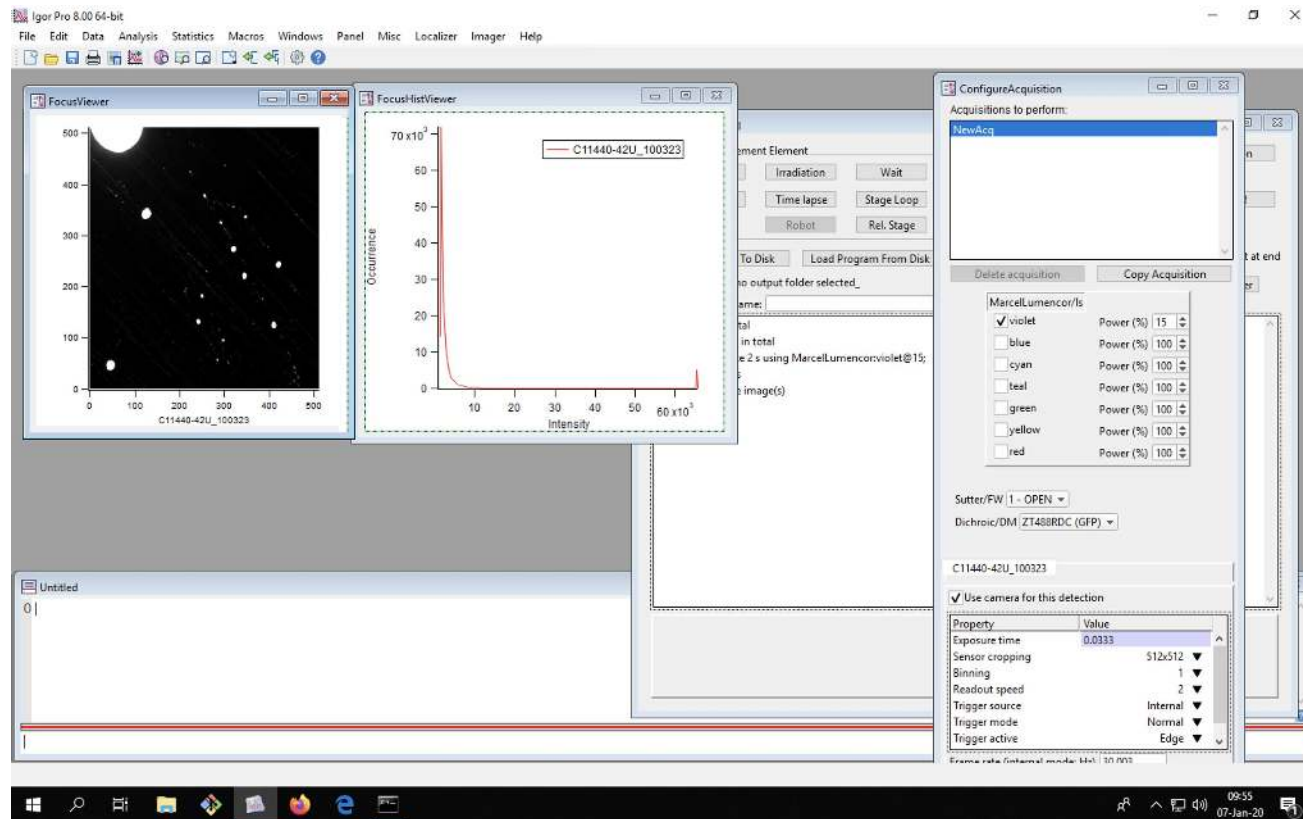
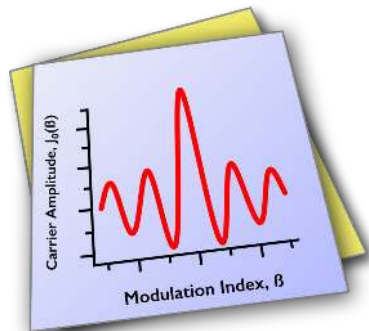
- Communication with **GUI**



