Longitudinal registration strategies

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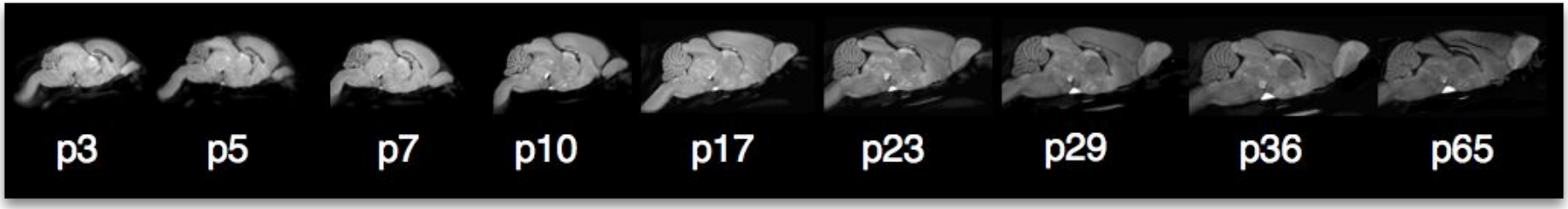
MISS

Challenges posed by longitudinal data

1. Gross alterations of brain morphology (size and shape) across development



2. Images from same individual register better than those from different individuals

Registration is flexible: There are multiple ways of combining temporal and spatial information

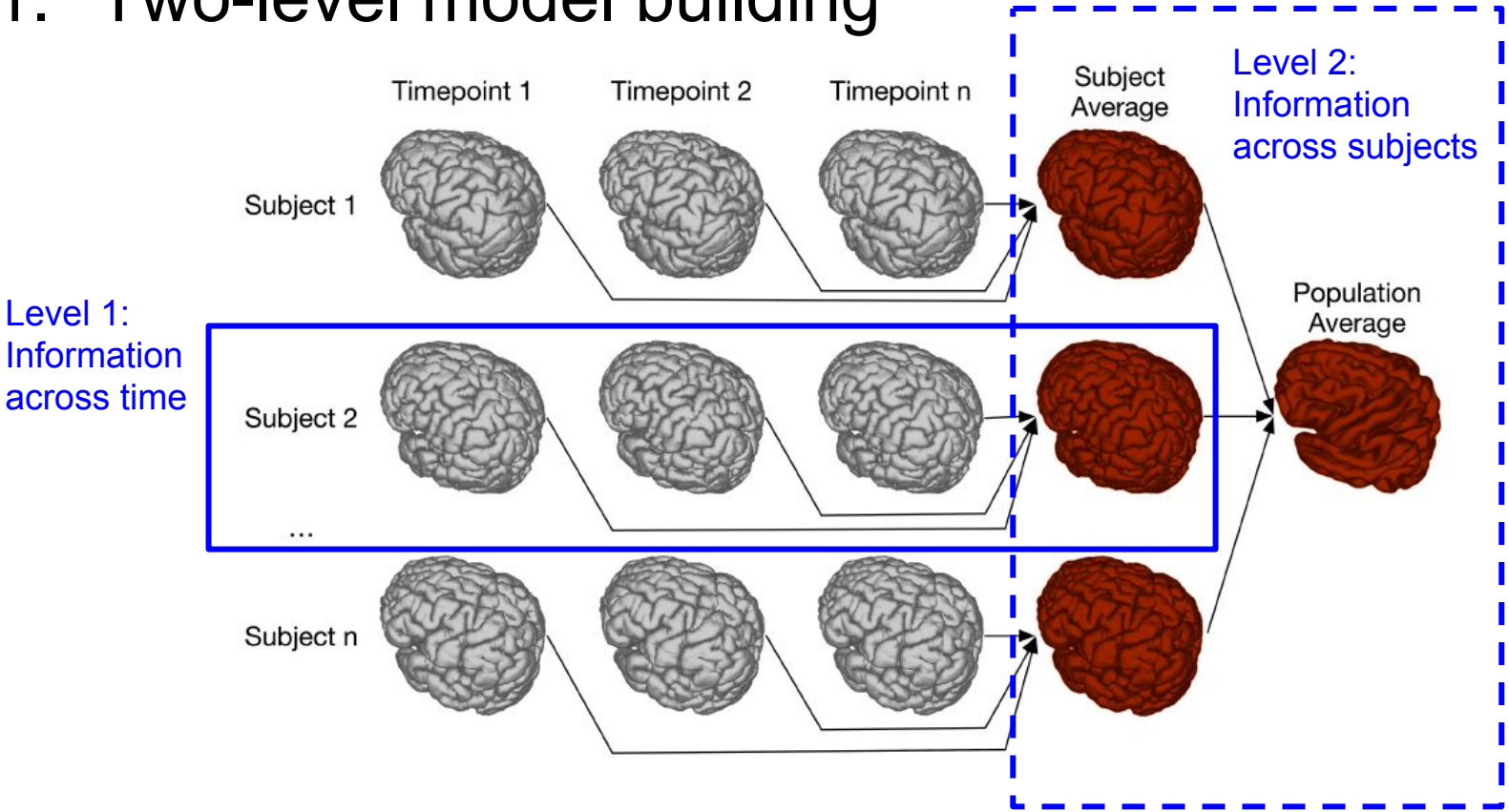
How do you combine information?

- Develop a hierarchical model of registration
- Allows us to move up in complexity as we go up the hierarchy
- We typically use registrations that are hierarchical at MICe
- Spatial or temporal information can be contained in level 1 and/or level 2 of our registration

Pydpiper

- Pydpiper is a development toolkit, written in Python, for creating modular, distributed pipelines.
  - Replace or modify the parameters
  - Modularized, discrete stages can be removed, modified, or replaced
  - Parallelization: remotely distributes stages to computing clusters
  - Interdependencies
  - Executors
- Pydpiper allows us to efficiently program our registration strategies.

