POY VERSION 4

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GOALS OF THE PROJECT

- Multiple phylogenetic inference criteria
- Support from pre-aligned sequences, to complete genomes, developmental sequences, and morphology
- Good performance
- Analytic, educational, and research tool
- High quality control

THIS TALK

- Phylogenetic analysis features
- Performance
- Flexibility
- Quality control

PHYLOGENETIC ANALYSIS FEATURES

TRANSFORMATIONS SUPPORTED

- Substitutions
- Insertions and Deletions
- Inversions
- Translocations
- Horizontal Gene Transfer
- Other transformations

GOALS

	Static	Dynamic Homologies	
	Matrix	Unaligned	Rearrangements
Parsimony			
Likelihood			
Bayesian			

POY VERSION 3

	Static	Dynamic Homologies	
	Matrix	Unaligned	Rearrangements
Parsimony			
Likelihood			
Bayesian			

POY VERSION 4

	Static	Dynamic Homologies	
	Matrix	Unaligned	Rearrangements
Parsimony			
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Bayesian			

ALGORITHMS

- **Random Addition Sequence**
- SPR
- **TBR**
- Sectorial Search
- Tree Fusing
- Ratchet
- Perturbation
- Simulated Annealing
- Tree Drifting
- Branch and Bound
- Multiple new heuristics
- **Direct Optimization**
- Affine-DO
- Fixed States
- Iterative improvement
- Exhaustive (Affine-)DO
- Local search for GTAP with rearrangements

POY VERSION 4

	Static	Dynamic Homologies	
	Matrix	Unaligned	Rearrangements
Parsimony			
Likelihood			
Bayesian			

PERFORMANCE

COMMON COMMENTS

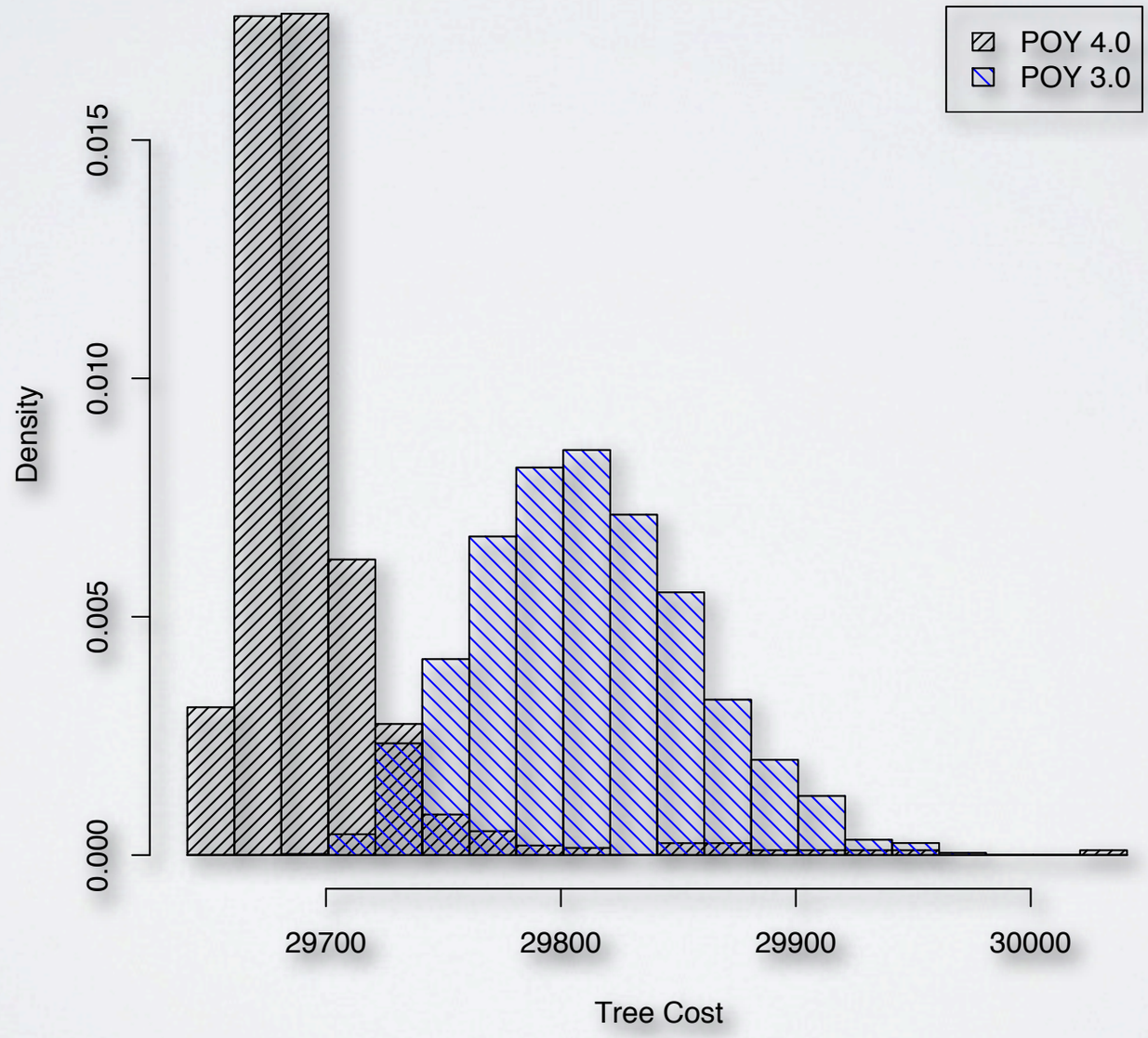
- POY is slow (needs a cluster)
- POY's trees are very inaccurate
- POY doesn't scale (only small data sets really)

VERSION COMPARISON

Version 3 with Version 4
100 terminals, 8 genes, 35 morphological characters
(subset of Faivovich *et al*., 2005)
1000 iterations Random Addition Sequence followed by TBR

SPEED COMPARED WITH POY 3

Random Addition Sequence followed by TBR



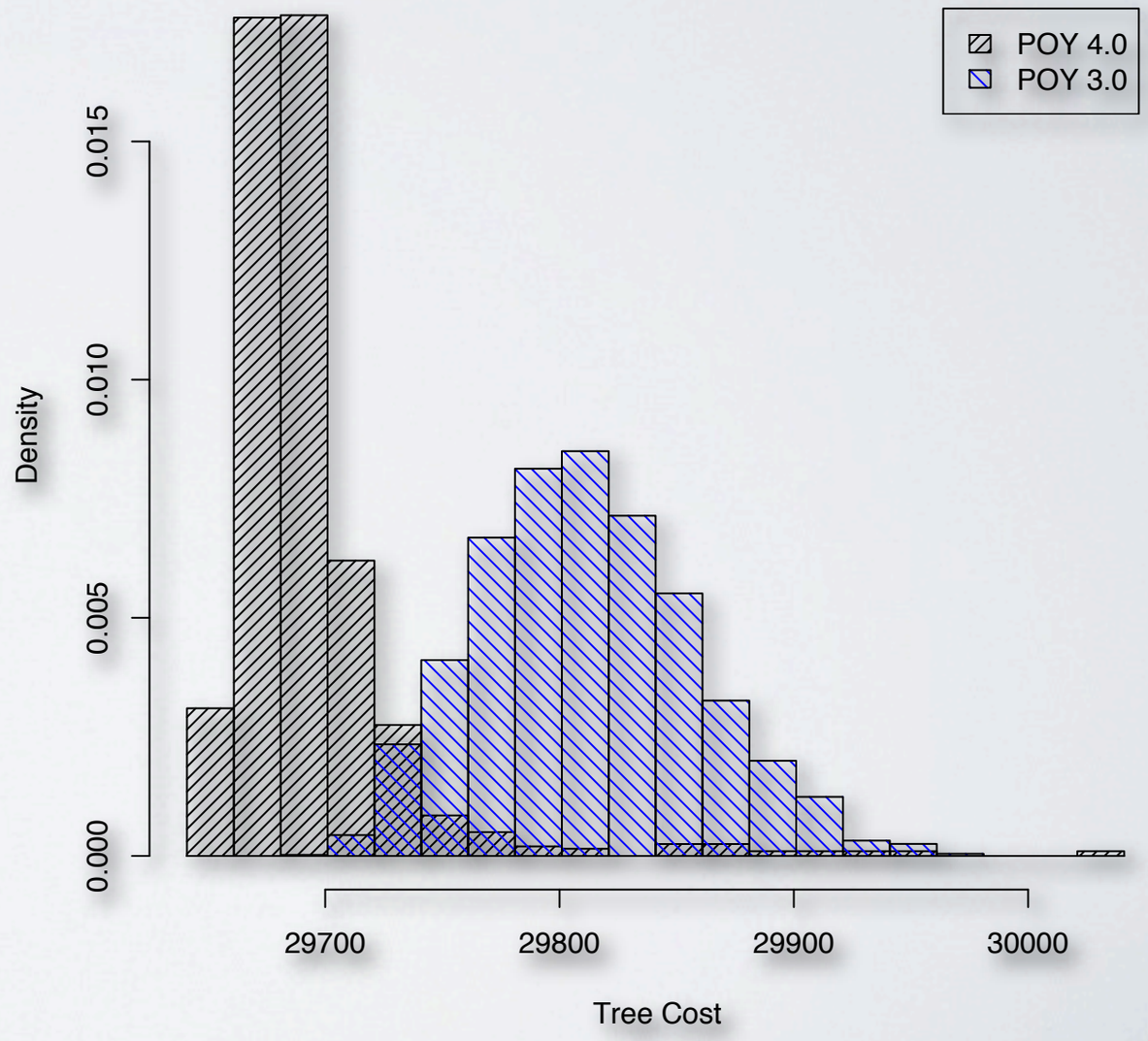
SPEED COMPARED WITH POY 3

Random Addition Sequence followed by TBR

POY 4 + Dual core workstation

=

POY 3 + 5000 core cluster



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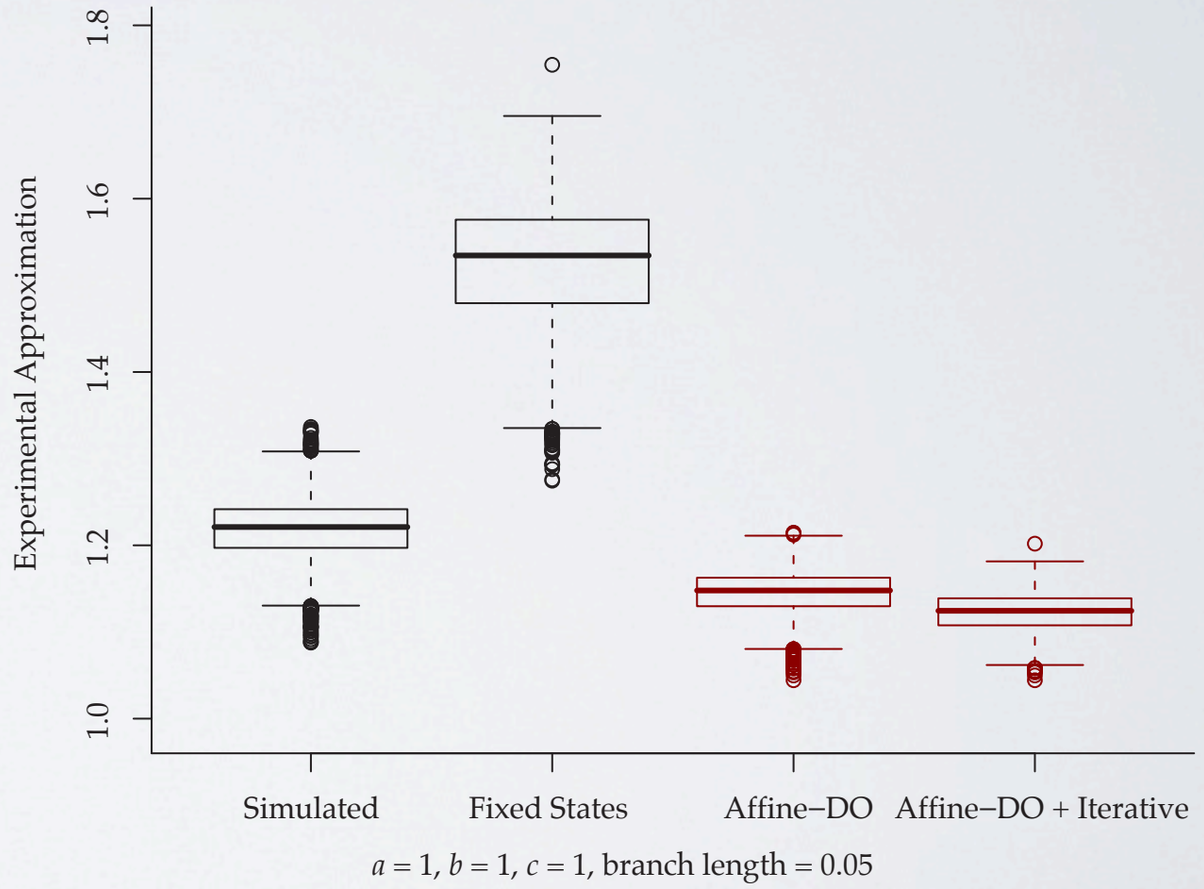
COMPARED WITH PRE-ALIGNED SEQUENCE