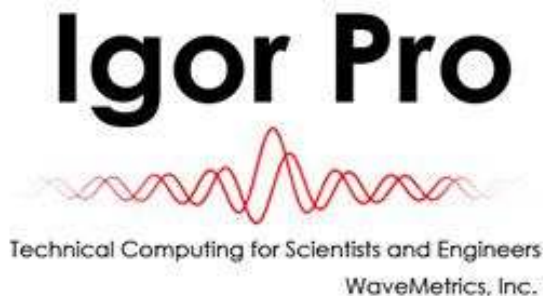
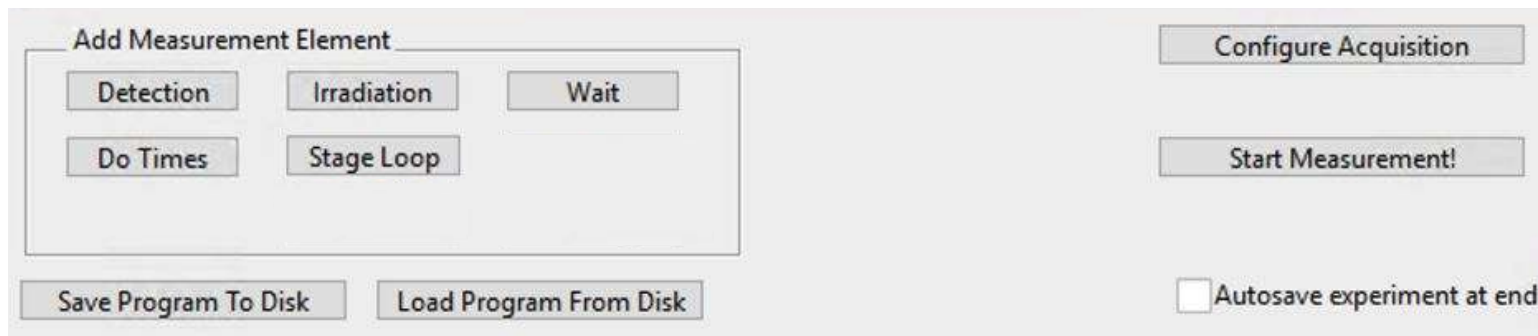
GUI

Igor Pro

Technical Computing for Scientists and Engineers
WaveMetrics, Inc.



GUI: Example

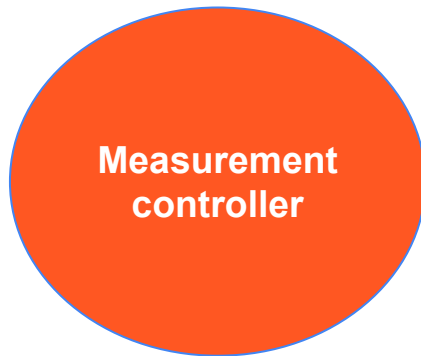


```
do 5 time(s) in total
    irradiate 2 s using Marcellumencor:violet@15;
    wait 3 s
    acquire image(s)
wait 10 s
acquire image(s)
```

Solution: Controller DSL

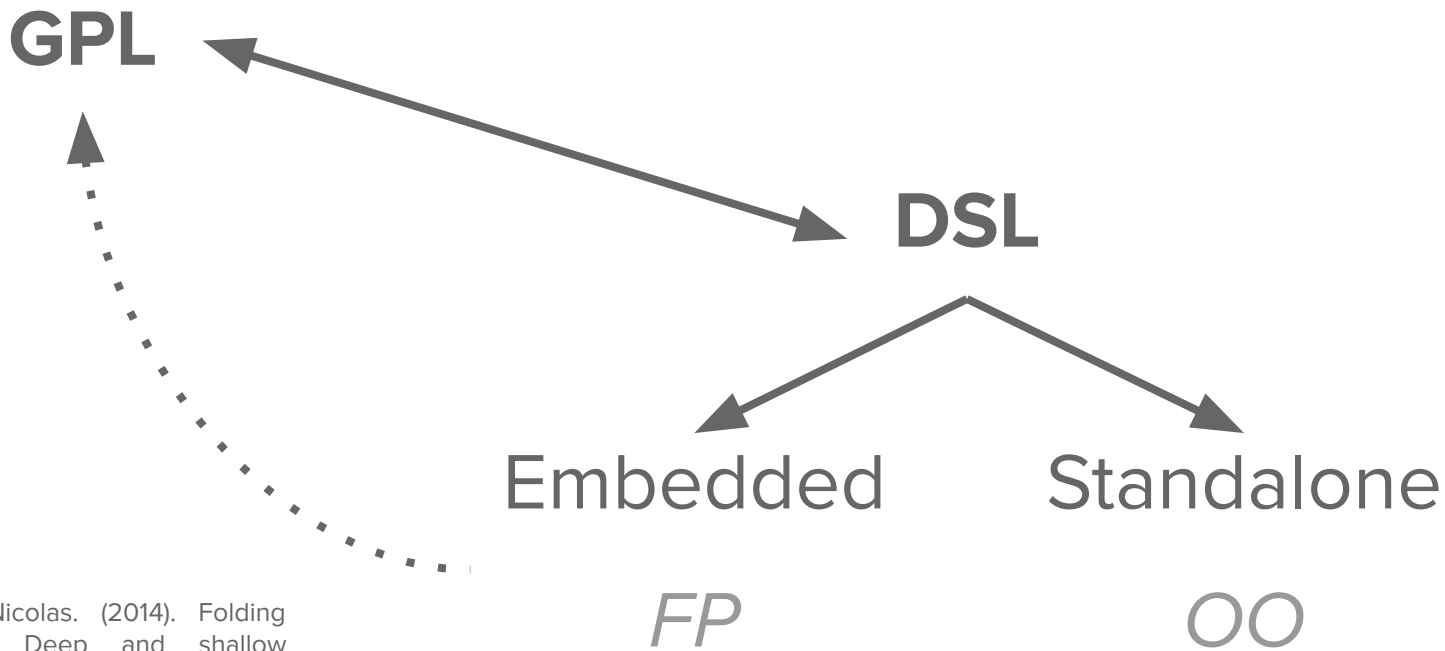
- Representing and reasoning over **domain-specific knowledge**