1. Two-level model building



https://wiki.mouseimaging.ca/display/MICePub/twolevel_model_building

```
twolevel_model_building.py \
--num-executors=600 \
--init-model=[init model] \
--pipeline-name=test \
--lsq12-protocol=[lsq12protocol.csv] \
--nlin-protocol=[nlin-protocol.pl] \
--registration-method=ANTS \
--output-dir=test \
--no-run-maget \
--default-job-mem=8 \
--maget-no-mask \
--csv-file=TwoLevelFiles.csv
```

Each row = same subject

https://wiki.mouseimaging.ca/display/MICePub/twolevel_model_building

Pros, cons and when to use two-level

Pros:

- Unique features within subject are maintained

Cons:

- If there are gross morphological changes across time, Level 1 registration will not be that good (eg. neonate and adult)

When to use:

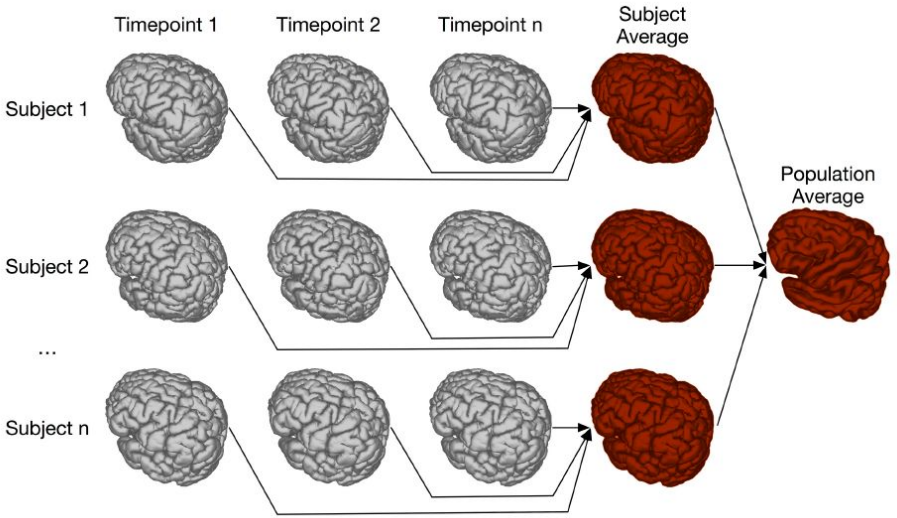
- Changes across individuals are greater than those across time (eg. timepoints are p20, p30 and p40)

Two-level registration: activity!

3 subjects, 3 timepoints.

List the transformation needed to go from subject 2, timepoint 1, to population average

1. Register with all subject 2 timepoint images to create subject 2 consensus
2. All subject consensus averages registered
3. Population average

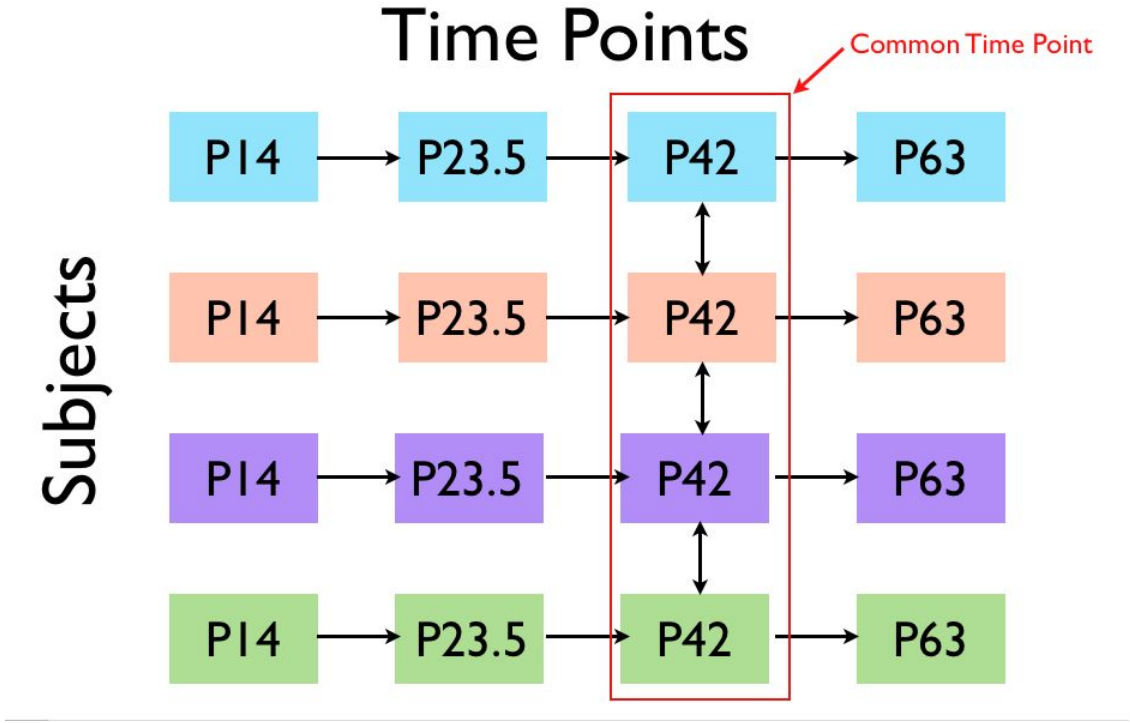


Levels 1 and 2 for registration types

Registration Type	Level 1	Level 2
Two-Level	• Same subject, including all timepoints. • `Information across time`	• Across subject consensus averages • `Information across subjects`
Registration Chain		
Tamarack		
Overlapping Group-Wise		

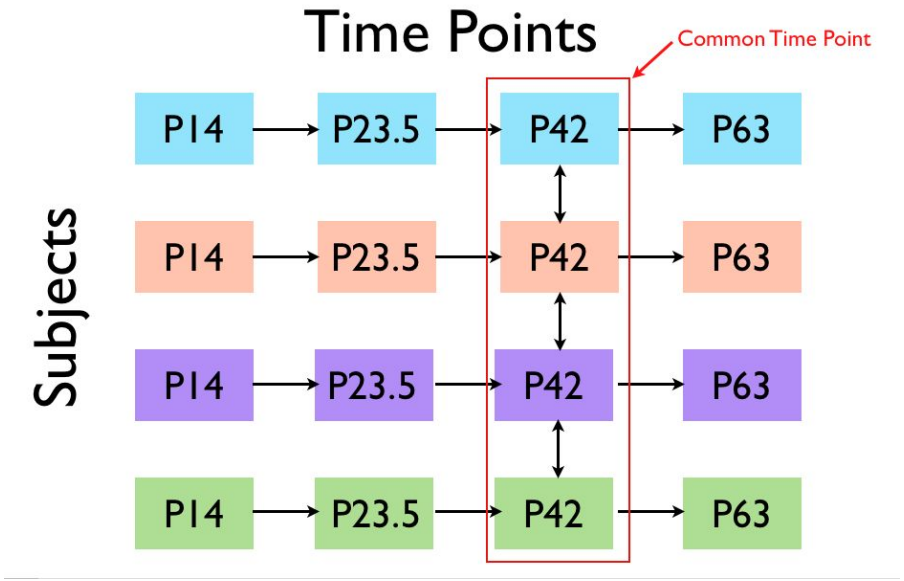
Types of Registrations	Pros	Cons	When to use
Two-Level	• Unique features within subject are maintained	• If there are gross morphological changes, registration will not be as good (i.e. neonate & adult)	• Changes across individuals are greater than those across time • ie. p20, p30, p40
Registration Chain			
Tamarack			
Overlapping Group-wise			

