

What comes next? Beyond integration of visual and computational interactive data analysis

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A longitudinal study

- 30 subjects (8 F, 22M)
challenged with enterotoxigenic
E. coli
- 16S profiling of stool samples
one day before, day of and 9
days after
- Diarrhal symptoms recorded
- Ciprofloxacin (antibiotic) given after
symptoms (or 9 days if no
symptoms)

RESEARCH ARTICLE | OPEN ACCESS

Individual-specific changes in the human gut microbiota after challenge with enterotoxigenic *Escherichia coli* and subsequent ciprofloxacin treatment

Mihai Pop, Joseph N. Paulson, Subhra Chakraborty, Irina Astrovskaya, Brianna R. Lindsay, Shan Li, Héctor Corrada Bravo, Clayton Harro, Julian Parkhill, Alan W. Walker, Richard I. Walker, David A. Sack and O. Colin Stine 

BMC Genomics 2016 17:440 | <https://doi.org/10.1186/s12864-016-2777-0> | © The Author(s). 2016

Received: 8 January 2016 | Accepted: 25 May 2016 | Published: 8 June 2016

Pop et al., 2016 BMC Genomics

A longitudinal study

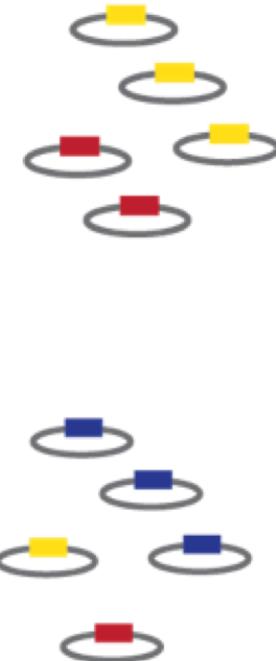
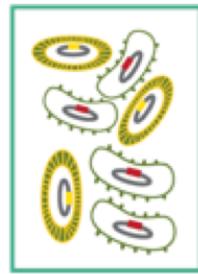
Questions

Is there an association between (pre-challenge) microbiome structure and response to challenge

Is there a time structure in the association between specific taxonomic units and presentation of symptoms

Microbiome survey - data generation

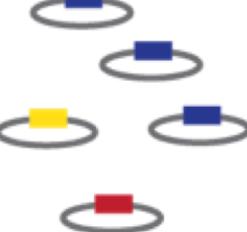
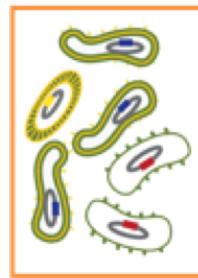
Case