DSL



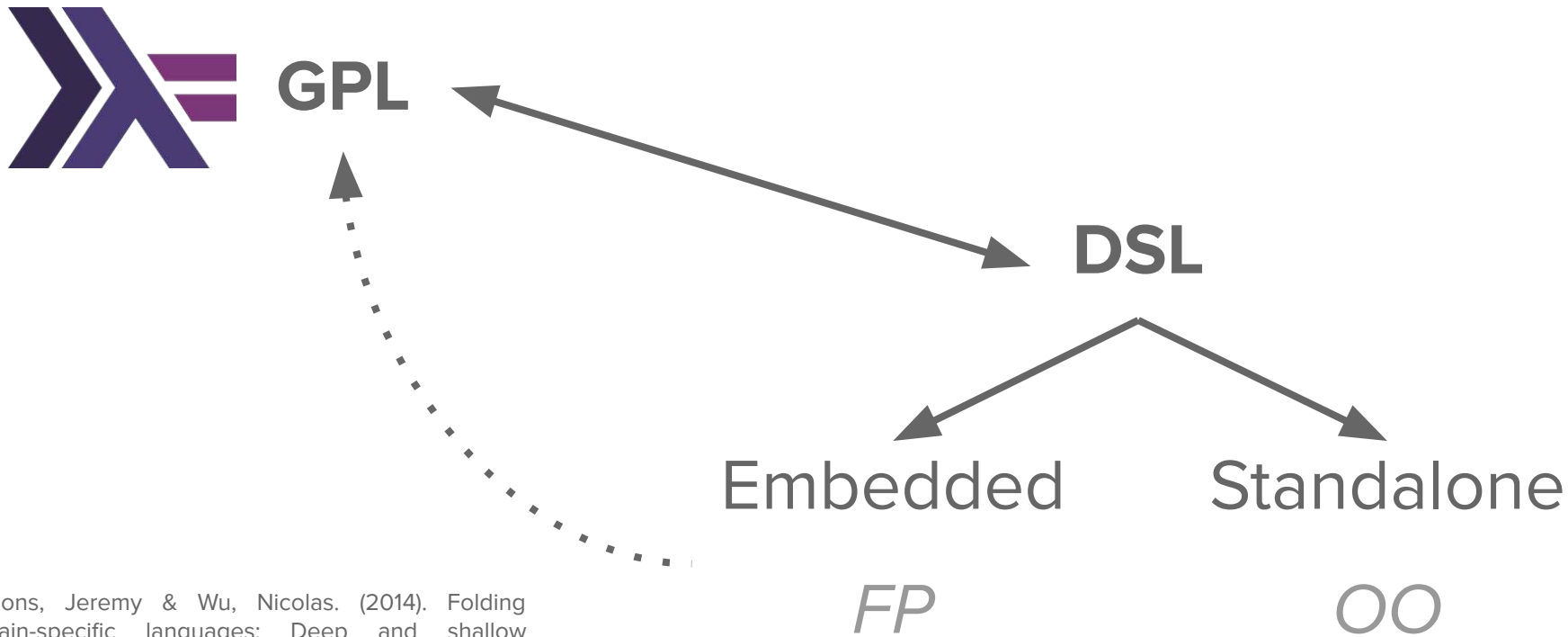
>>= Haskell

Why DSL? Why Haskell?