2. Registration Chain



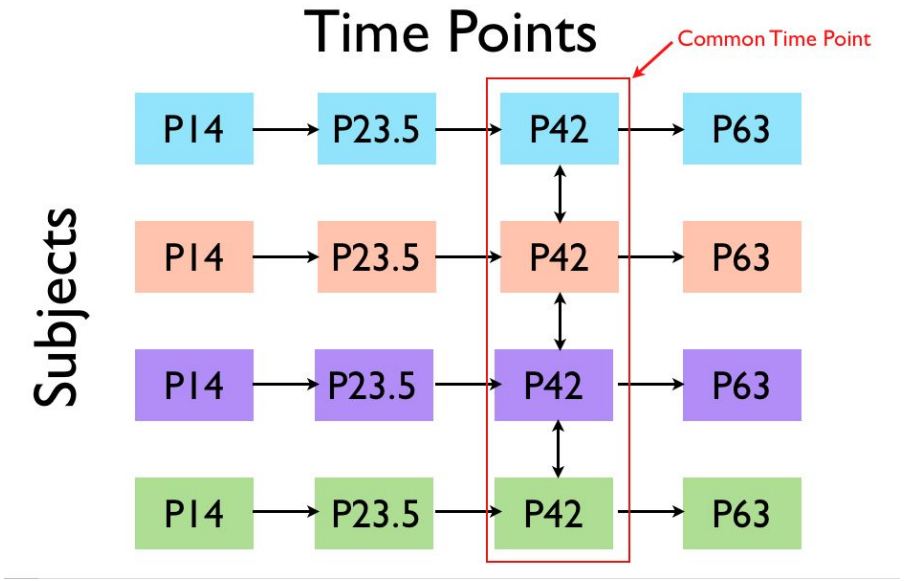
Registration Chain

- Registration between sequential timepoints within each subject.



Registration Chain

- Registration between sequential timepoints within each subject.
- Useful when subject brain differ greatly and have highly individualized time-courses
    - For example: tumour-prone mice

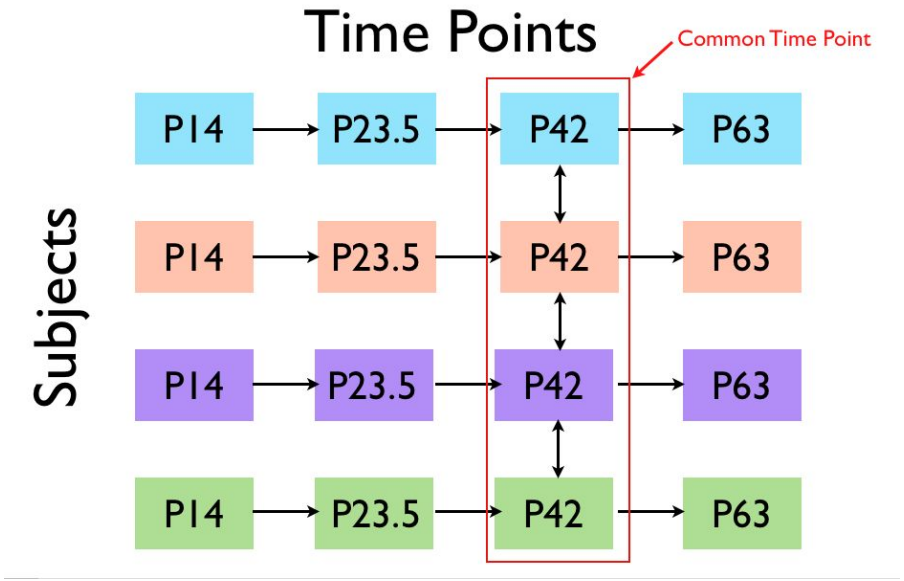


```
registration_chain.py \
--pipeline-name=test \
--num-executors 12 \
--latency-tolerance 1800 \
--lsq12-protocol [lsq12protocol.csv] \
--chain-common-time-point 3 \
--pride-of-models [initmodelmapping.csv] \
--chain-csv-file list_of_files.csv
```

https://wiki.mouseimaging.ca/display/MICePub/Longitudinal+Registration+Tools

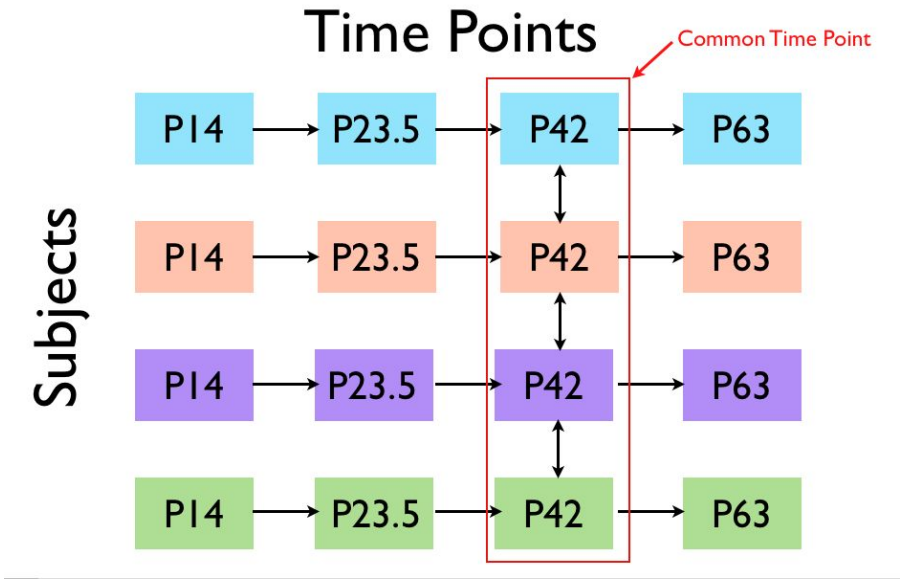
Registration Chain

What do the determinants tell us?