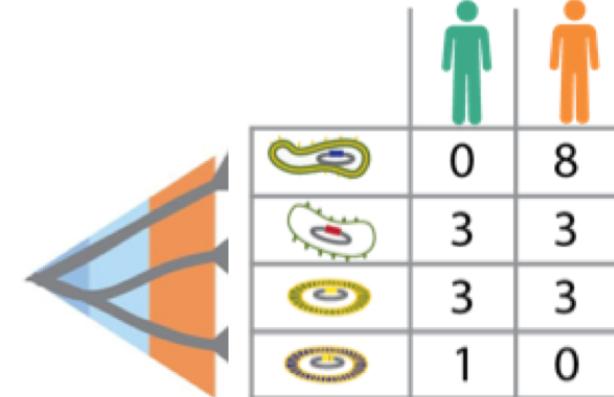
Sequencing



Control



Features with
Hierarchy



This talk

Metaviz

<http://metaviz.org>

Interactive visualization methods for metagenomic data

Features for longitudinal data in development

This talk

metagenomeSeq

<http://bioconductor.org/packages/metagenomeSeq>

Statistical methods for metagenomic data analysis

Including longitudinal data

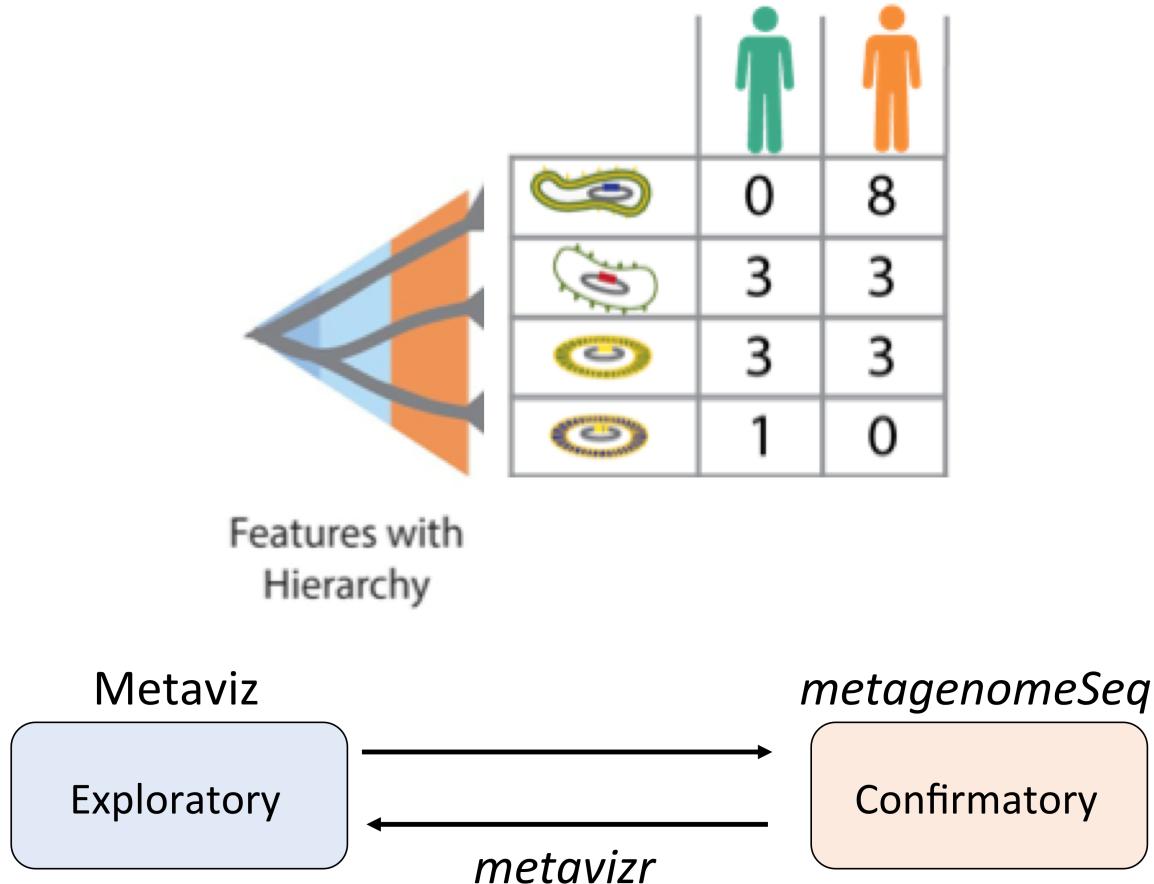
This talk

metavizr

<http://bioconductor.org/packages/metavizr>

Integration between R/Bioconductor infrastructure and interactive
visualization

This talk



Metaviz

Wagner et al., 2018 Nucleic Acids Research

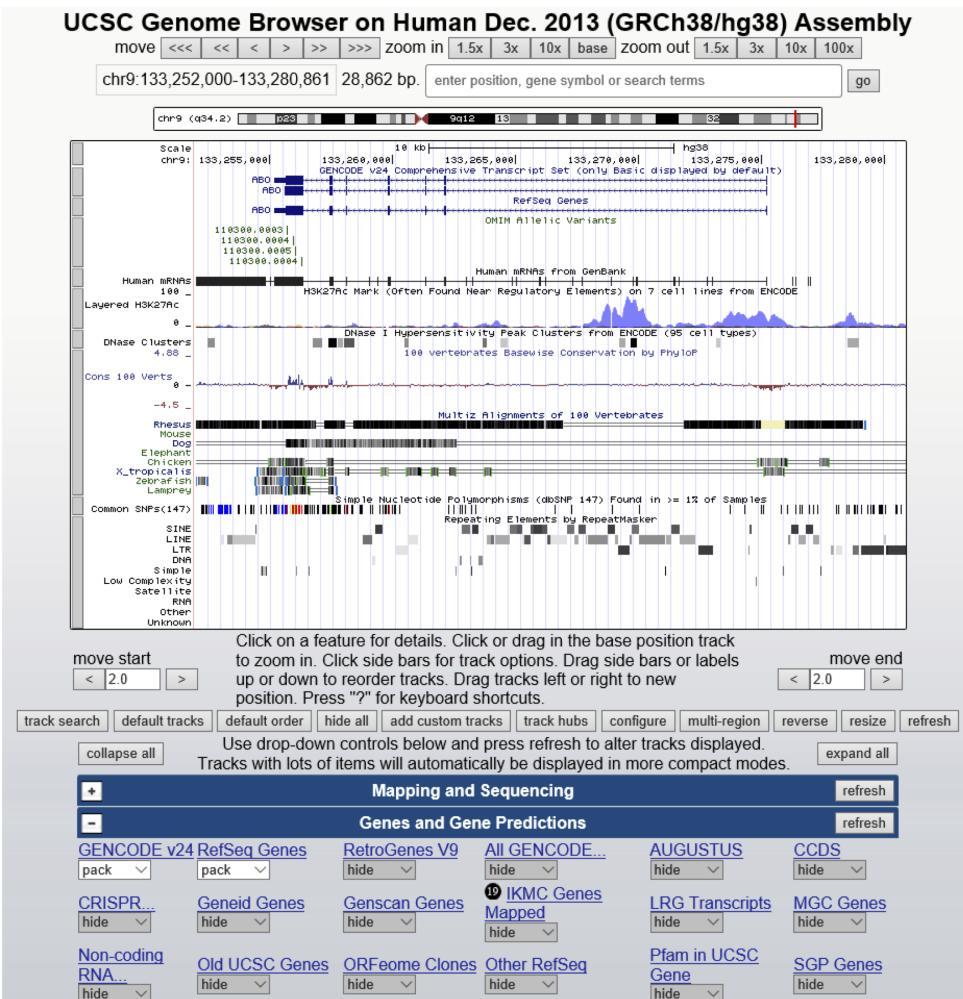
Genome Browsers

Benefits

- Perspective arises naturally to provide quick, intuitive navigation
- Genes and annotations integrated

Track-based

- Sequences and measurements are laid out across screen

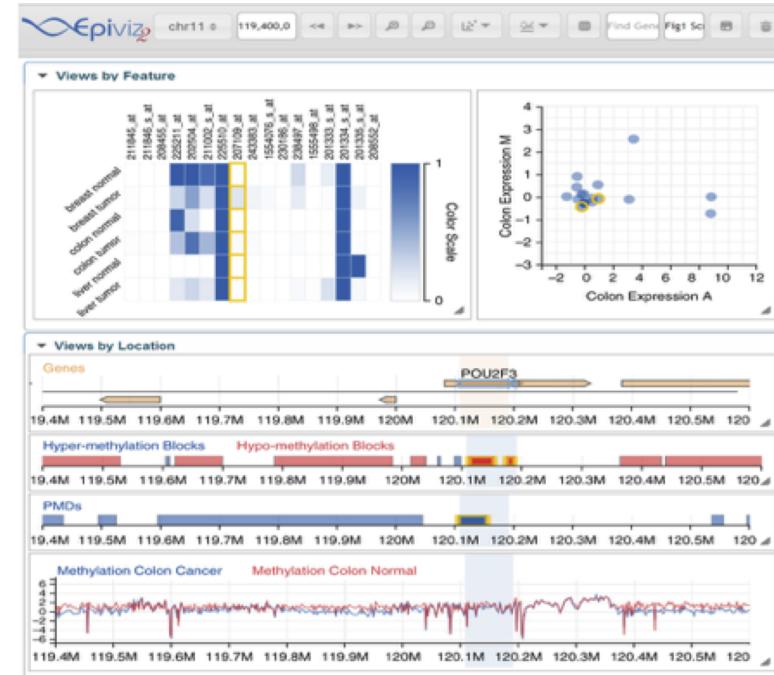


Epiviz: Interactive Visualization for Functional Genomics

Separate track-based and non track-based visualization

Data visualizations updated based on user interaction

Integrated with R/Bioconductor



Chelaru et al. 2014, Nat. Methods

Microbiome data visualization challenges

Features with a hierarchy

- Need to view multiple levels of hierarchy made of thousands of nodes

Need to support population surveys of many samples

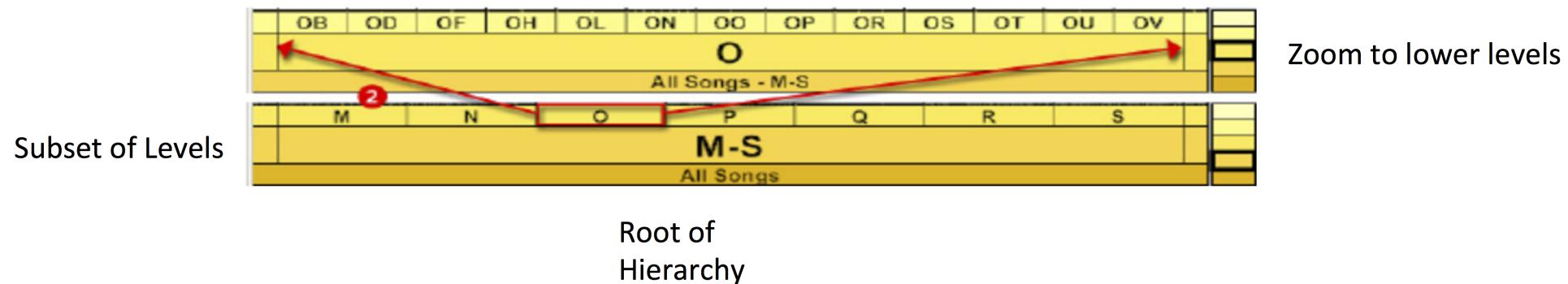
Support quantitative measurements with heatmaps, scatterplots, and boxplots