- Ogden and Rosenberg, 2007 (POY 3)
  - POY = 10 RAS + TBR with non-affine gap costs
  - Simulate with affine gaps
- None of the pre-aligned sequence methods support affine gaps as transformation events

IMPROVED AFFINE GAP SUPPORT IN POY 4

- Only program of this performance and scalability for (affine) tree alignment



COMPARISONS WITH PRE-ALIGNED SEQUENCES

- Lehtonen, 2008
  - POY's inference is better even using non-affine cost with a better search (using POY 4).
- Wheeler, 2009
  - POY's trees are much shorter.
- Liu, *et al.*, 2009
  - POY's phylogenies with unaligned sequences are very competitive.

COMPARED WITH PRE-ALIGNED SEQUENCE

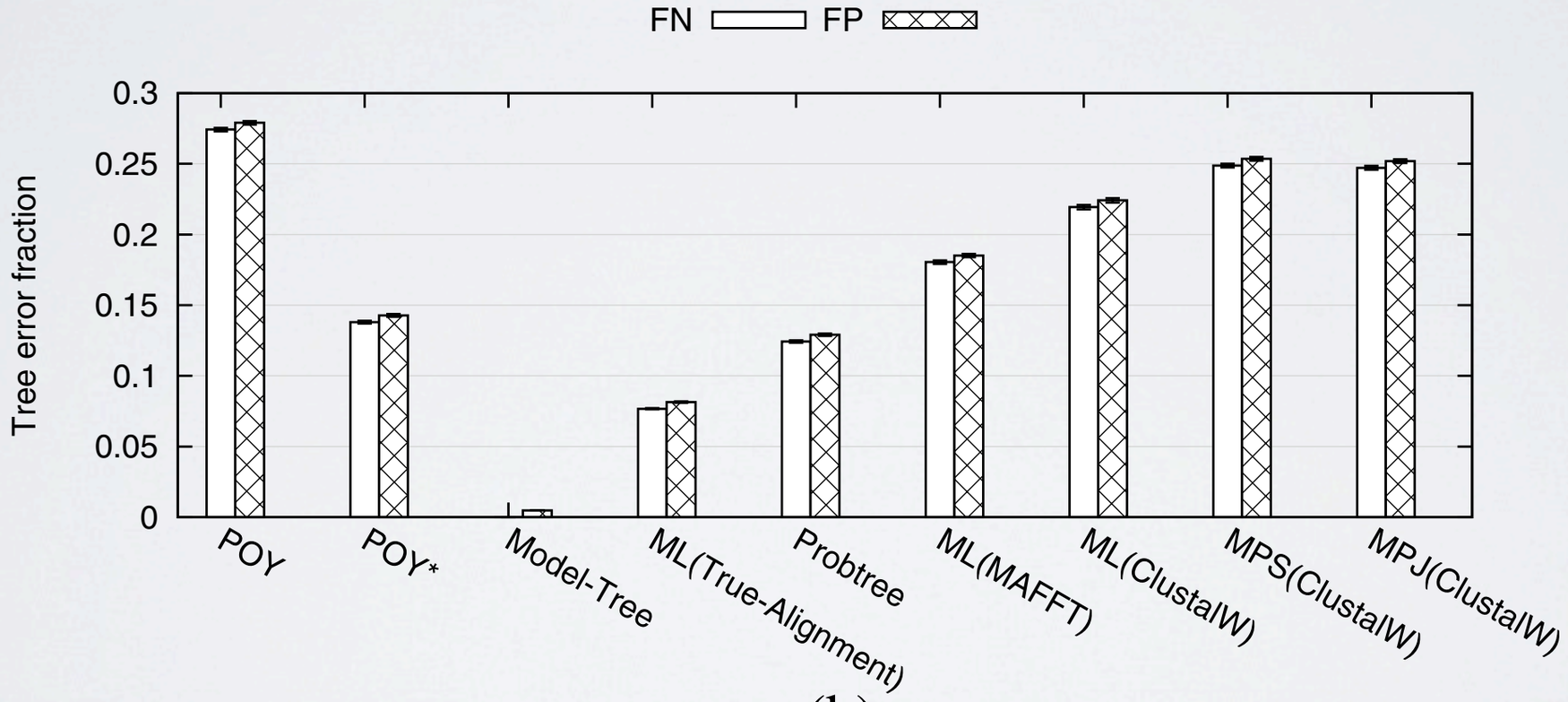
ML = RAxML with GTRMIX

PS (X) = POY score for a tree generated by method X

POY = 1 Random Addition Sequence followed by TBR

POY* = Probtree + TBR in POY

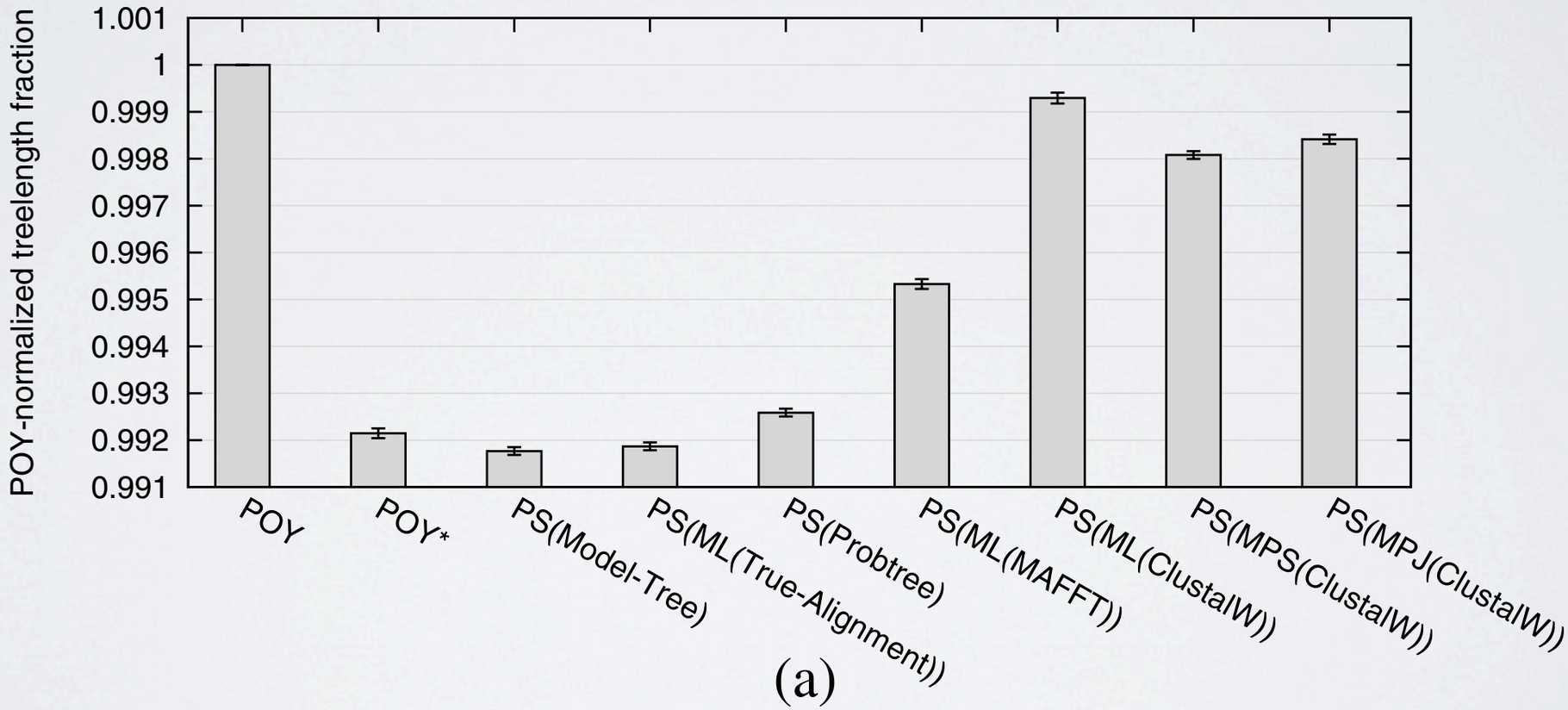
COMPARED WITH PRE-ALIGNED SEQUENCE



(b)

Liu, *et al.*, 2009

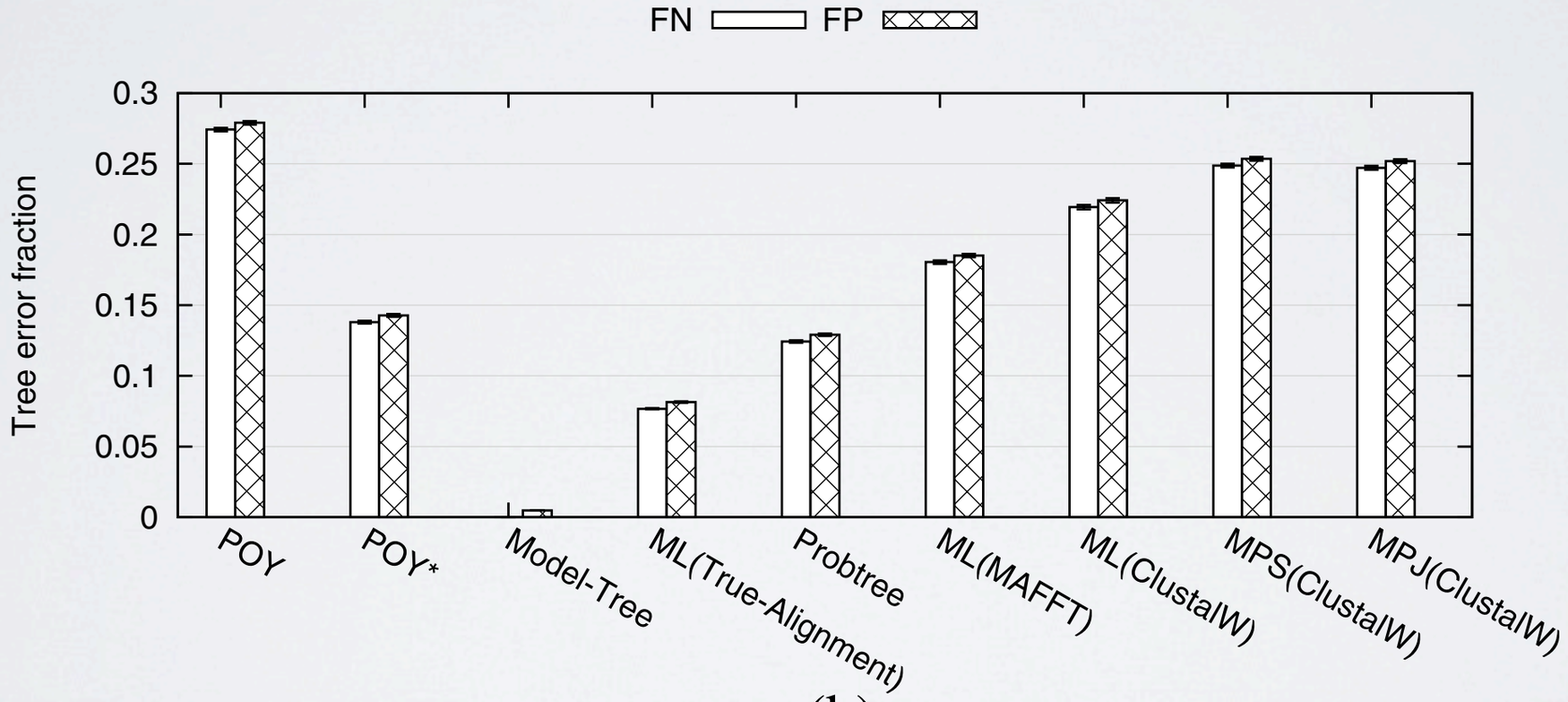
COMPARED WITH PRE-ALIGNED SEQUENCE



(a)