Gibbons, Jeremy & Wu, Nicolas. (2014). Folding domain-specific languages: Deep and shallow embeddings (functional Pearl). Proceedings of the ACM SIGPLAN International Conference on Functional Programming, ICFP. 49. 10.1145/2628136.2628138.

Why DSL? Why Haskell?



Gibbons, Jeremy & Wu, Nicolas. (2014). Folding domain-specific languages: Deep and shallow embeddings (functional Pearl). Proceedings of the ACM SIGPLAN International Conference on Functional Programming, ICFP. 49. 10.1145/2628136.2628138.

DSL Fragment

```
data StagePosition      = StagePosition { x :: Double
                                          , y :: Double
                                          , z :: Double }
```

```
data MeasurementElement = MEDetect
                        | MEWait Double
                        | MEIrradiate Double ( String, Double )
                                          -- duration ( light source , power )
                        | MEDoTimes Int Prog
                        | MESTageLoop [ StagePosition ] Prog
                        | ...
```

```
type Prog               = [ MeasurementElement ]
```

DSL: Example

```
do 5 time(s) in total
  irradiate 2 s using MarcelLumencor:violet@15;
  wait 3 s
  acquire image(s)
wait 10 s
acquire image(s)
```

```
[ MEDoTimes 5 [ MEIrradiate 2 ( MarcelLumencor:violet , 15 )
                , MEWait 3
                , MEDetect ]
  , MEWait 10
  , MEDetect ]
```

Deep embedding

`executeProg :: Prog → IO ()`

`executeProg prog = foldMap executeME prog`

`executeME :: MeasurementElement → IO ()`

`executeME MEDetect = executeDetection >> putStrLn “detecting...”`

`executeME (MEWait dur)`
`= threadDelay (round $ dur * 1e6)`
`>> putStrLn “waiting...”`

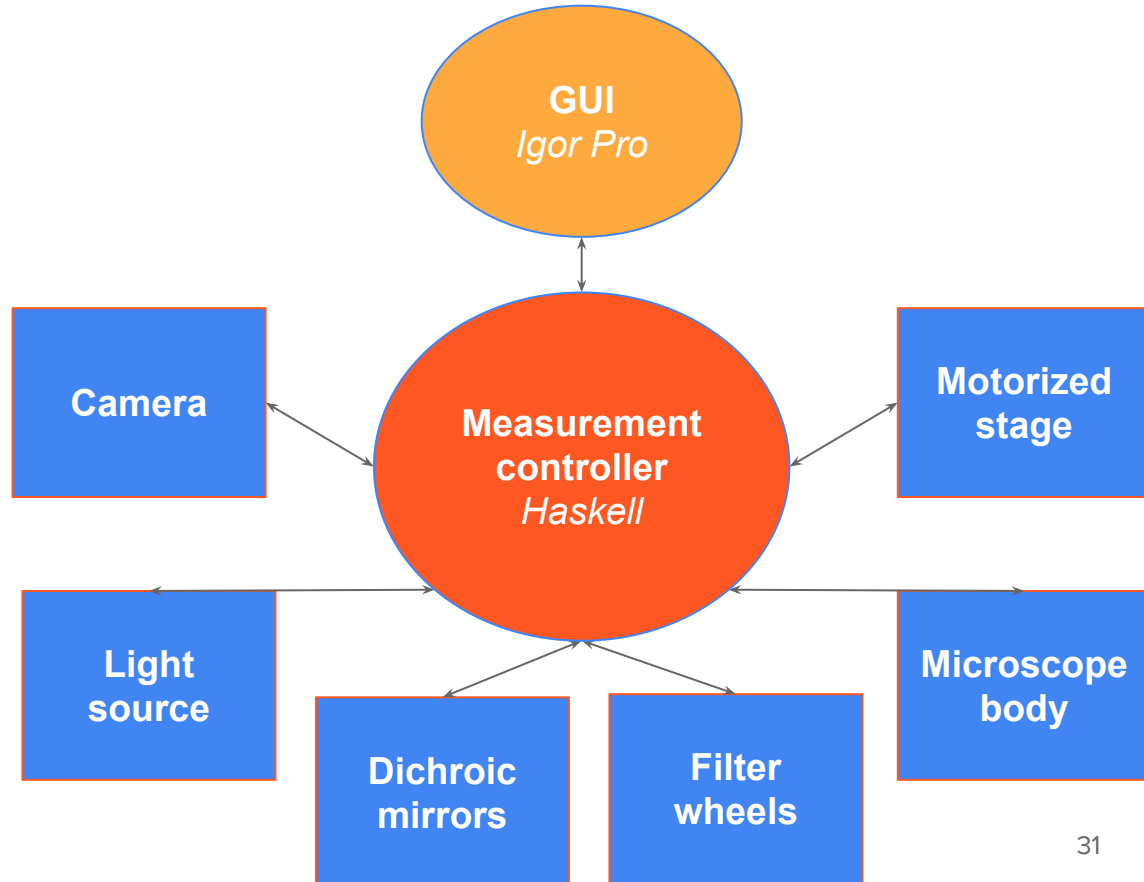
`executeME (MEIrradiate dur params)`
`= executeIrradiation dur params`
`>> putStrLn “irradiating...”`