Hierarchical navigation

Information Visualization technique for hierarchical data

Examine data at different levels and perform feature selection

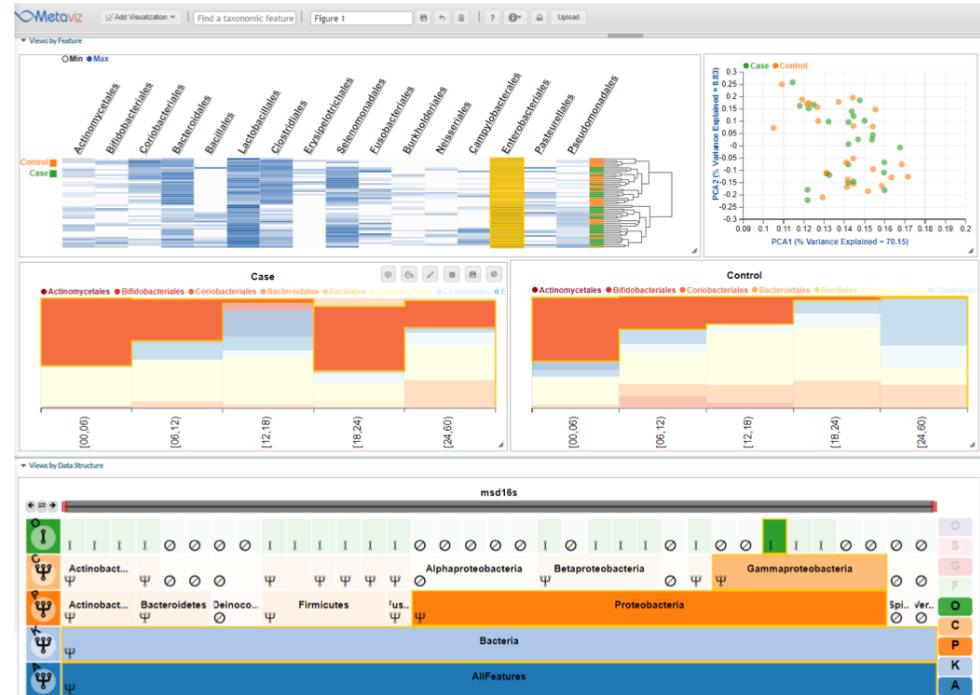
FacetZoom



Metaviz

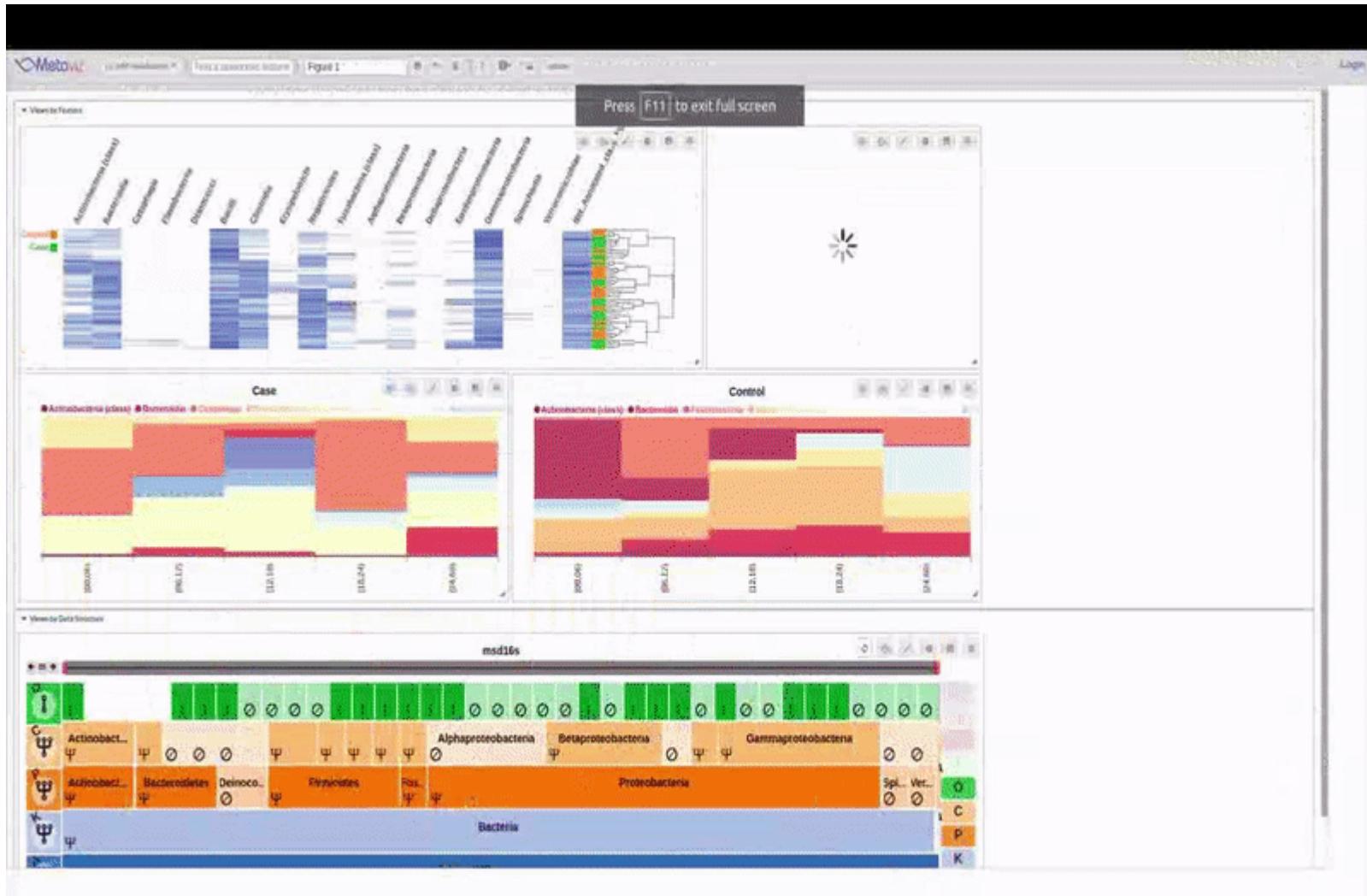
Integrated, interactive taxonomic feature selection

Statistically guided visual analysis
Intuitive navigation for mechanism
for hierarchical metagenomic data