Liu, *et al.*, 2009

COMPARED WITH PRE-ALIGNED SEQUENCE



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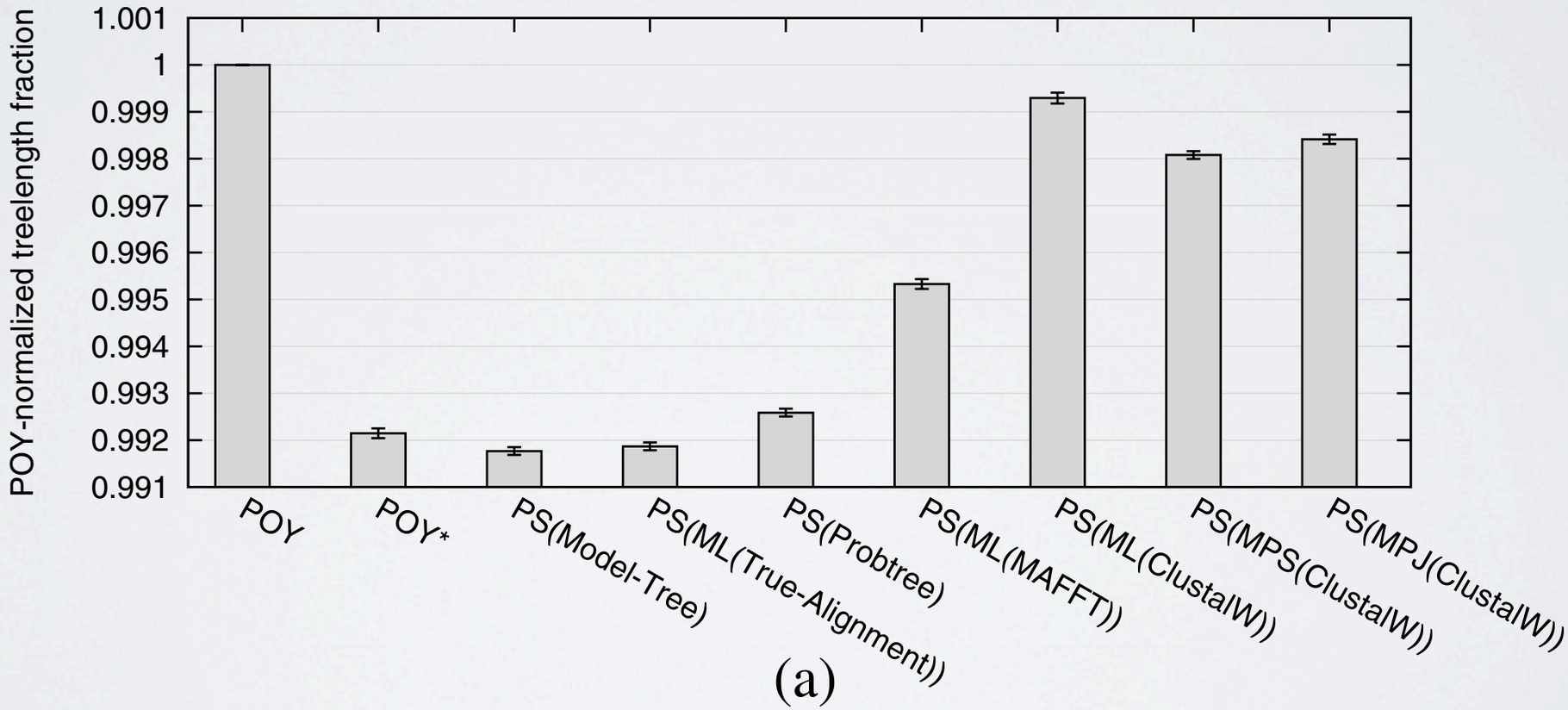

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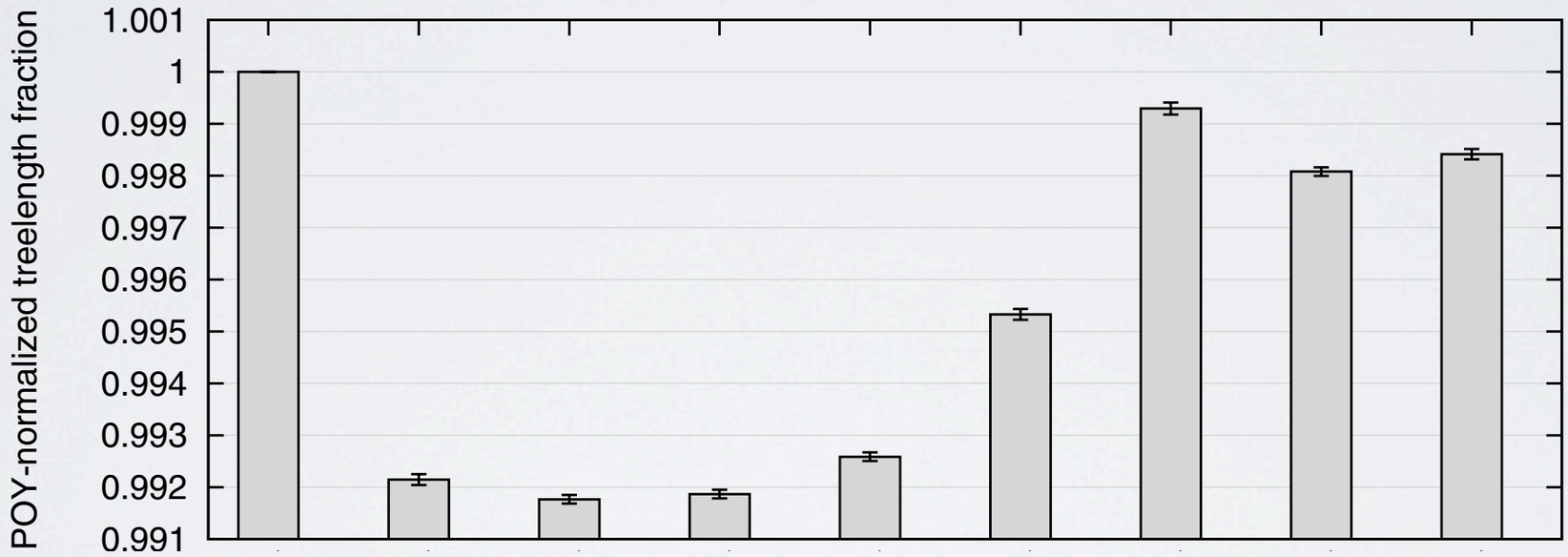
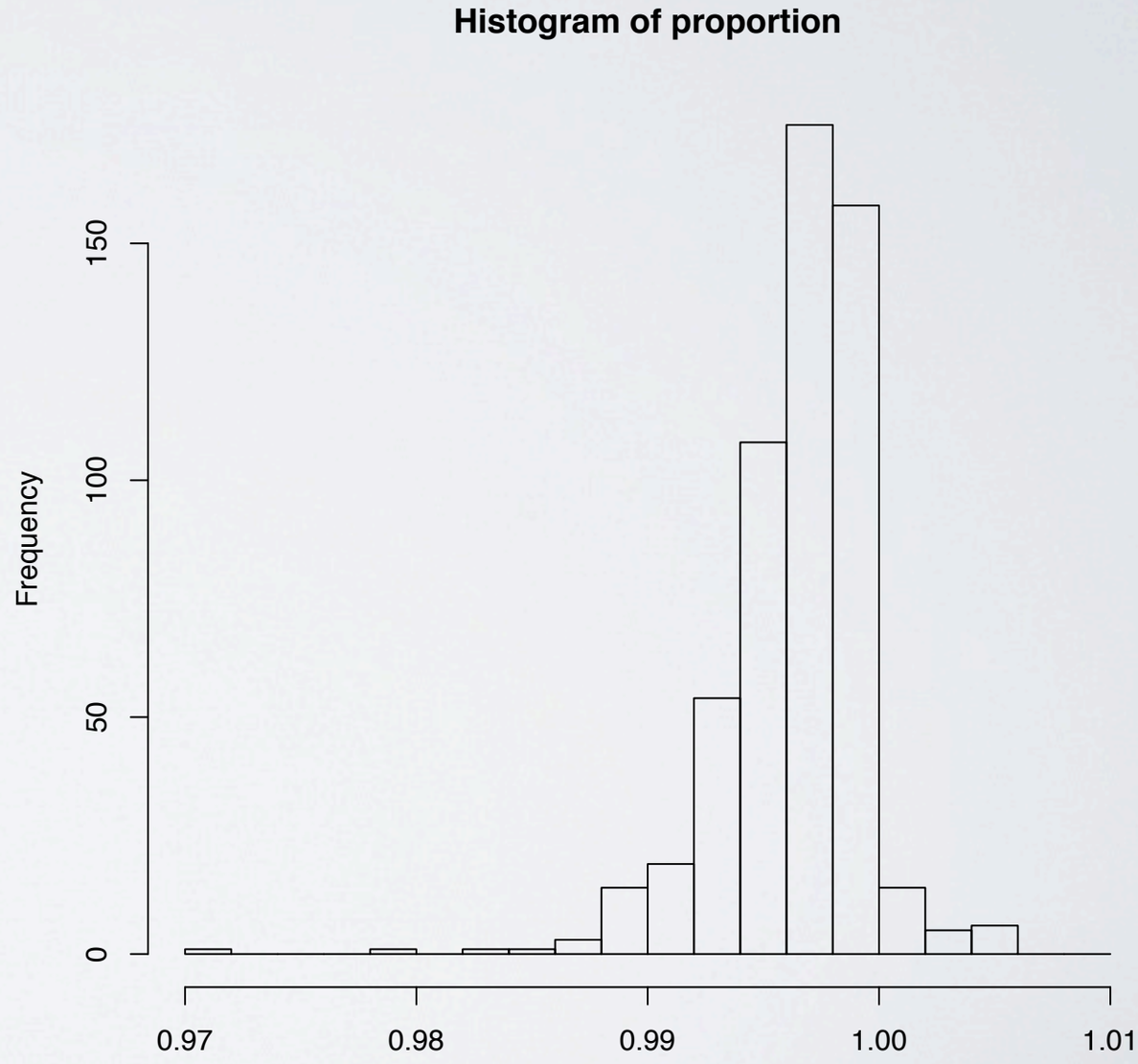


DOES POY DO WELL?

- Better heuristic in POY
- Time limit of 2 hours
- POY produces shorter trees than POY*



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SCALABILITY

SCALABILITY METHODS

- New algorithms
- Functional programming and data structures
- Script analysis and optimization

FUNCTIONAL PROGRAMMING

- No global variables (well .... there are two counters).
- No side effects (interfaces are purely functional).