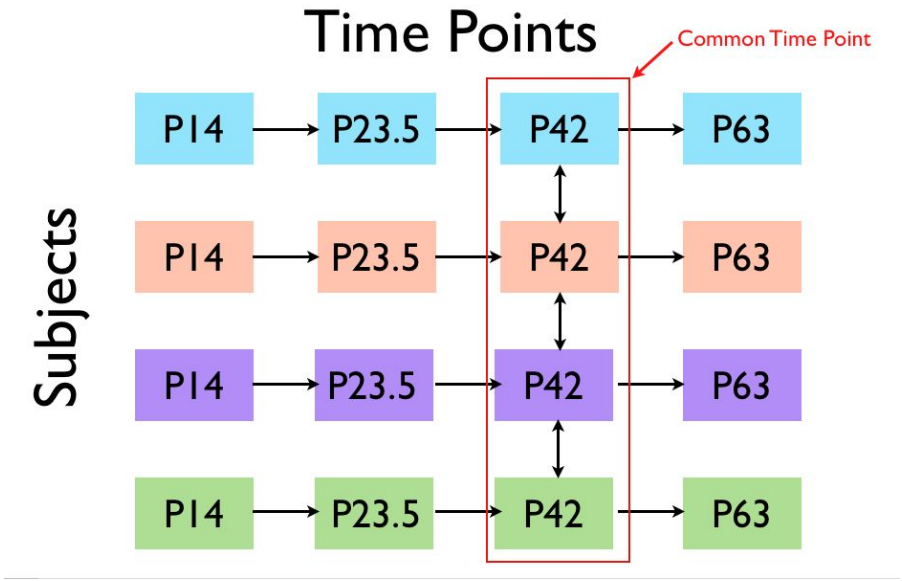
Registration Chain

- Level 1 determinants tell us the volumetric development of a subjects



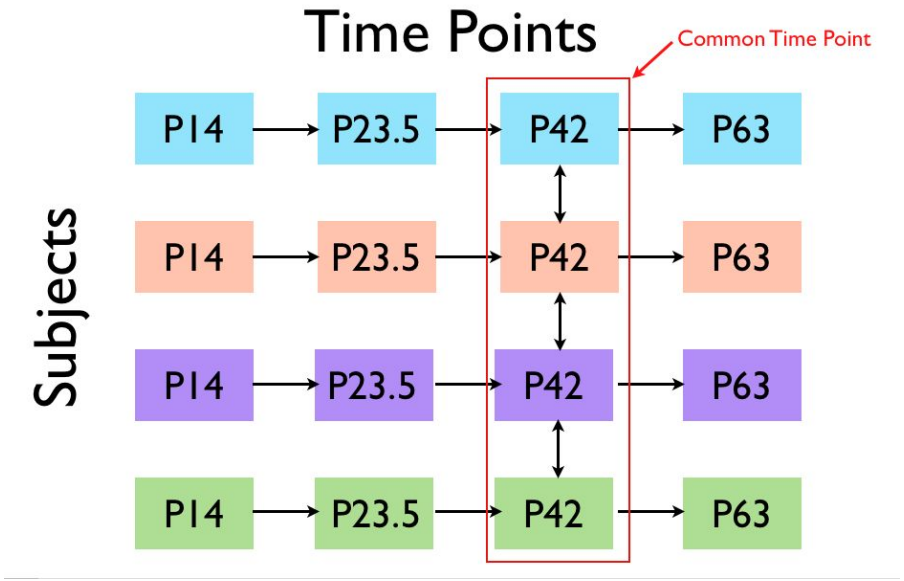
Registration Chain

- Level 1 determinants tell us the volumetric development of a subjects
- Level 2 determinants tell us the volumetric differences between subjects



Registration Chain

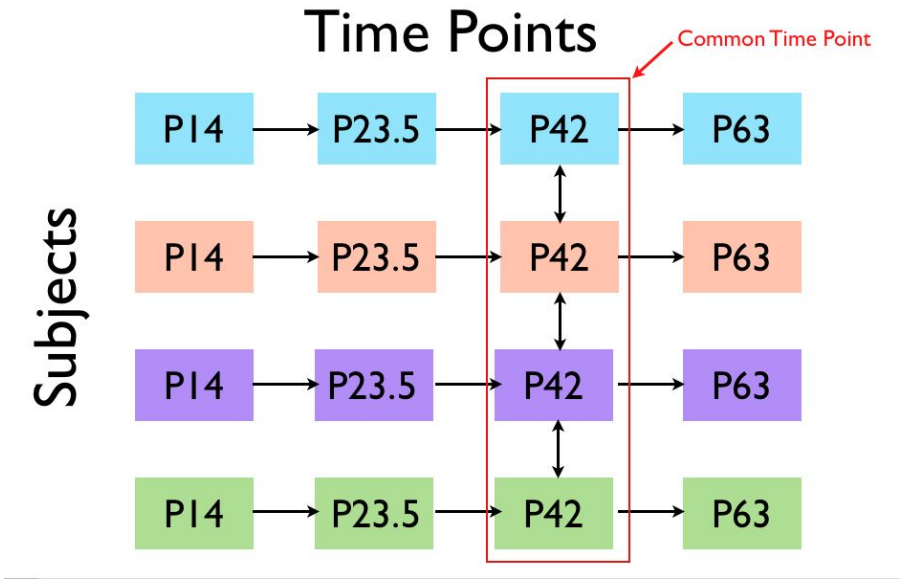
List the transformation needed to go from P23.5 in subject 1 to P14 in subject 3?



Registration Chain

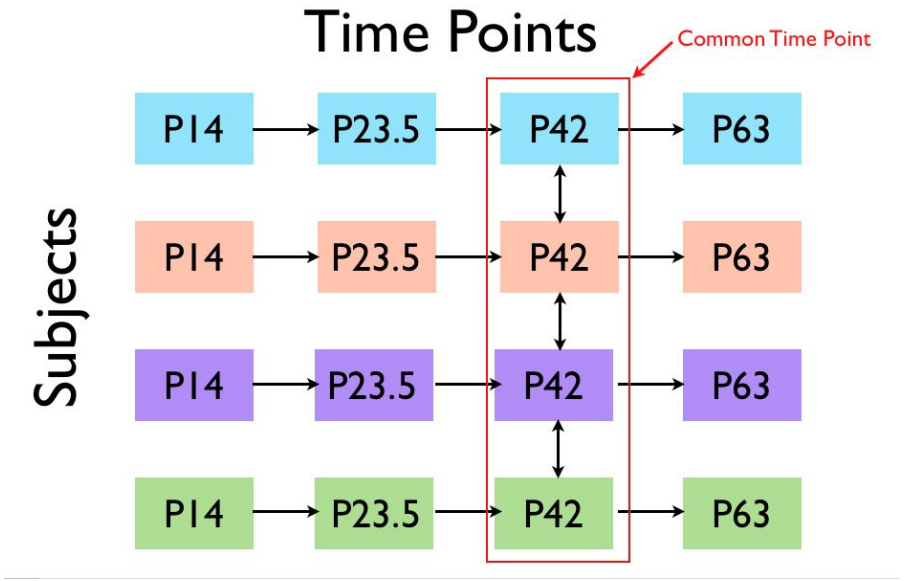
List the transformation needed to go from P23.5 in subject 1 to P14 in subject 3?