Wagner et al., 2018. Nucleic Acids Research

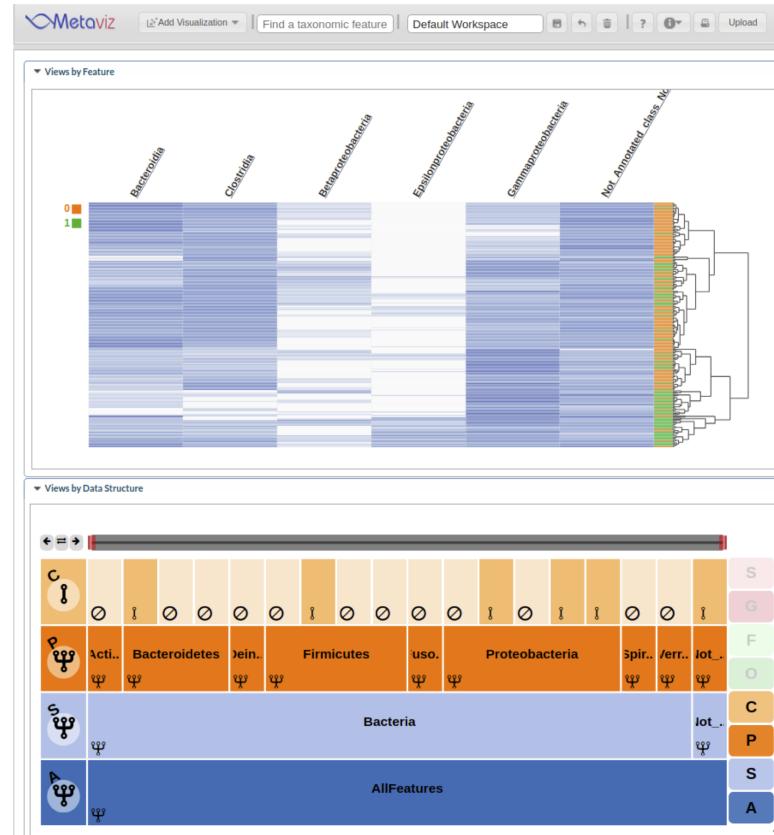
Metaviz



Integration with Bioconductor

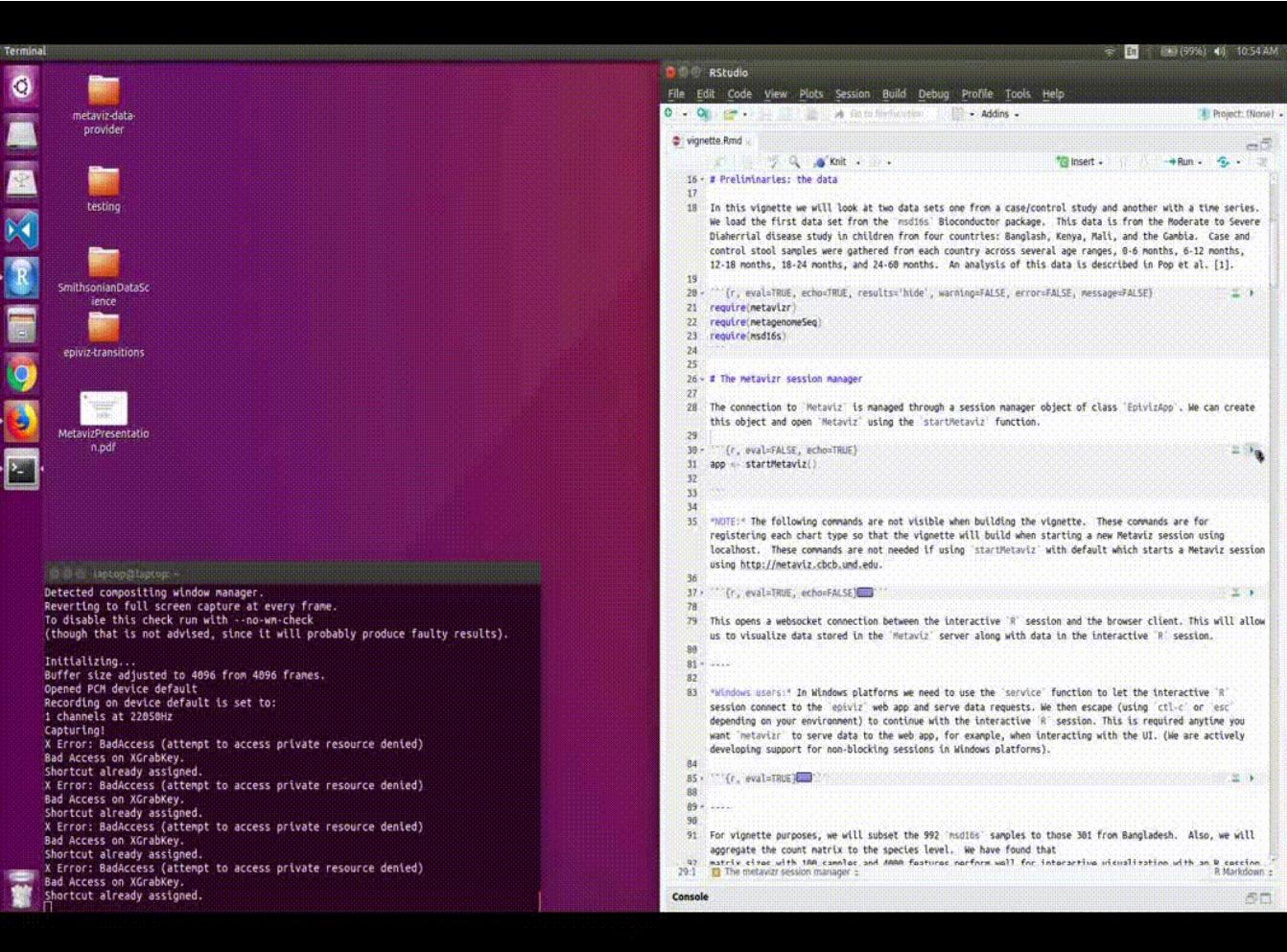
Compute differential abundance
with metagenomeSeq

Explore results through interactive
visualization

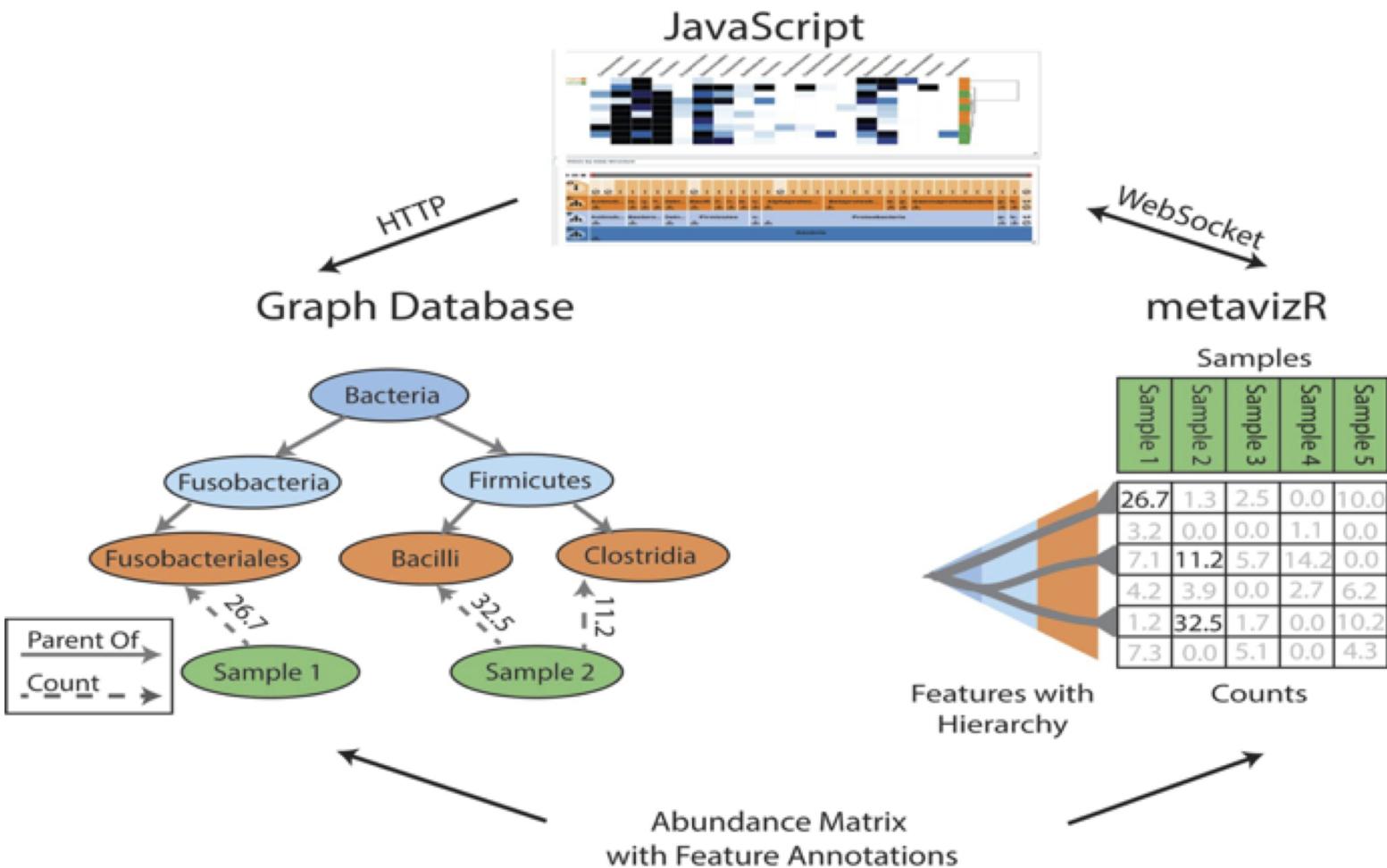


<http://bioconductor.org/packages/metavizr>

Integration with Bioconductor



Architecture



Deployment options

University of Maryland Metagenome Browser (14k metagenomes)