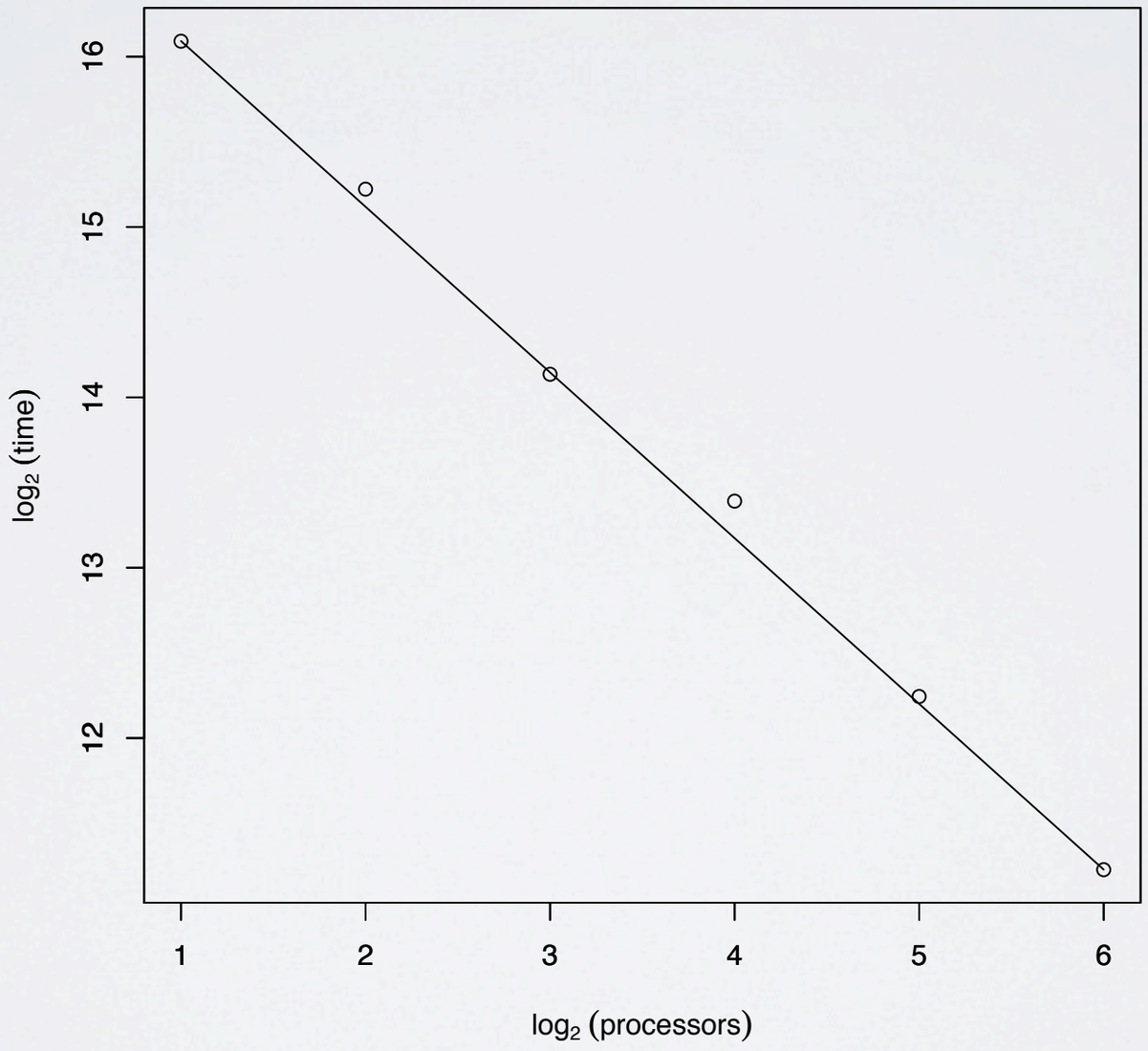
SCRIPT ANALYSIS AND OPTIMIZATION

```
read ("file")              (* Non-Composable *)
build (1000)               (* Parallelizable *)
swap ()                    (* Parallelizable *)
redraw ()                  (* Linnearizable  *)
select ()                  (* Composable     *)
report (graphtrees)        (* Non-Composable *)
quit ()                    (* Non-Composable *)
```

SCRIPT ANALYSIS AND OPTIMIZATION

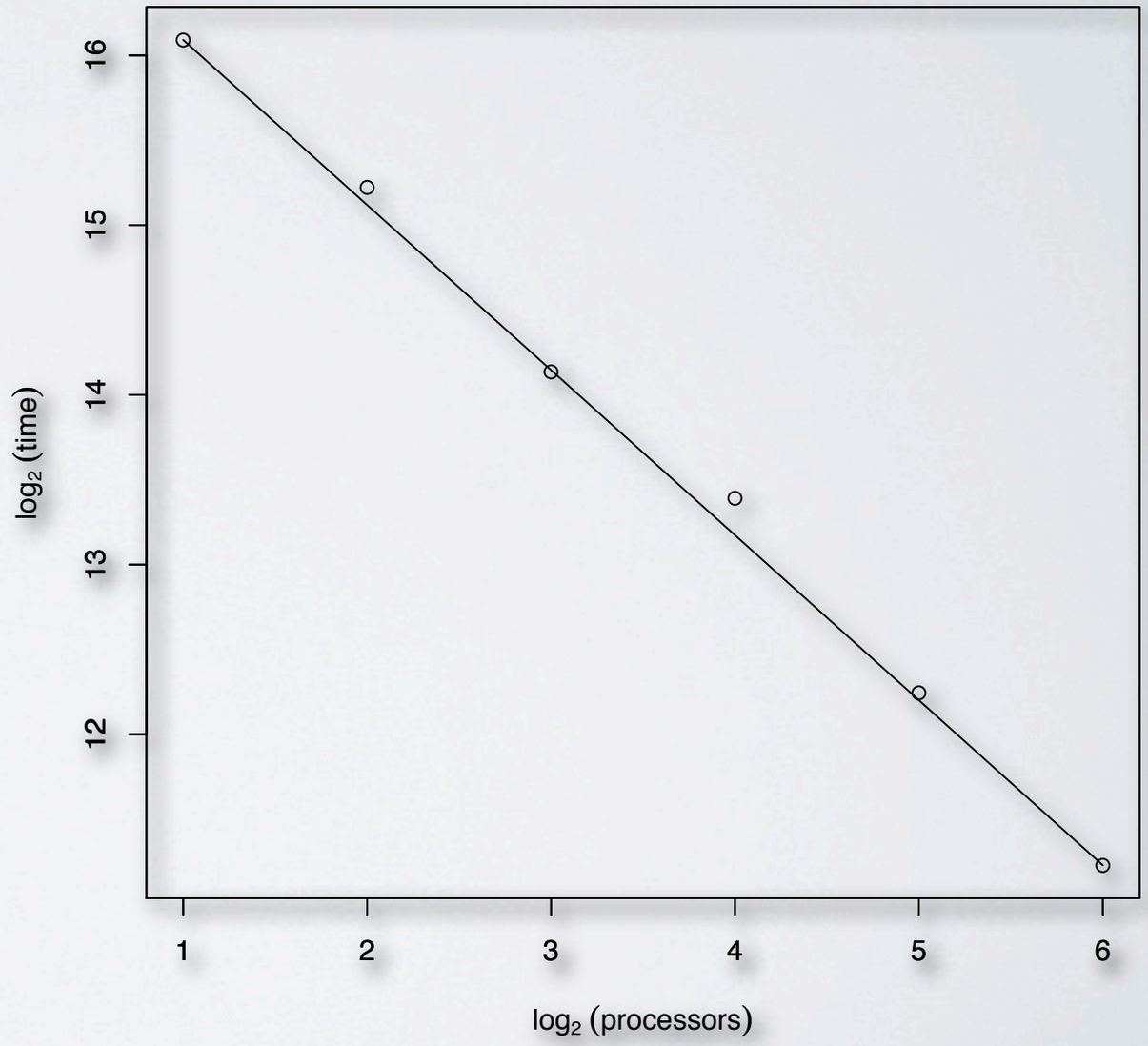
```
beginning of the program
read an input file
I will calculate the following in separate processors (if available)
processor group 1:
  in parallel:
    build some trees from scratch
    swap the trees in memory
    while keeping the following invariant:
      eliminate repeated trees
      select the optimal trees
  eliminate repeated trees
  select the optimal trees
processor group 2:
  redraw the screen
  output the trees in memory
  close POY
```

SCRIPT ANALYSIS AND OPTIMIZATION



SCALABILITY EXAMPLE

- Linear scalability + limited memory consumption



LARGEST ANALYSES
(TO MY KNOWLEDGE)

- In terminals: ~1.700 terminals, 4 genes (~ 4.000 bp)

- Simulations of 1.000 sequences in a modern workstation within 72 hours

- In genome length: >800.000 bp and 342 genes for 6 terminals

- Linear scalability in parallel execution

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POY 4 ADVANTAGES

- Shorter time
- Better tree costs
- Indels consistently treated within the optimality criterion

WARNING!

- The simulations are easy to attack
- The results depend on the model used
- The data are ideal, not real (e.g. patterns of missing fragments)

FLEXIBILITY

FLEXIBILITY

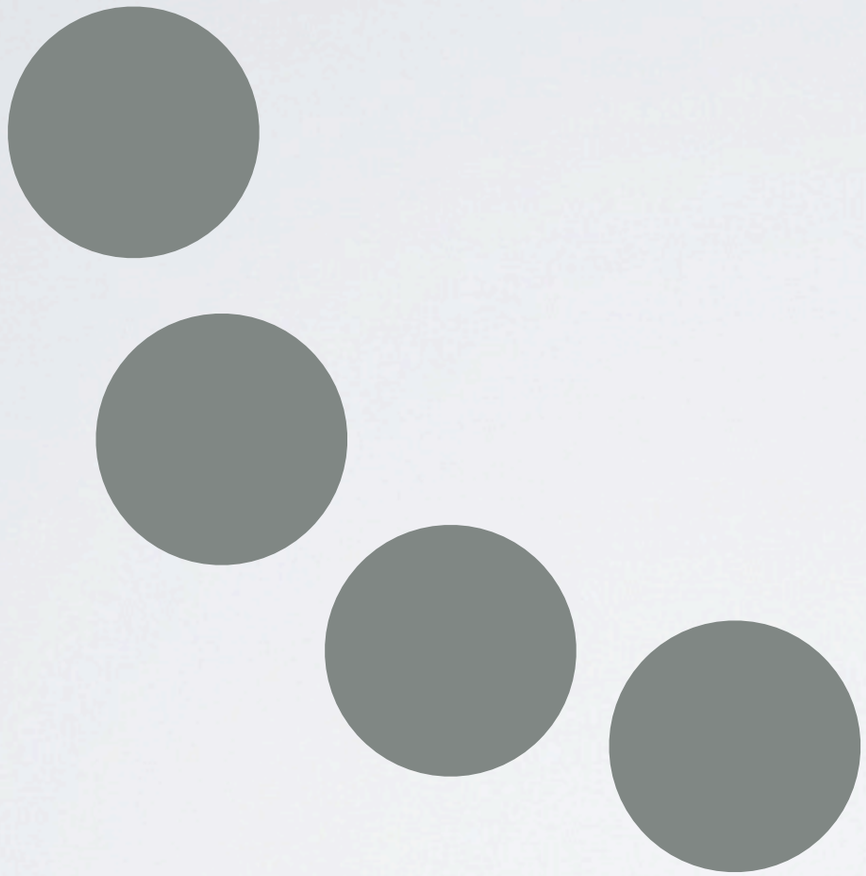
- Open source
- OCaml and C
- Plugin architecture to add functions
- New character types can be easily added
- Extensions to the Objective CAML language to inject POY scripts
- Extensive documentation
- Many file formats supported

QUALITY CONTROL

QUALITY CONTROL

- OCaml helps *a lot*
- Release early, release often
- Provide very active support to users
- Distributed unit tests in multiple architectures with distributed version control