1. Subject 1 P23.5 → Subject 1 P42
2. Subject 1 P42 → consensus average
3. consensus average → Subject 3 P42
4. Subject 3 P42 → Subject 3 P23.5
5. Subject 3 P23.5 → Subject 3 P14



Registration Chain

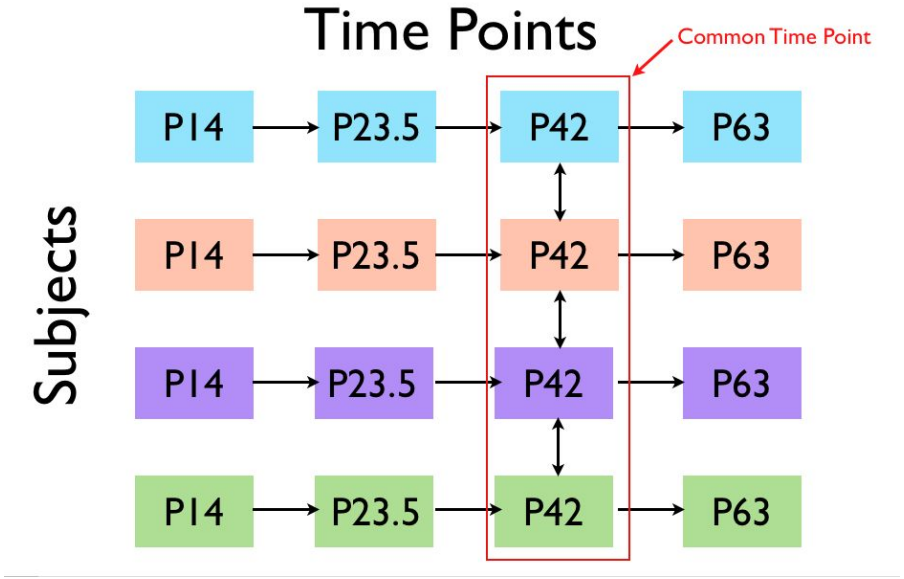
Disadvantages?



Registration Chain

Disadvantages?

- Model building (high SNR consensus) happens last
- Transformation error can propagate to dependent timepoints
- If subject is missing a single timepoint, subject is ignored



Levels 1 and 2 for registration types

Registration Type	Level 1	Level 2
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Registration Chain	• Within subject, across sequential timepoints • `Information across time`	• Across final timepoint consensus averages • `Information across subjects`
Tamarack		
Overlapping Group-Wise		

Types of Registrations	Pros	Cons	When to use
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Registration Chain	• Captures gross differences across time and across subjects	• Consensus averaging (increases SNR) happens last, therefore noise gets propagated • Requires a balanced design	• Gross changes across time and across subjects • i.e tumour in one subject, not in the other
Tamarack			
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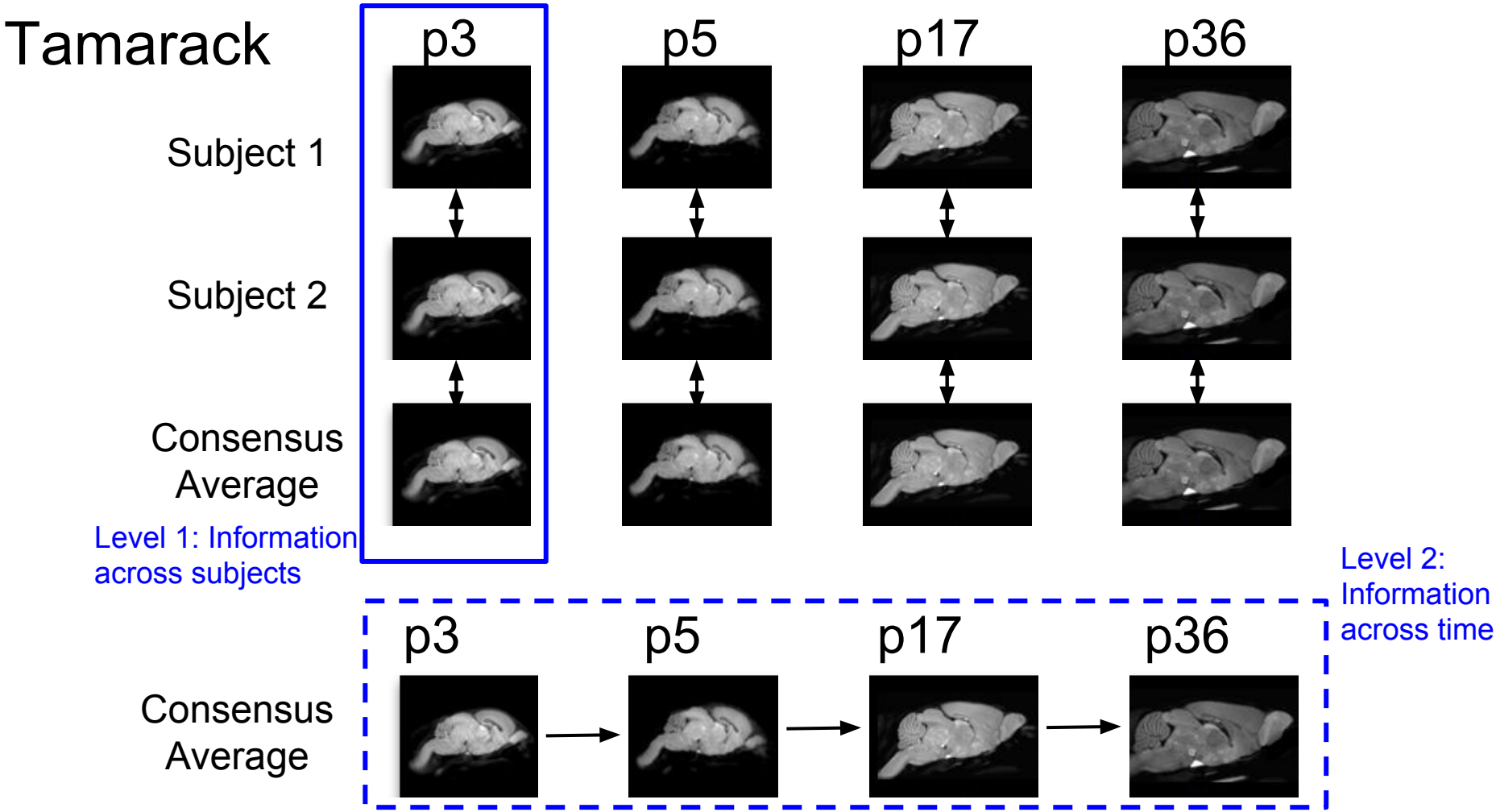
3. Tamarack


Tamarack
p3
p5
p17
p36
Subject 1
Subject 2
Consensus Average
Level 1: Information across subjects
Level 2: Information across time
p3
p5
p17
p36
Consensus Average

Pros, cons and when to use Tamarack

Pros:

- Works well for subtle changes in neonatal data
- Preserves cross-sectional differences across time

Cons:

- Does not work when there are gross changes across subjects
- Introduces biases when there is a correlation analysis

When to use:

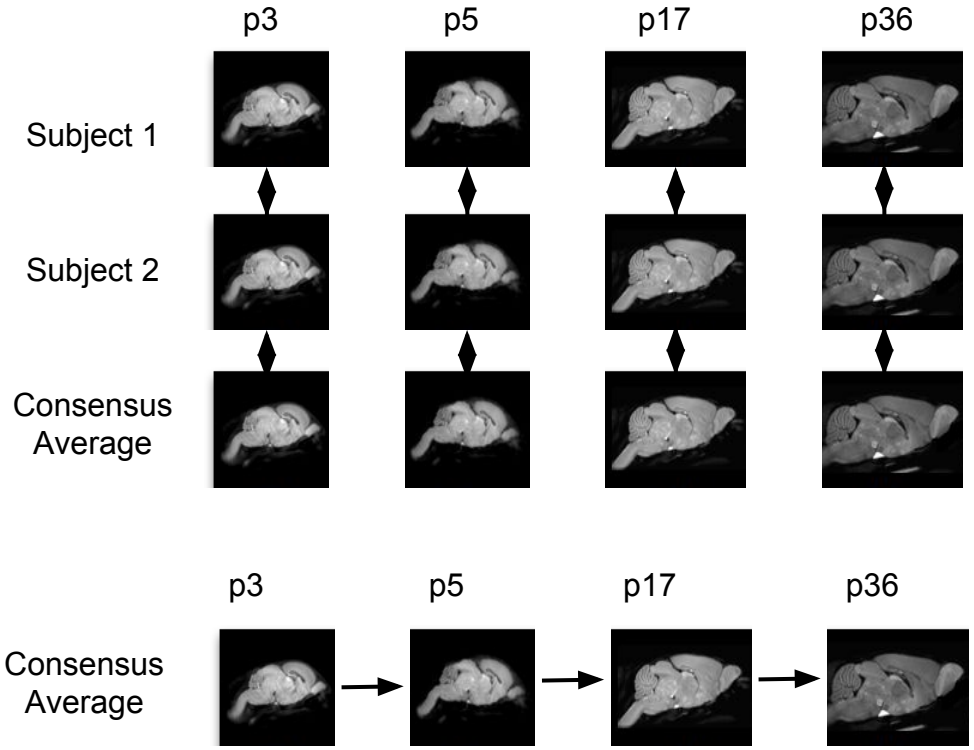
- Gross morphological changes across time, but subtle across subjects (eg. development of sex differences)

Tamarack registration: activity

2 subjects, 4 timepoints.

List the transformations needed to go from subject 1 at p3 to p36 consensus average

1. Register with all p3 images together
2. p3 consensus average → p5 avg
3. p5 avg → p17 avg
4. p17 avg → p36 avg



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Tamarack	• All subjects at each time point • `Information across subjects`	• Consensus averages across sequential timepoints • `Information across time`
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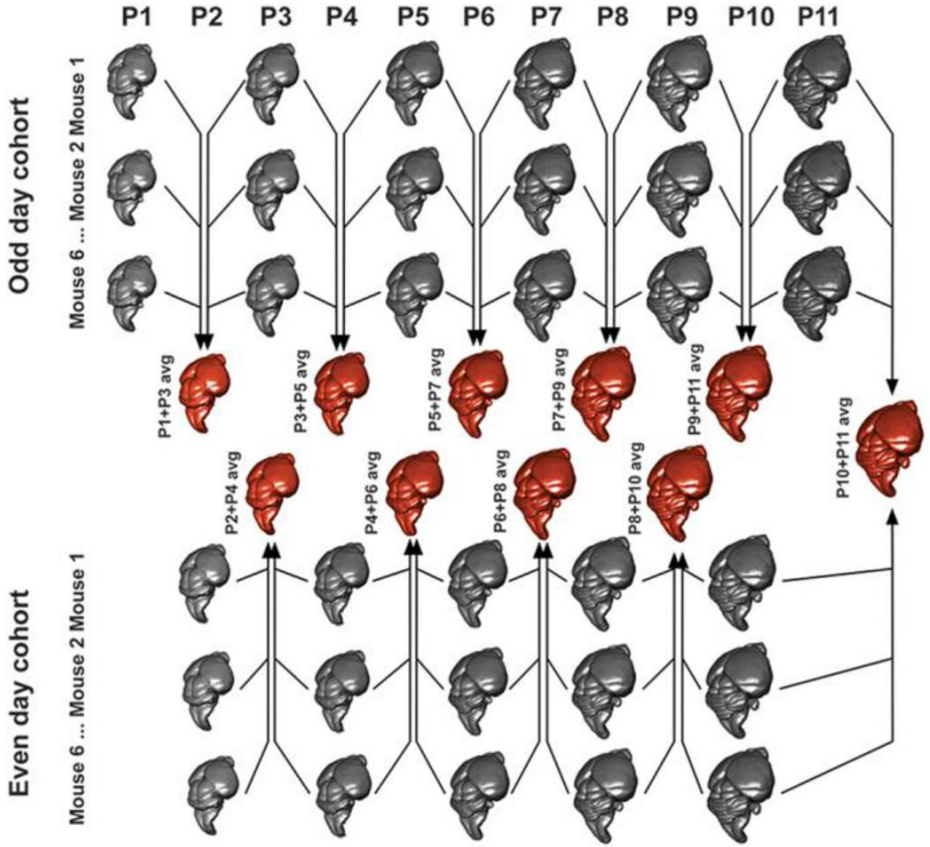
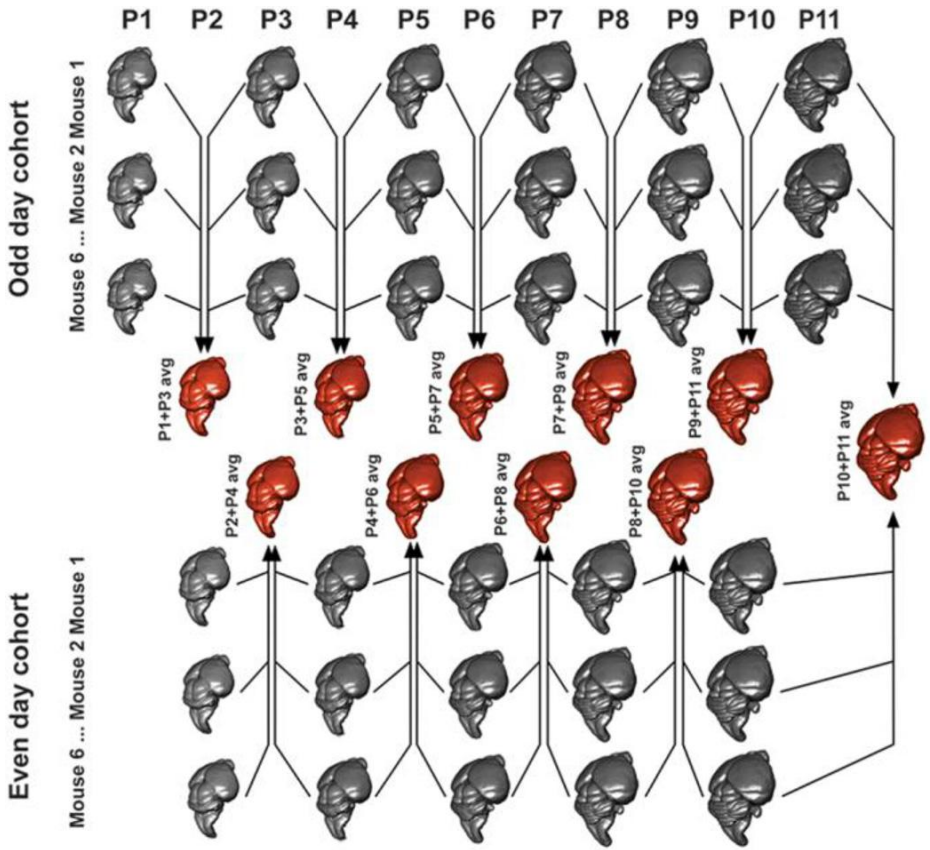
Tamarack	• Works well with subtle changes in neonatal data • Preserves cross-sectional differences over time	• Does not work when there are gross changes across subjects • Introduces biases when there is a correlation analysis	• Gross morphological changes across time, but subtle across subjects • i.e. sex differences
Overlapping Group-wise			