<http://metaviz.cbc.umd.edu>

metavizr

<http://bioconductor.org/packages/metavizr.html>

Local install

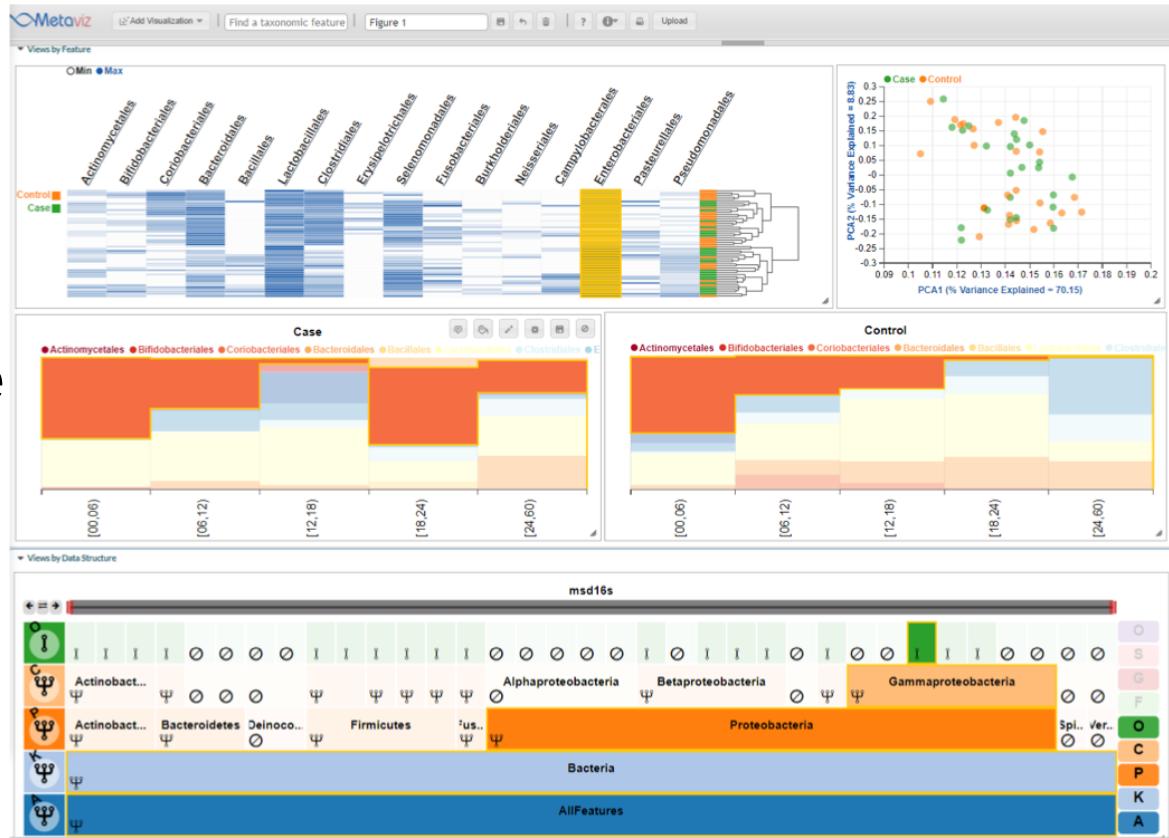
<https://github.com/epiviz/Metaviz>

<https://github.com/epiviz/metaviz-data-provider>

Metaviz for longitudinal designs

How can we effectively display longitudinal data characteristics

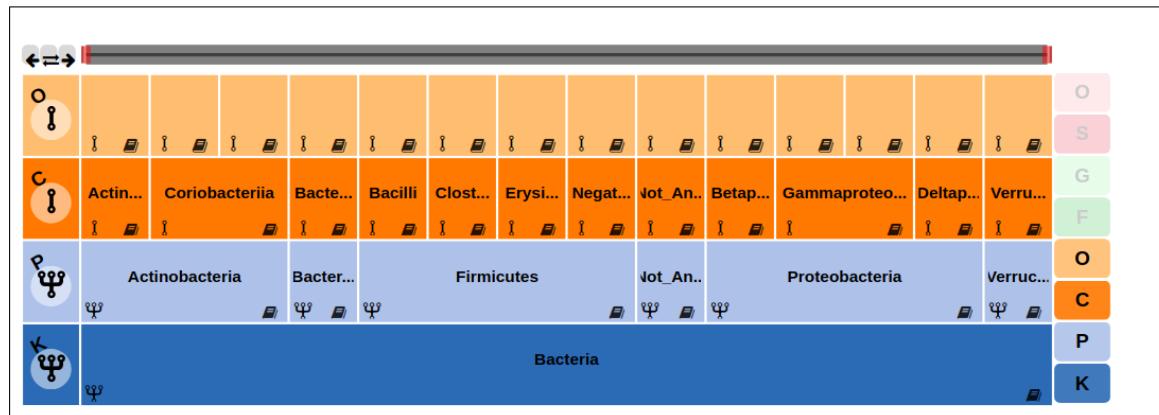
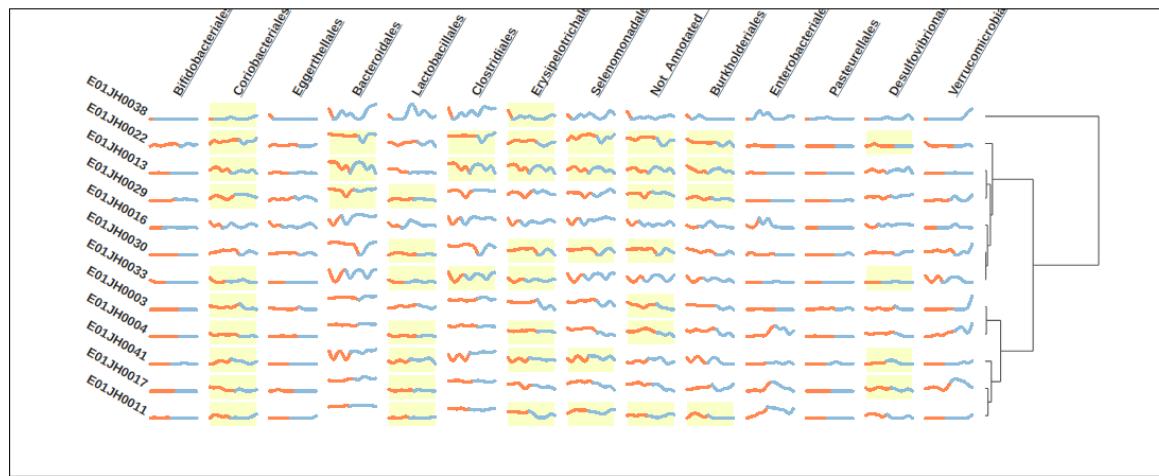
E.g., heatmap is not effective