QUALITY CONTROL



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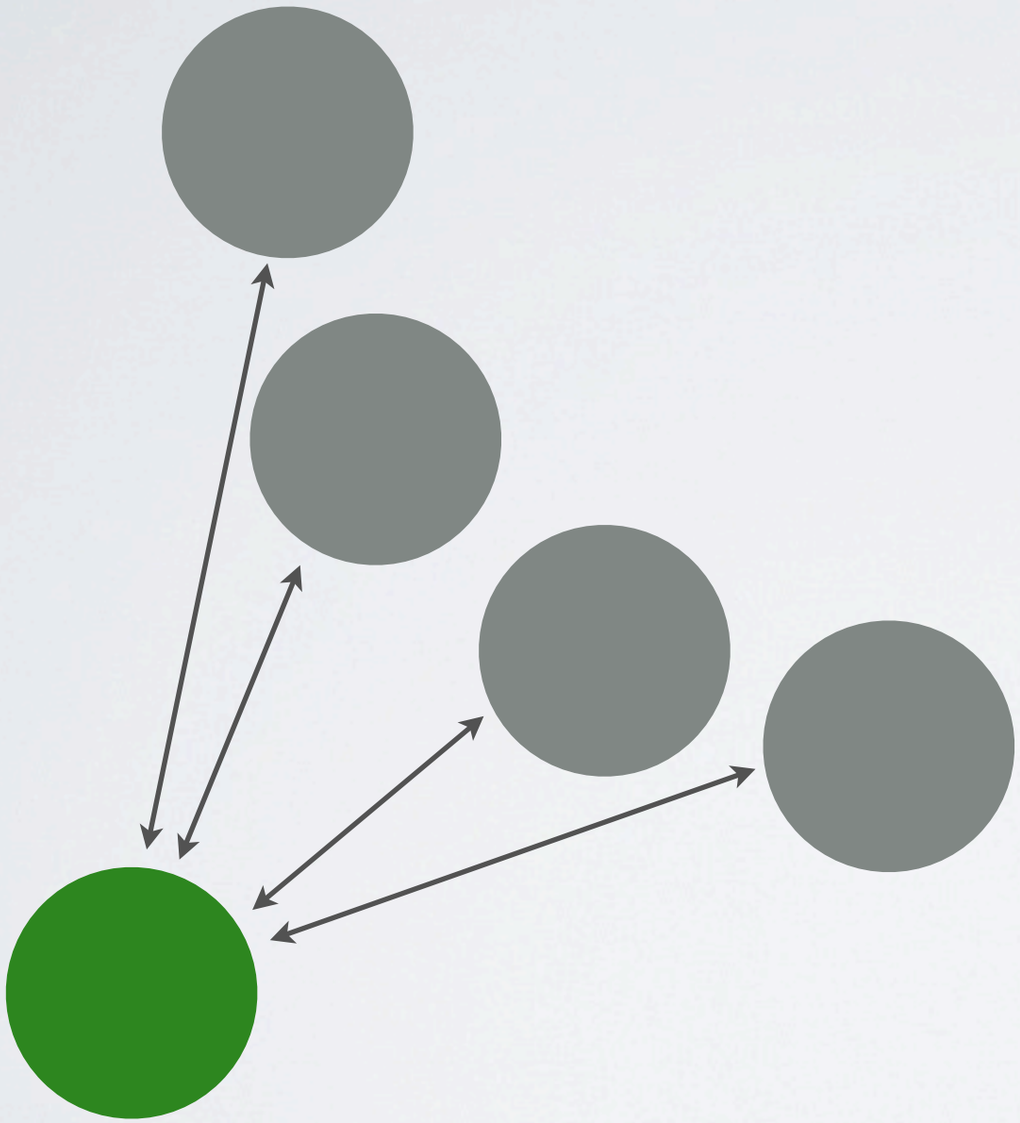

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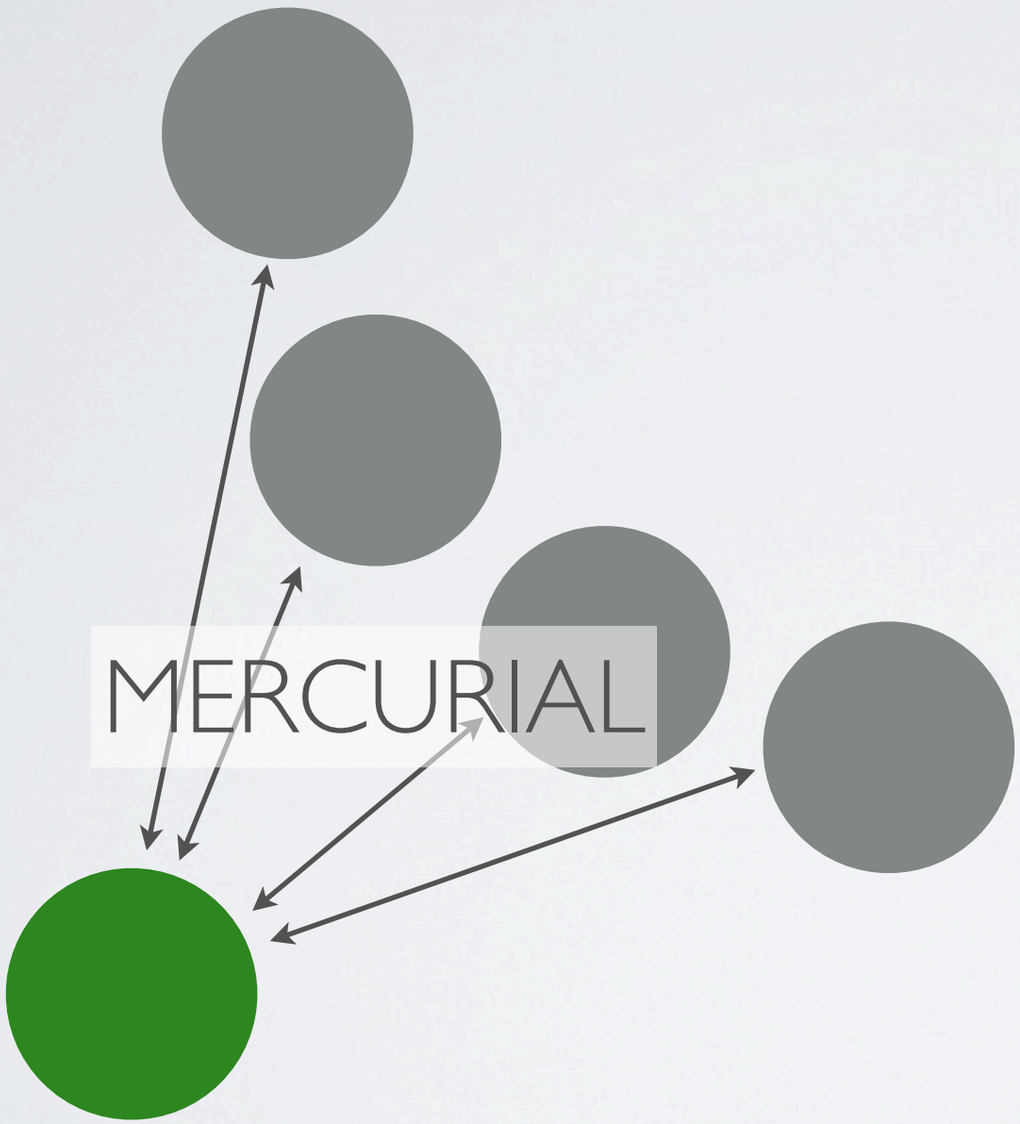

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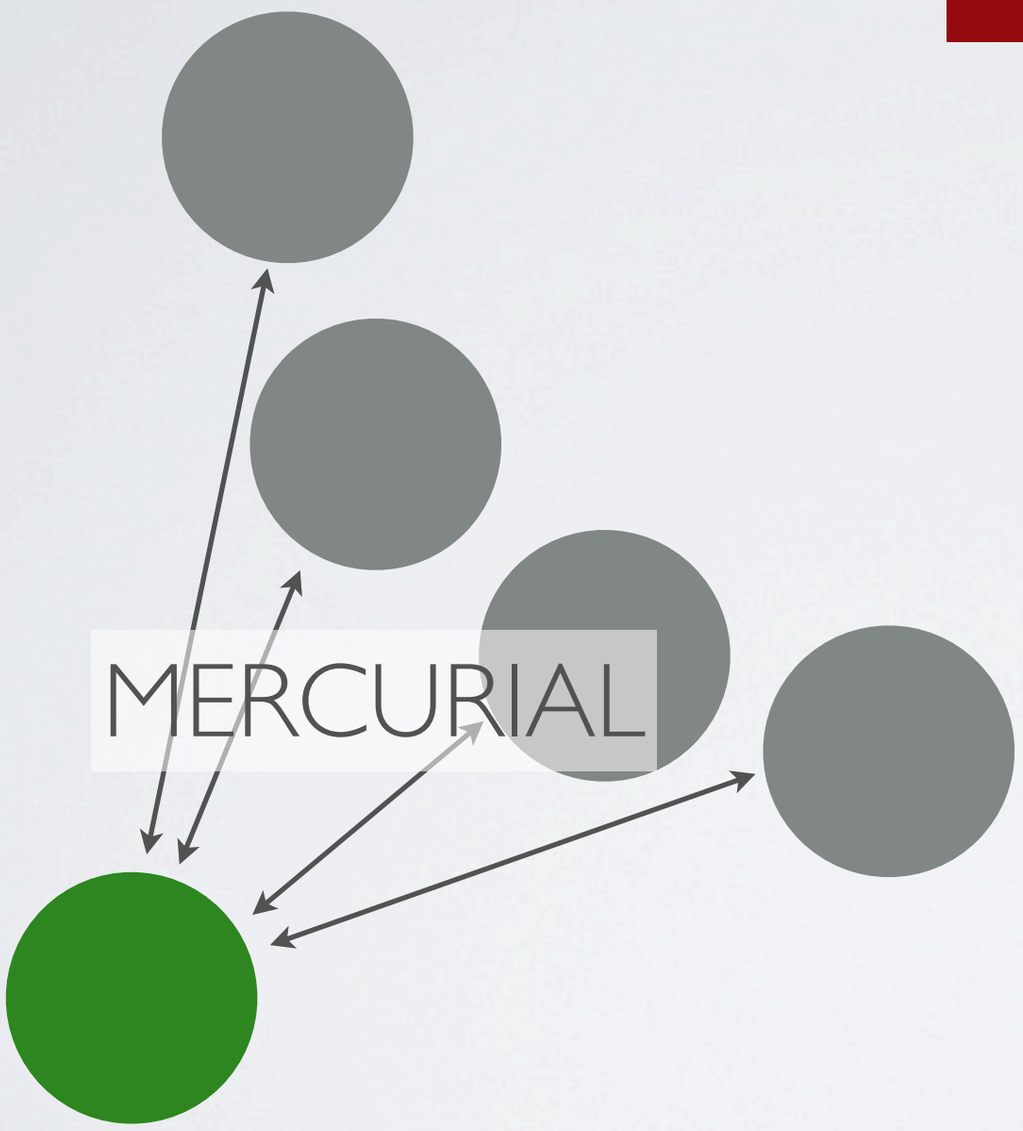