4. Overlapping group-wise



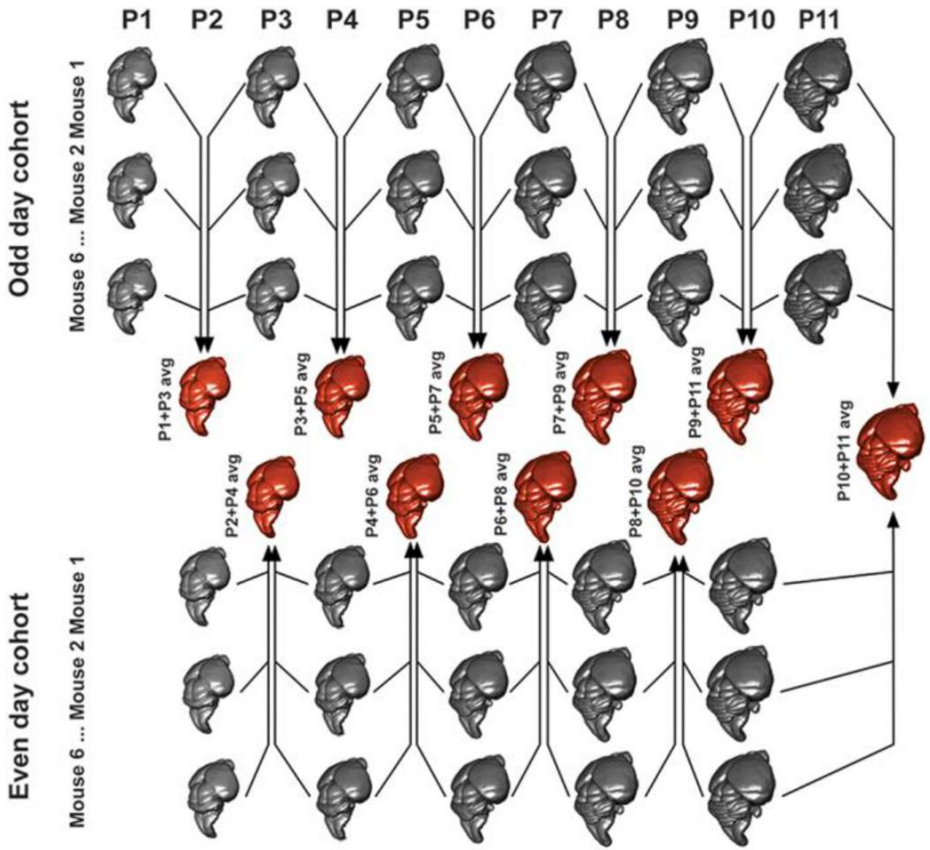
Overlapping group-wise

- Register adjacent timepoints of each cohort.
- Register last timepoint in each cohort together.
- Useful when brain undergoes gross changes over time.
- And when subjects brains evolve similarly.
- Provides information on variability of temporal changes



Overlapping group-wise

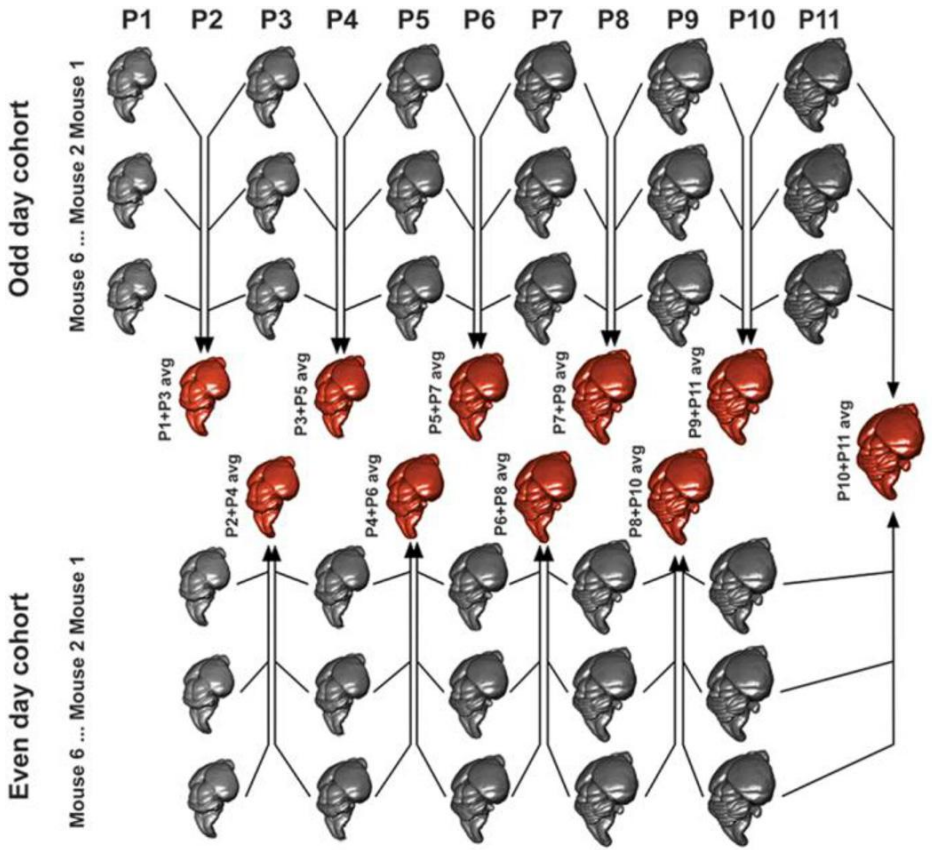
What do the level 1 and level 2 determinants tell us?



Overlapping group-wise

What do the level 1 and level 2 determinants tell us?