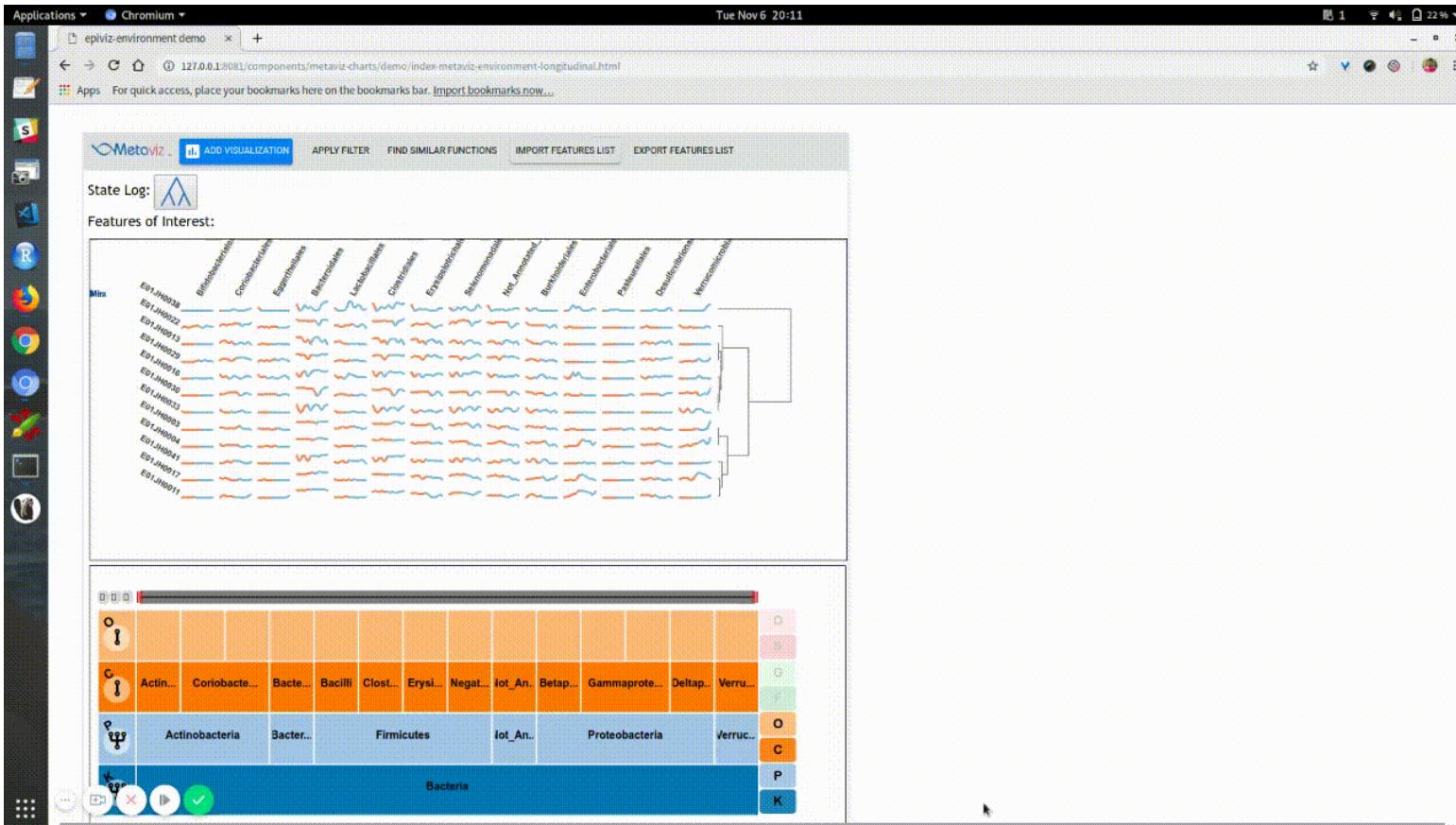
Metaviz for longitudinal designs

How can we effectively display longitudinal data characteristics

Sparkline Matrix



Metaviz for longitudinal designs



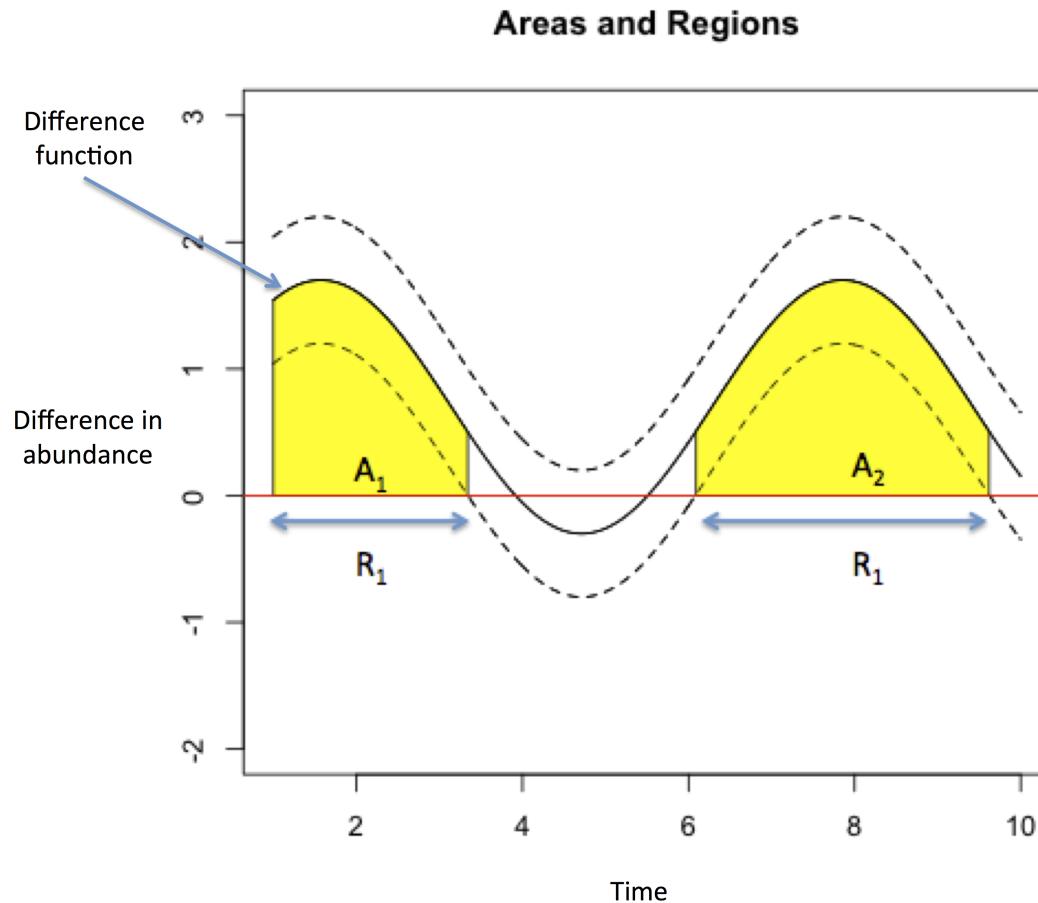
metagenomeSeq

Paulson et al., 2017. biorxiv

Paulson et al., 2013. Nat. Methods