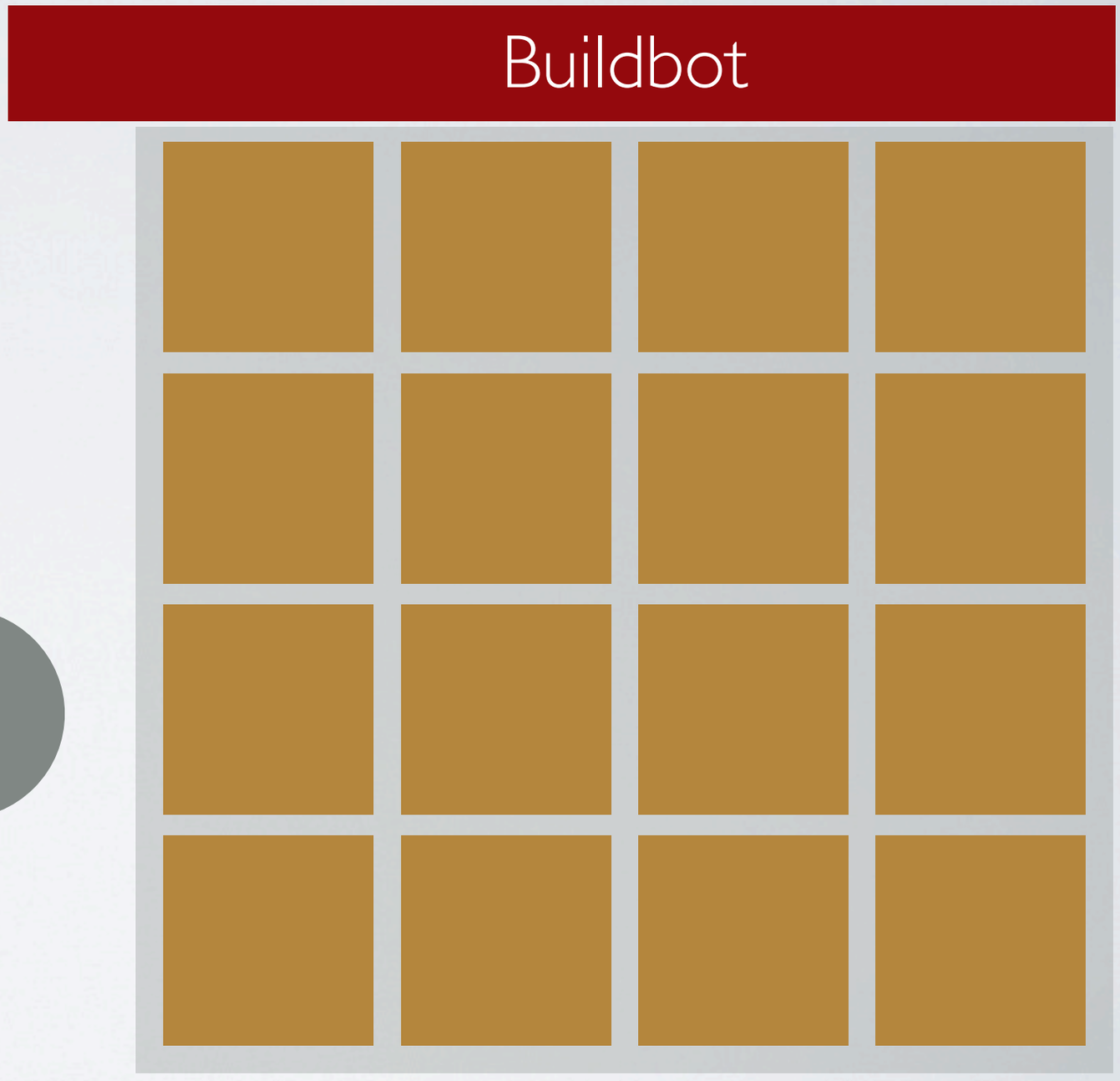

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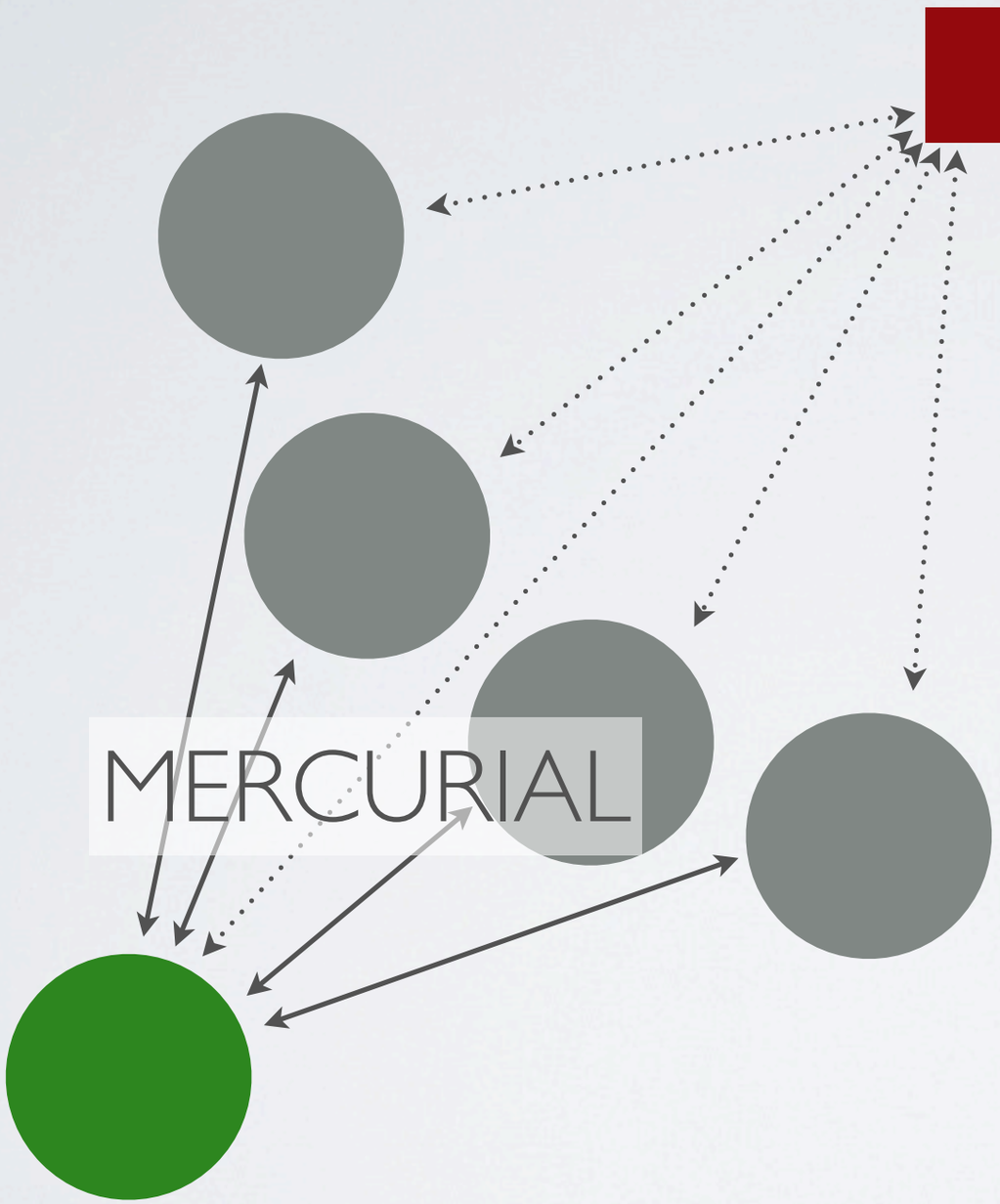