`executeME (MEDoTimes n pr)`
`=`
`mapM_ (\prs → executeProg prs) (take n . repeat $ pr)`
`>> putStrLn “times...”`

`executeME (MEStageLoop poss pr)`
`=`
`mapM_ (\pos → setStagePosition pos >> executeProg pr) poss`
`>> putStrLn “stage looping...”`

Solution: Controller vs Hardware

- Controlling **hardware**



Hardware



Camera



Light
source



Dichroic
mirrors



Motorized
stage

Filter
wheels

Microscope
body



Hardware: Example

do 5 time(s) in total

irradiate 2 s using Marcellumencor:violet@15;

wait 3 s

acquire image(s)

wait 10 s

acquire image(s)

[MEDoTimes 5 [MEIrradiate 2
(Marcellumencor:violet , 15)
, MEWait 3
, MEDetect]

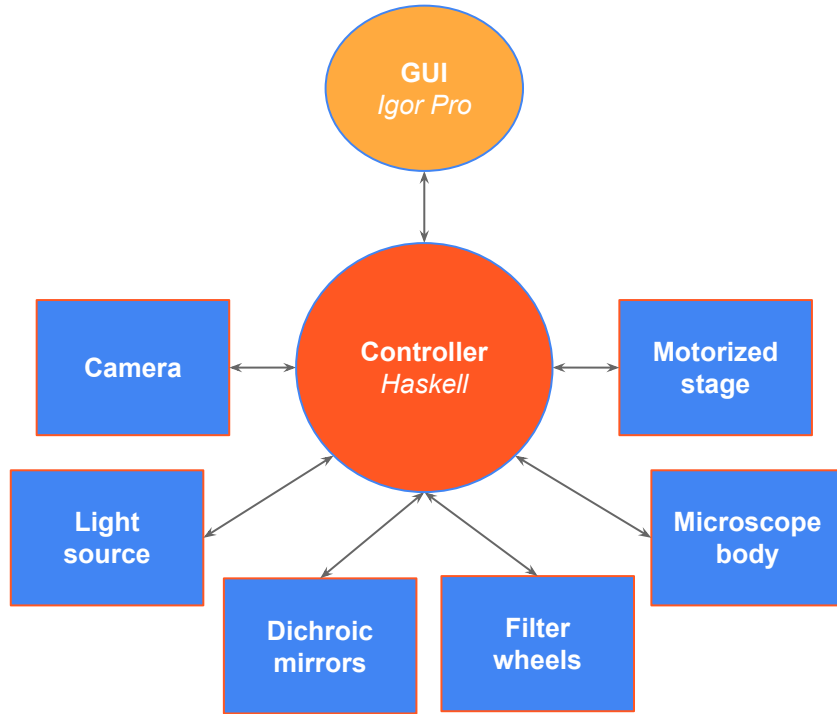
, MEWait 10
, MEDetect]



Results



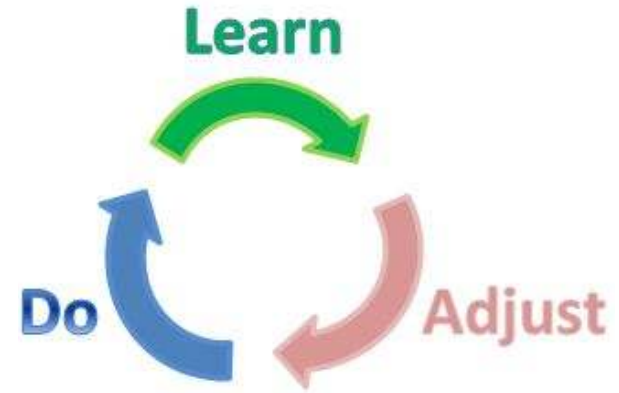
Results



usable software



feedback loop



Compared to already existing SW

- **Modularity**
 - easily extendible for new hardware
 - works with several hardware setups
- Arbitrary long, **complex** programs