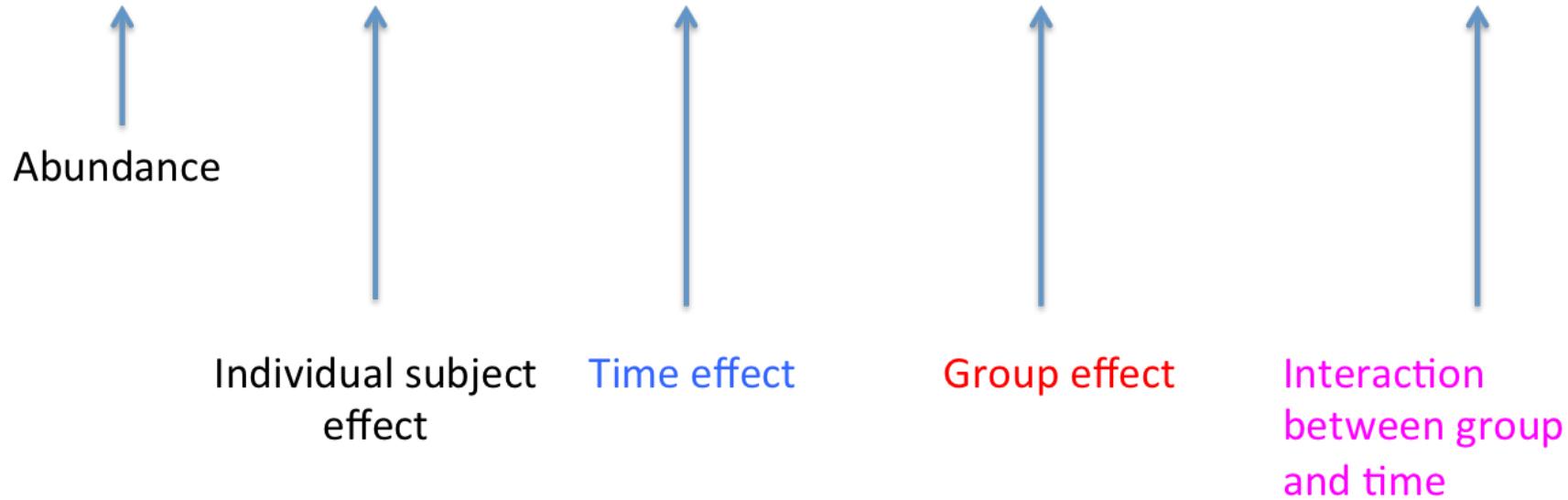
Statistical modeling

Detect intervals of differential abundance between two groups of interest.



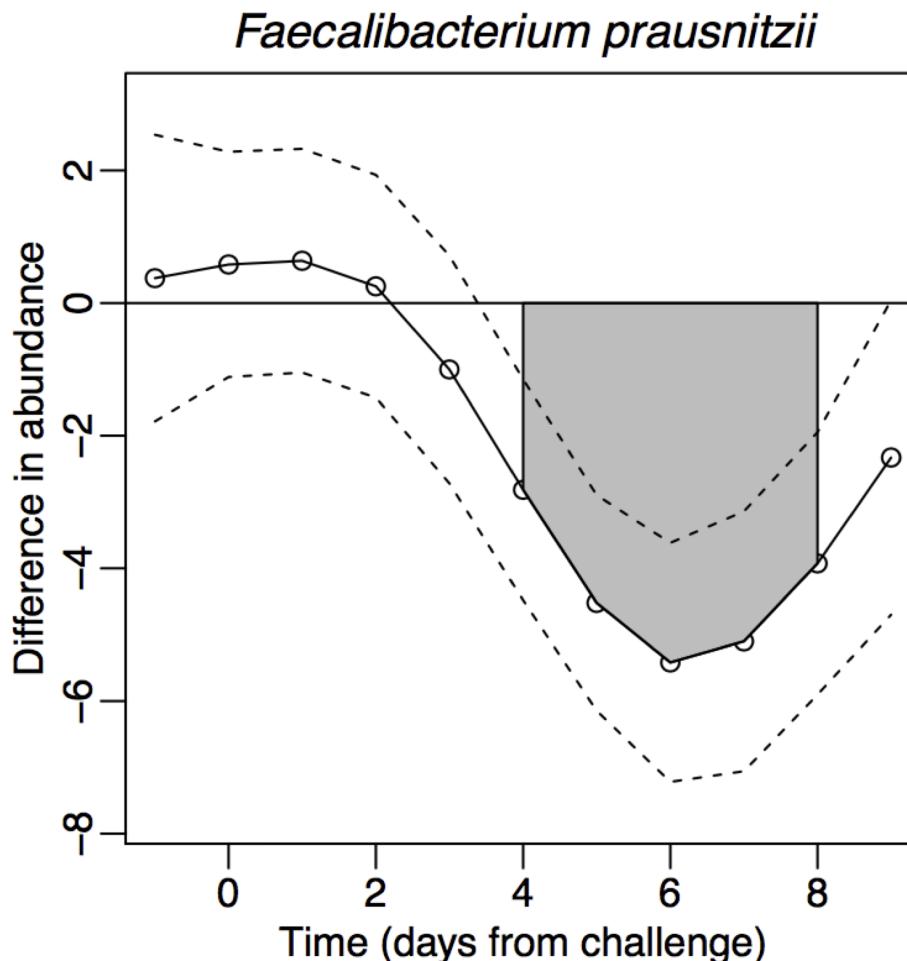
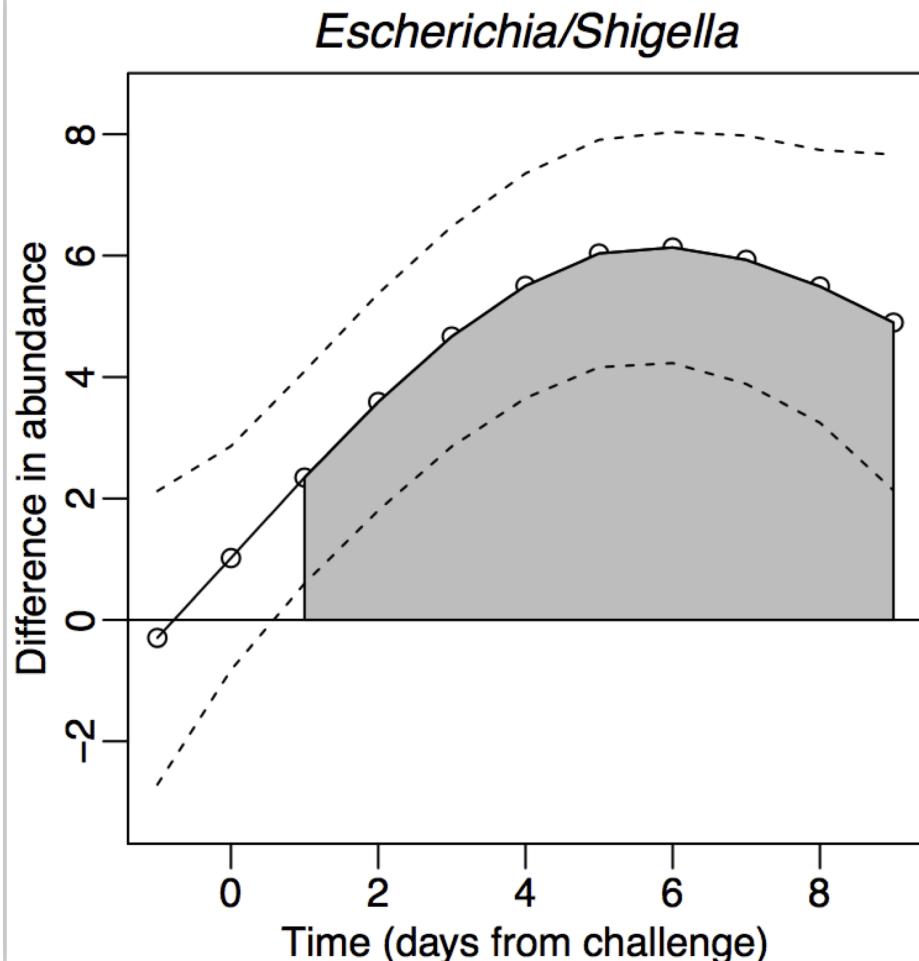
Statistical modeling

$$f_i(t, x_k) = \beta^T x_k + f_1(t) + f_2(I\{k \in i\}) + f_{12}(t, I\{k \in i\})$$