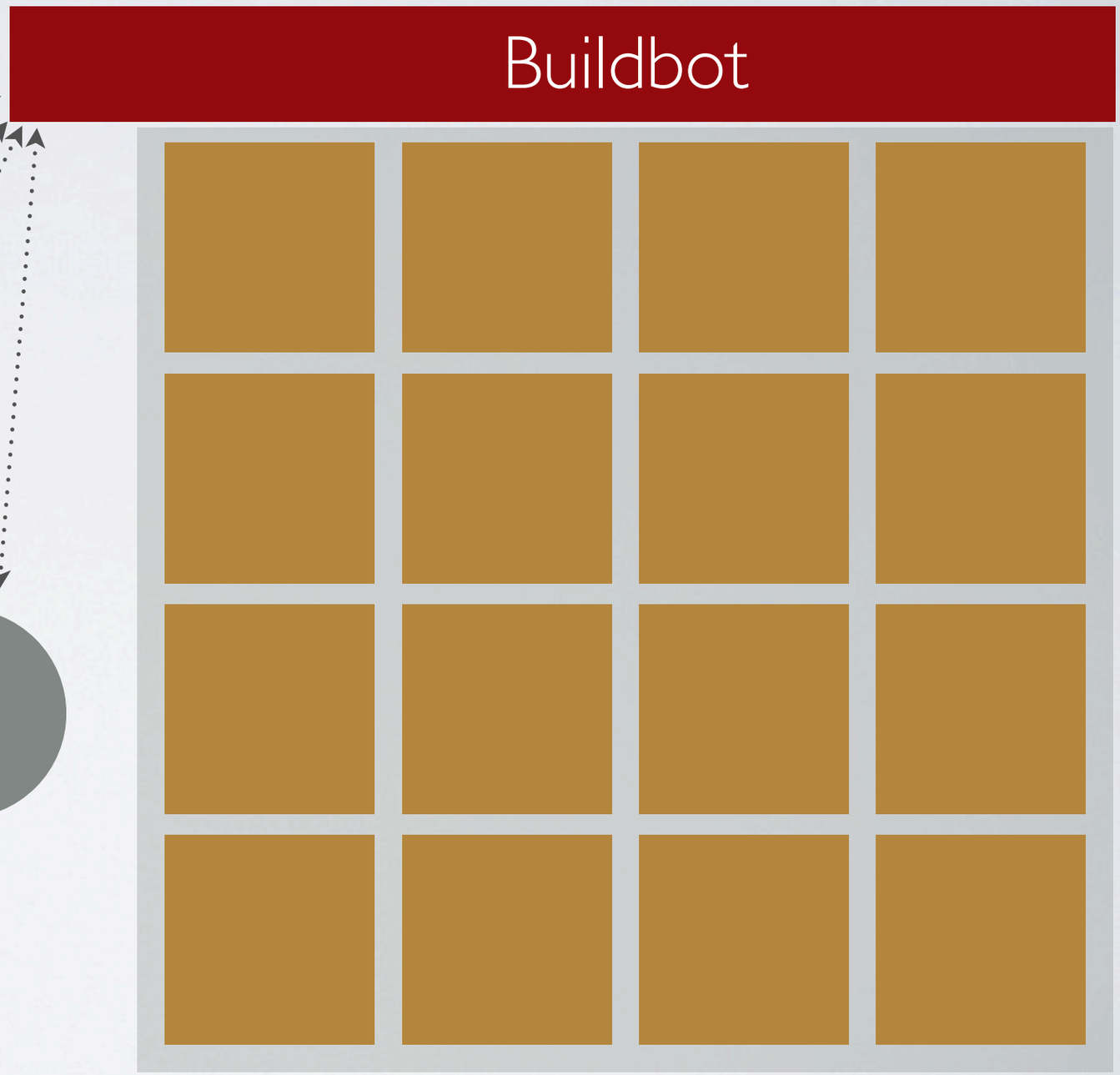

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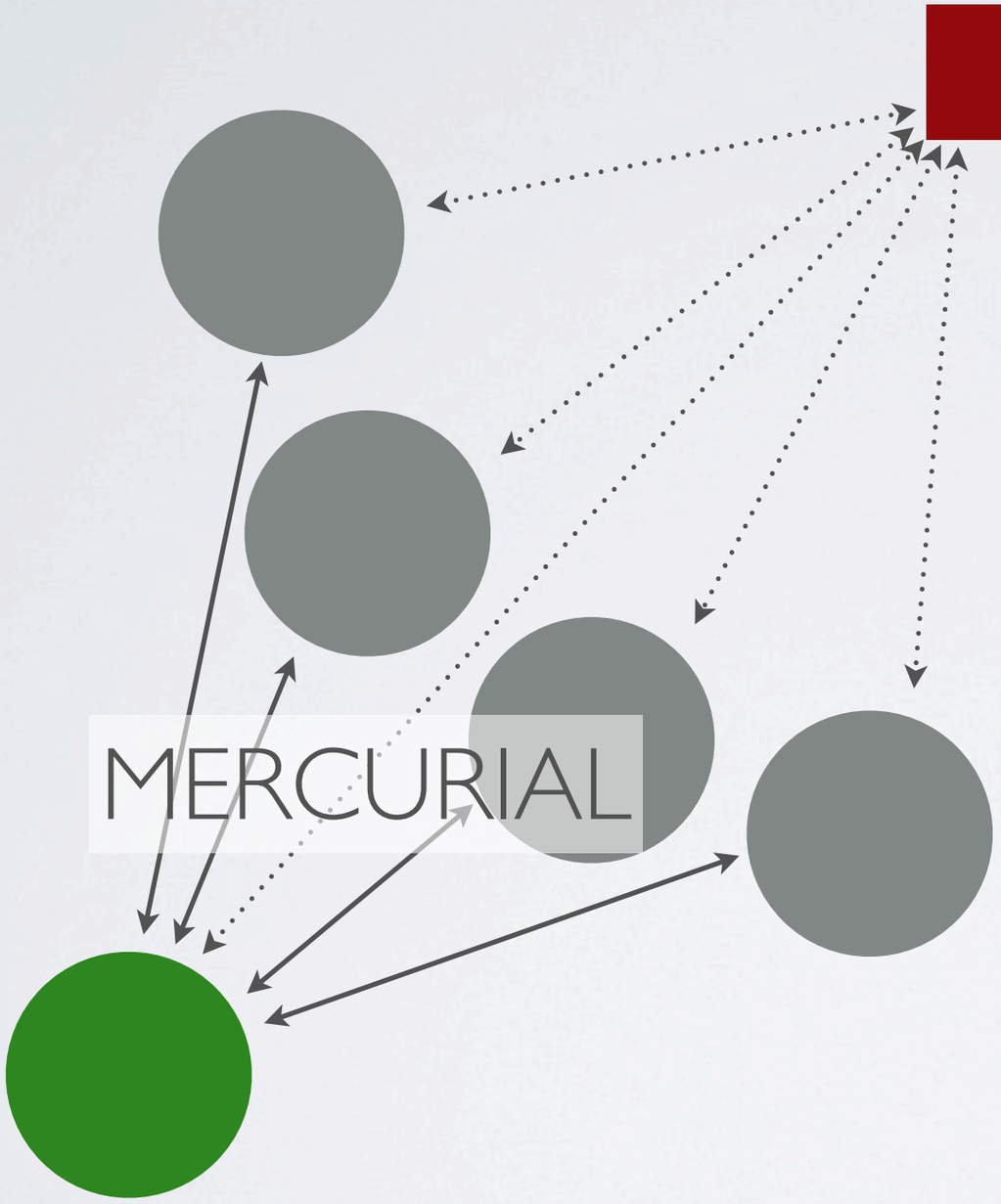
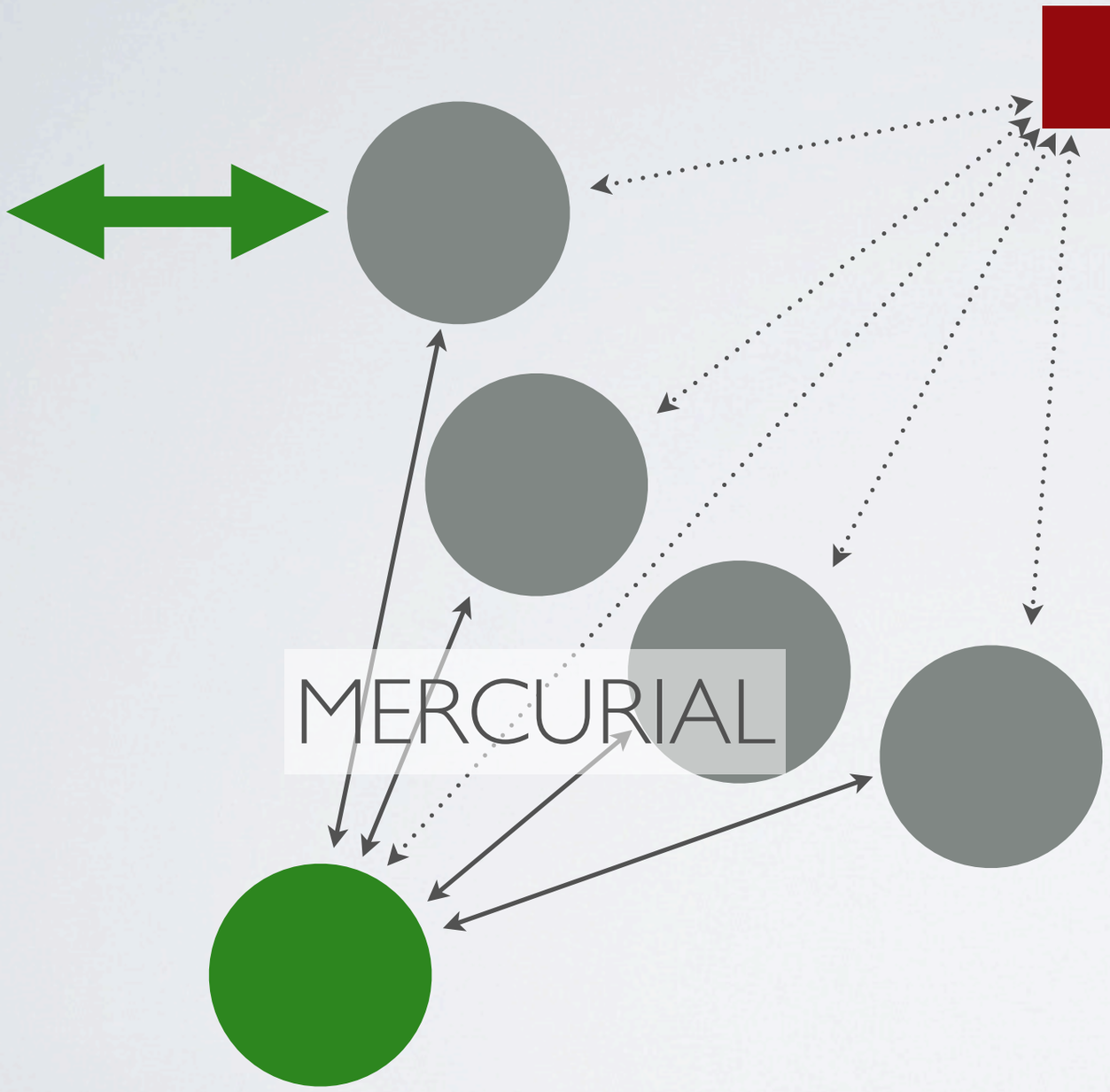


Buildbot

ON COMMIT
NIGHTLY
WEEKELY

Test Farm

QUALITY CONTROL



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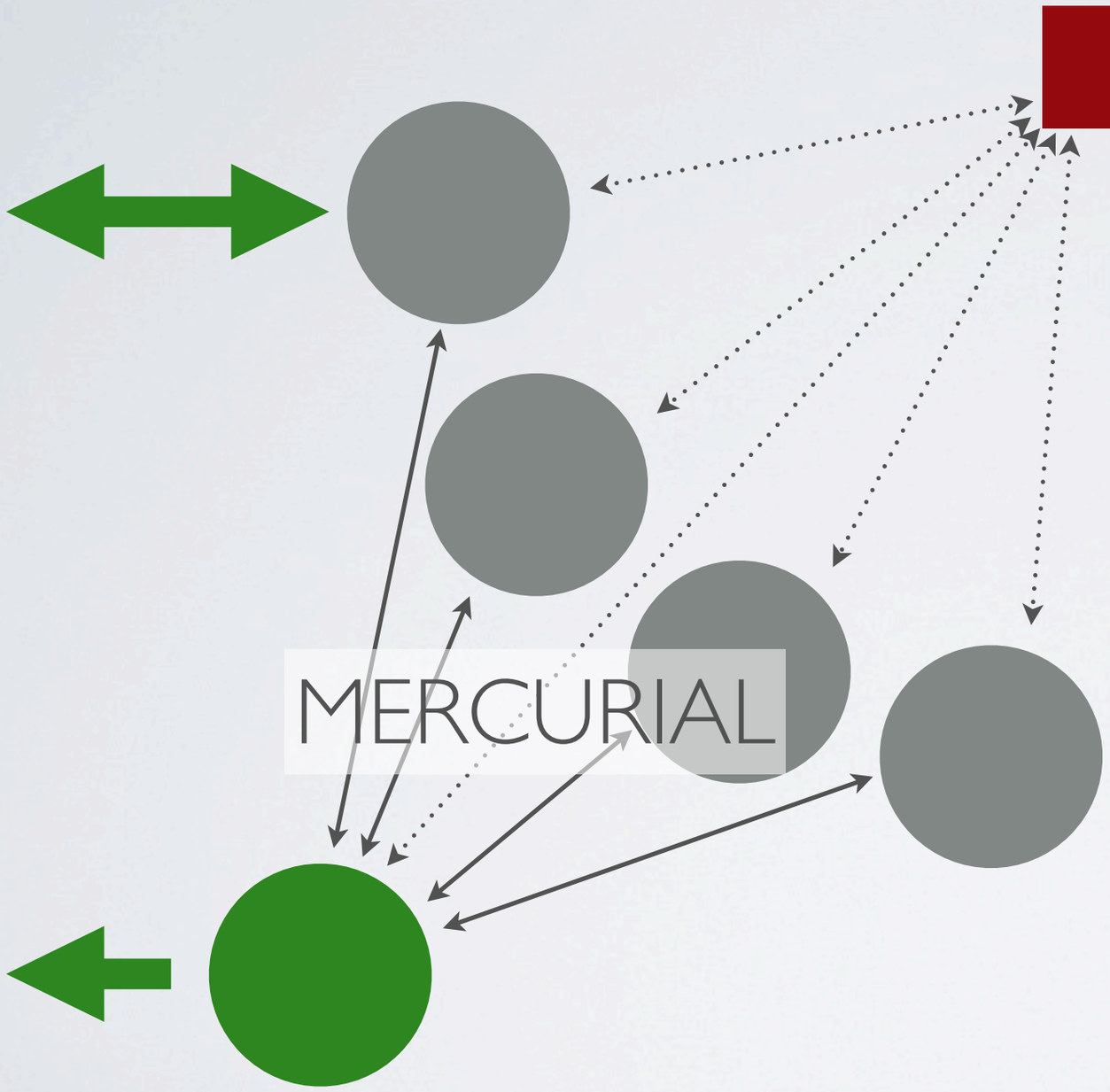