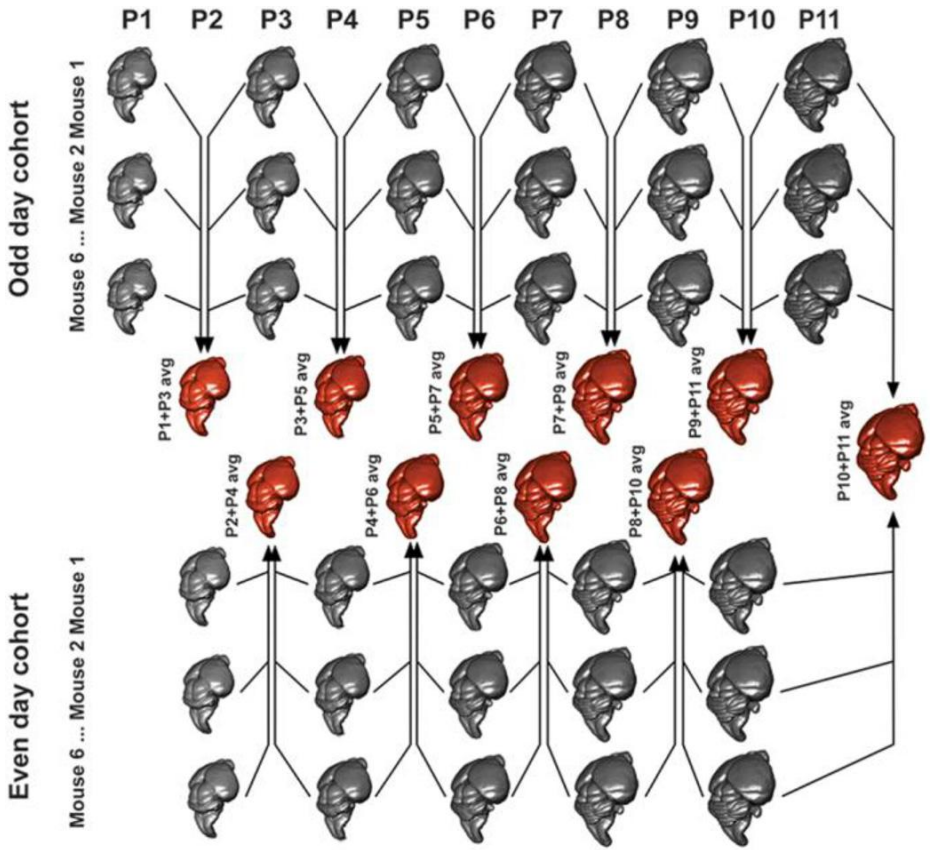
- Level 1 determinants tell us intra-cohort spatiotemporal volumetry
- Level 2 determinants tell us inter-cohort spatiotemporal volumetry



Overlapping group-wise

What are the transformations needed to go from mouse 1 P1 to mouse 6 P2?

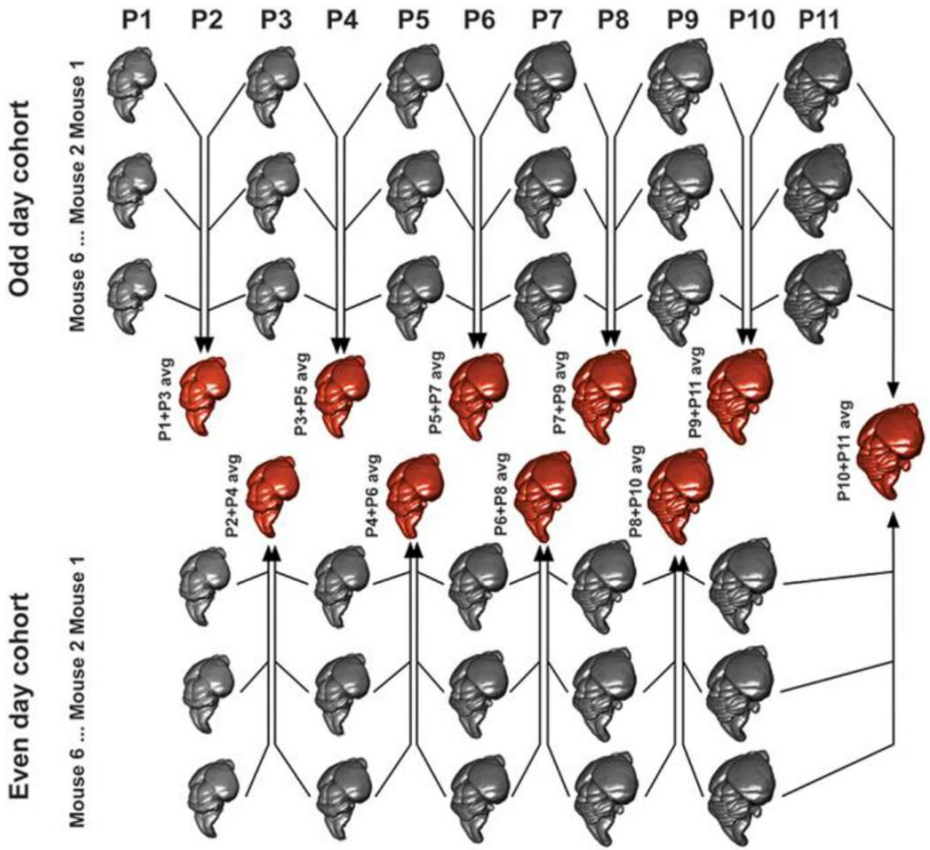
1. Mouse 1 P1 → P1+3 avg
2. P1+3 avg → P3+5 avg
3. P3+5 avg → P5+7 avg
4. P5+7 avg → P7+9 avg
5. P7+9 avg → P9+11 avg
6. P9+11 avg → P10+11 avg
7. P10+11 avg → P8+10 avg
8. P8+10 avg → P6+8 avg
9. P6+8 avg → P4+6 avg
10. P4+6 avg → P2+4 avg
11. P2+4 avg → Mouse 6 P2



Overlapping group-wise

What are the disadvantages?

- Balanced Design
- May introduce cohort biases



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Tamarack	• All subjects at each time point • `Information across subjects`	• Consensus averages across sequential timepoints • `Information across time`
Overlapping Group-Wise	• Within cohort • `Information across time and information across subject within same cohort`	• Across cohort • `Information across time and across subjects in different cohorts`

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Tamarack	• Works well with subtle changes in neonatal data • Preserves cross-sectional differences over time	• Does not work when there are gross changes across subjects • Introduces biases when there is a correlation analysis	• Gross morphological changes across time, but subtle across subjects • i.e. sex differences
Overlapping Group-wise	• Works well with subtle changes in neonatal data • Preserves cross-sectional differences over time • Exposes subtle temporal differences in subjects	• Requires a balanced design (no missing data!)	• Same as Tamarack, except you cannot have any missing data!