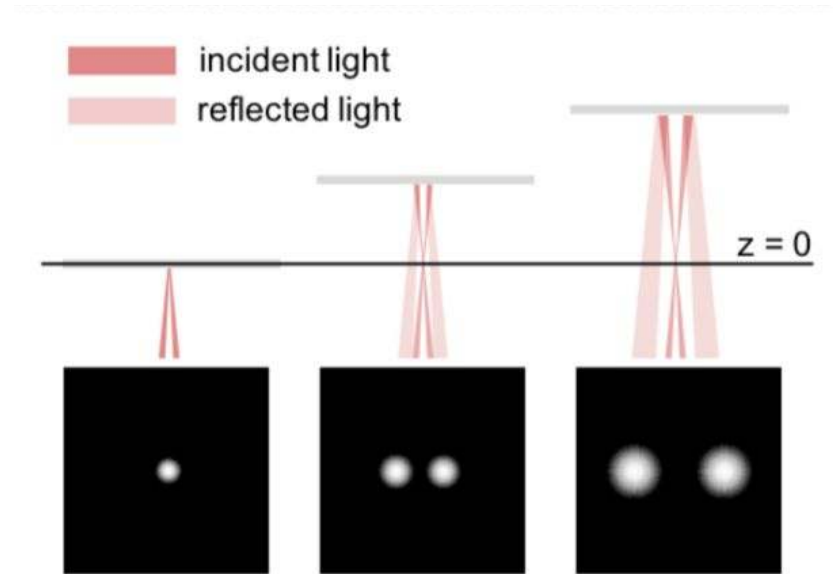
ThermoFisher
S C I E N T I F I C


PerkinElmer[®]
For the Better

Leica
M I C R O S Y S T E M S

Compared to already existing SW

- **Modularity**
 - easily extendible for new hardware
 - works with several hardware setups
- Arbitrary long, **complex** programs
- Also non-trivial, more complex tasks
 - E.g. **autofocus** system



Future Work

GUI

DSL for knowledge representation

Operational DSL for controlling HW/SW

Fluorescence Microscopy Applications

Future Work

GUI



DSL for knowledge representation

Operational DSL for controlling HW/SW

Fluorescence Microscopy Applications

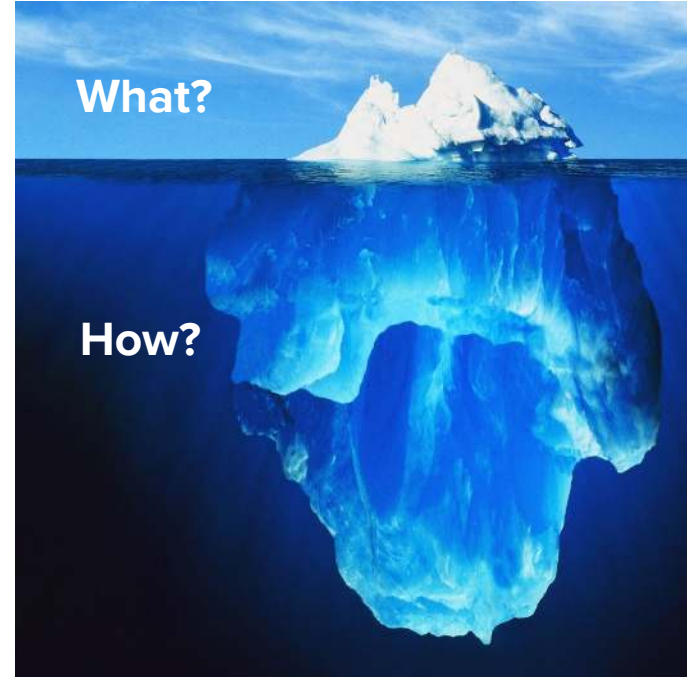
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Future Work

GUI

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Fluorescence Microscopy Applications



- Increase **performance**
 - optimal rescheduling
 - parallelizing
- **Safety** and **sanity checks**

Future Work

GUI

DSL for knowledge representation

Operational DSL for controlling HW/SW

Fluorescence Microscopy Applications



Future Work

“A system that can learn from scientists and operators, and vice versa.”

Thanks!