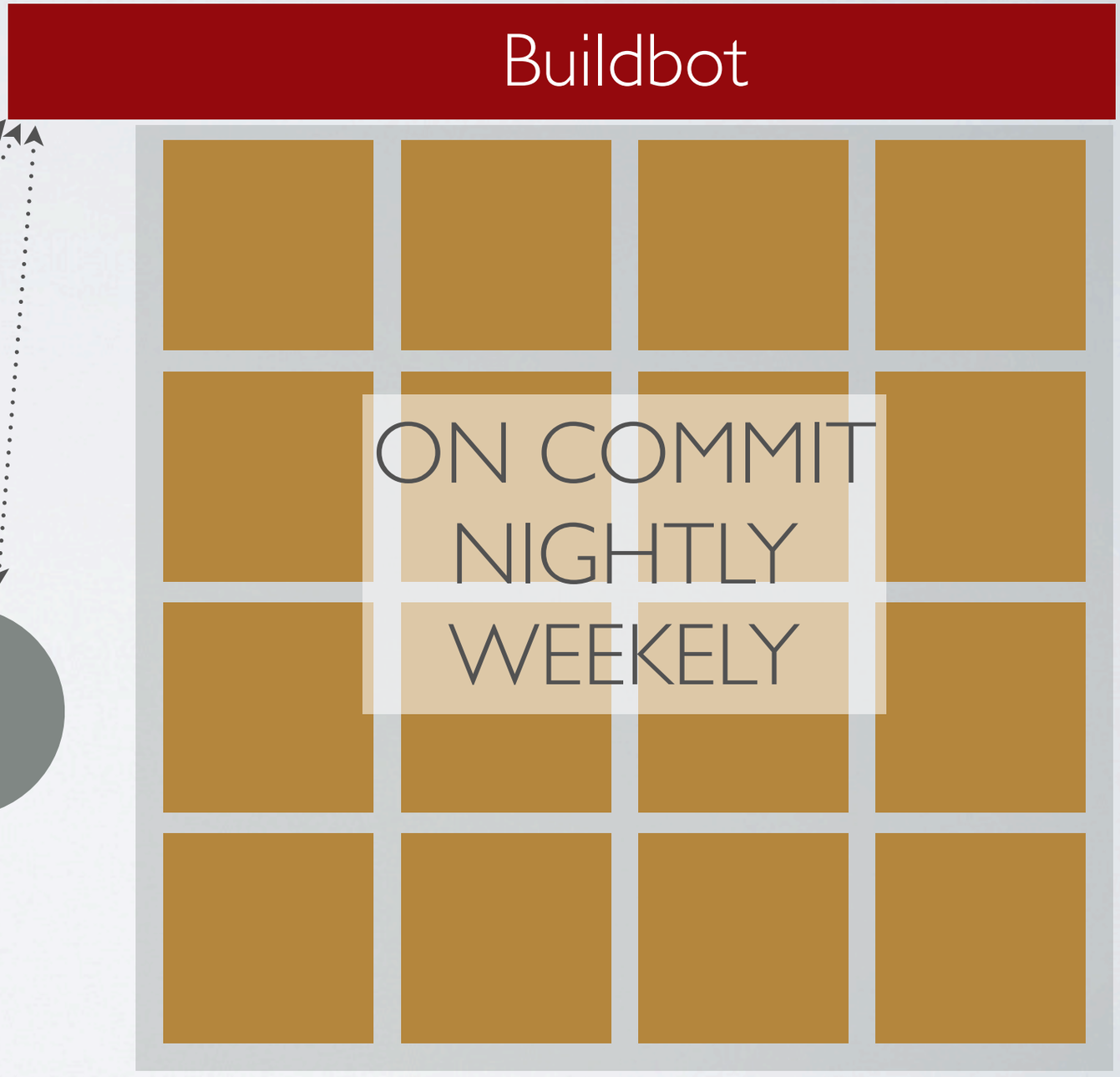

SUMMARY

- Phylogenetic analysis features
- Performance
- Flexibility
- Quality control

ACKNOWLEDGMENTS

- Le Sy Vinh
- Nicholas Lucaroni
- Ilya Bomash
- Lin Hong
- Illya Temkin
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- Dan Janies
- All the users that have tested and provided feedback

ACKNOWLEDGMENTS

- DoD - DARPA
- NSF - CIPRES
- American Museum of Natural History

POY 4

Website:

http://research.amnh.org/scicomp/projects/poy.php

Mailing list:

http://groups.google.com/group/poy4/

Source code and bug reports:

http://code.google.com/p/poy4/

TRANSFORMATIONS

CCTCCAATGATACGTTGAAAGGCGTTTATCGT

TRANSFORMATIONS

CCTCCAATGATACATTGAAAGGCGTTTATCGT

TRANSFORMATIONS

CCTCCA**C**TGATAC**A**TTGAAAGGCGTTTATCGT

TRANSFORMATIONS

CCTCCA**C**TGAAC**A**TTGAAAGGCGTTTATCGT

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CCTCCA**C**TGAAC**A**TTGAA**T**GGCGTTTATCGT

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CCTCCAATGATACGTTGAAAGGCGTTTATCGT

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TRANSFORMATIONS

CCTTGGTTCTCTTTACTGAGTGTCTTGGGCGACCGGCACGTTTACTTTGAAAAAATT

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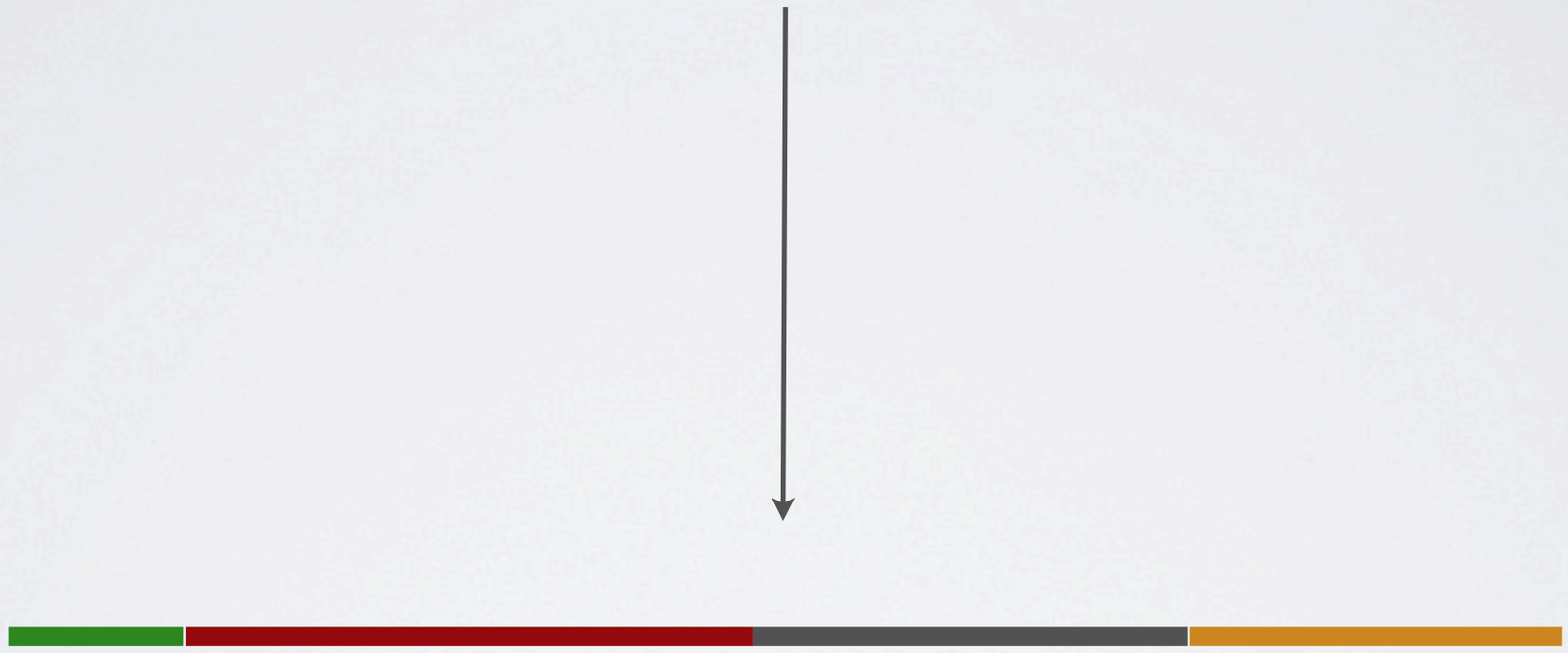
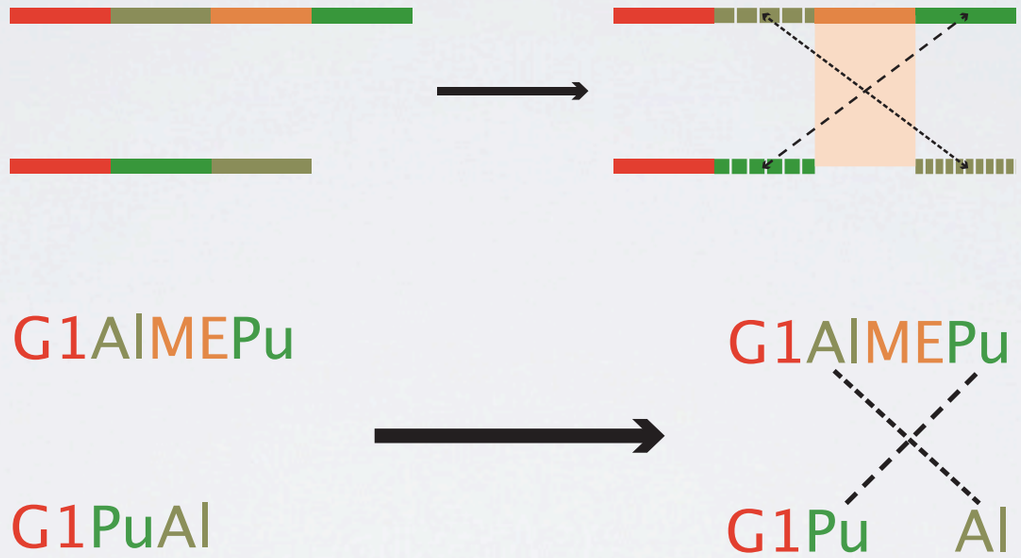
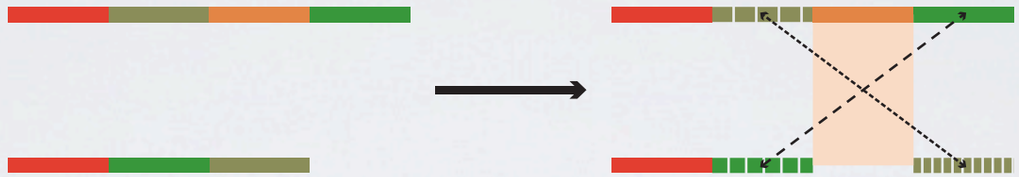


WHAT KIND OF ANALYSES POY SUPPORT?



REARRANGEMENTS



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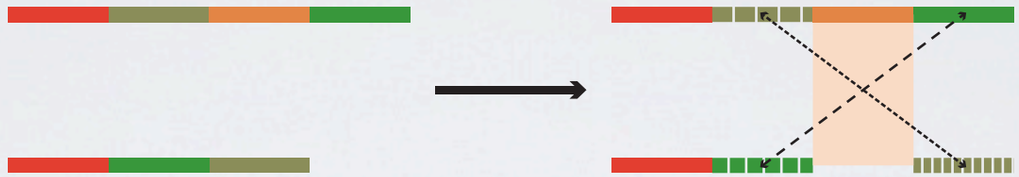

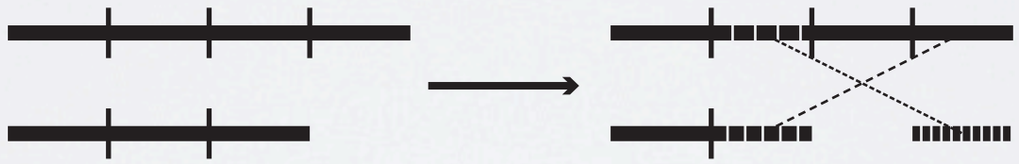

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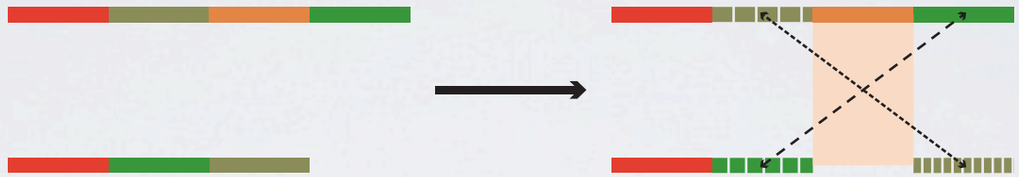

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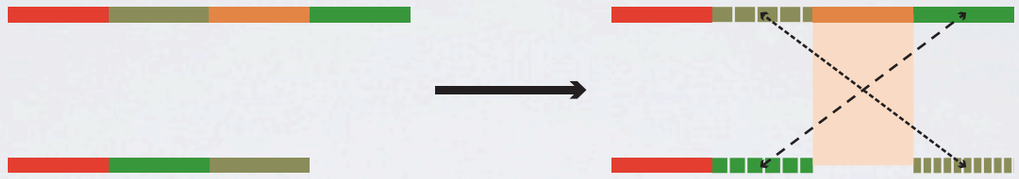

Breakpoint
Inversion
Double Cut and Join