Fit using smoothing-spline ANOVA (gss package)

Statistical modeling

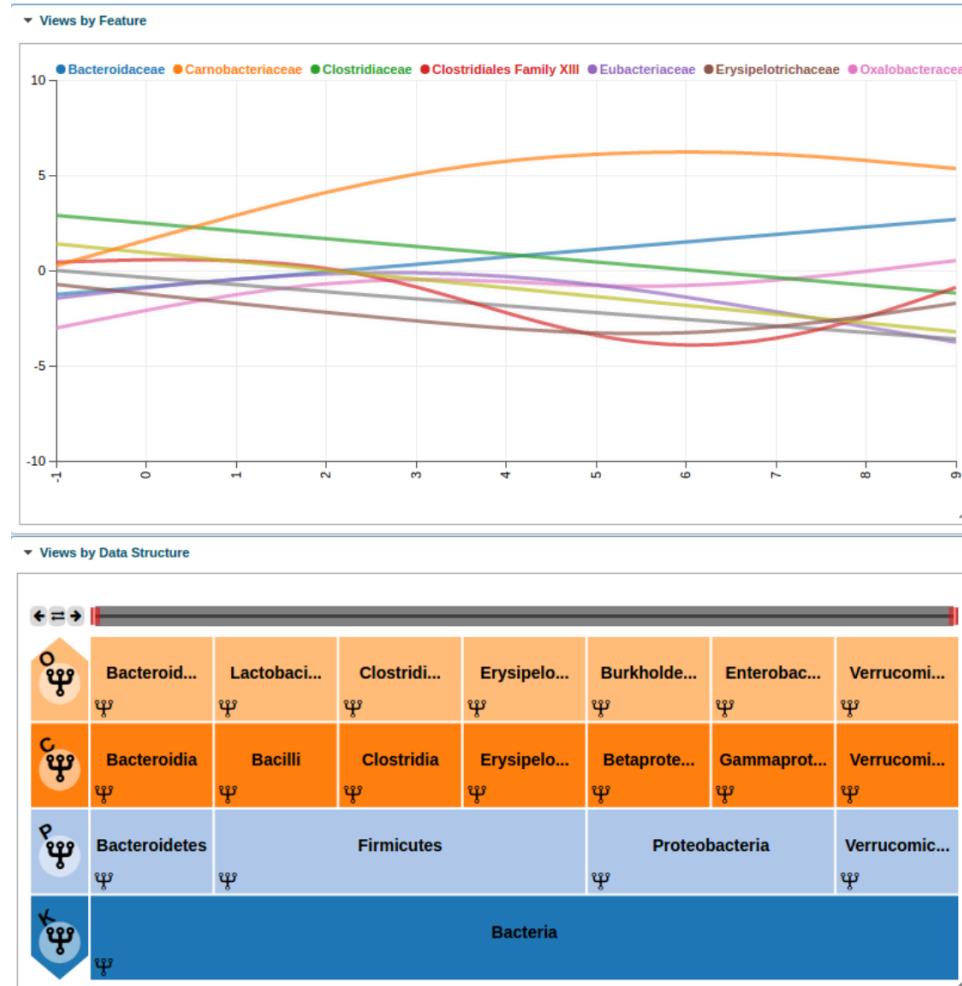


metavizr

<http://bioconductor.org/packages/metavizr>

Interactivity with spline model

```
library(metavizr)  
  
library(etec16s)  
  
data(etec16s)  
  
app <- startMetaviz()  
  
app$plot(etec16, type="TimeSeries",  
        formula=abundance~id+AntiG  
                  time*AnyDayDiarrhea  
)
```



Interactivity with spline model

Inference depends on model parameter (smoothness of function)

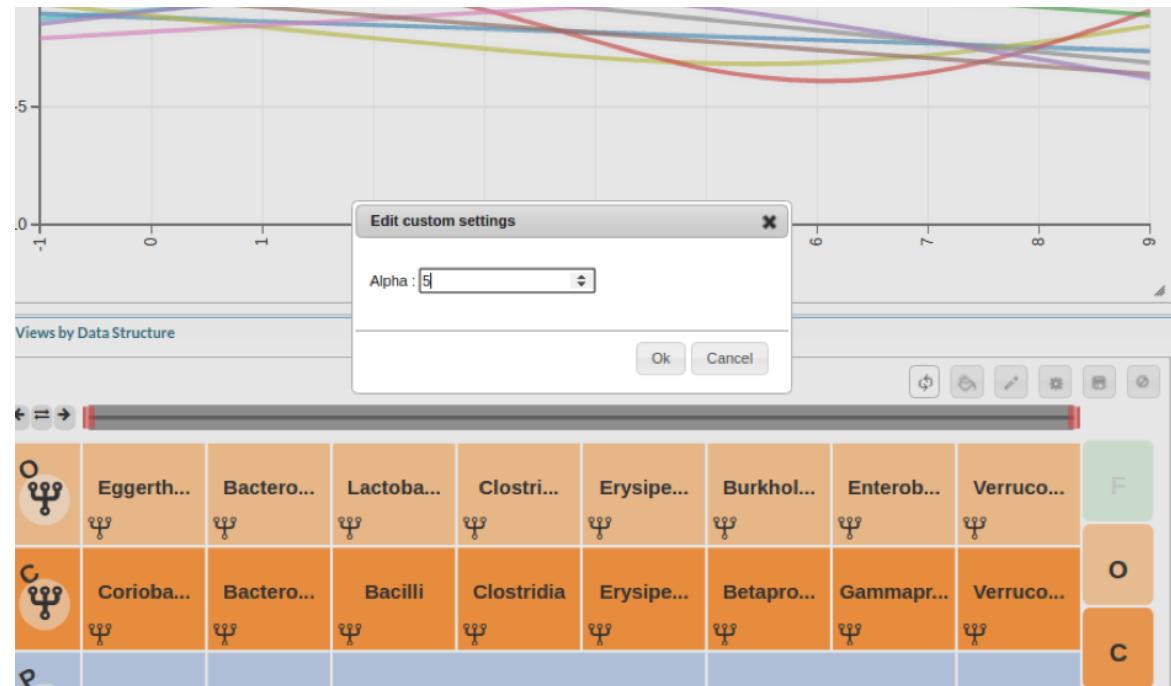
Use interactivity to explore sensitivity



Interactivity with spline model

Inference depends on model parameter (smoothness of function)

Use interactivity to explore sensitivity



Interactivity with spline model

Inference depends on model parameter (smoothness of function)

Use interactivity to explore sensitivity

High smoothness penalty



Interactivity with spline model

Inference depends on model parameter (smoothness of function)

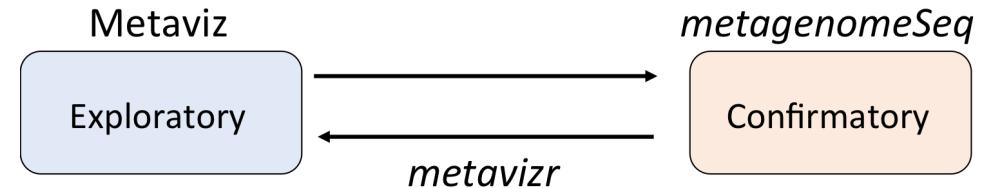
Use interactivity to explore sensitivity

Low smoothness penalty



Statistically guided visualization

Let's revisit the Data Analysis modes



How can we make the connection
between two modes of analysis
tighter?

Statistically guided visualization

One idea: statistically guided visual exploration via *proactive computation*

Back to Epiviz: epigenetic regulation of gene expression across multiple tumor types (Timp et al. 2016)



Statistically guided visualization

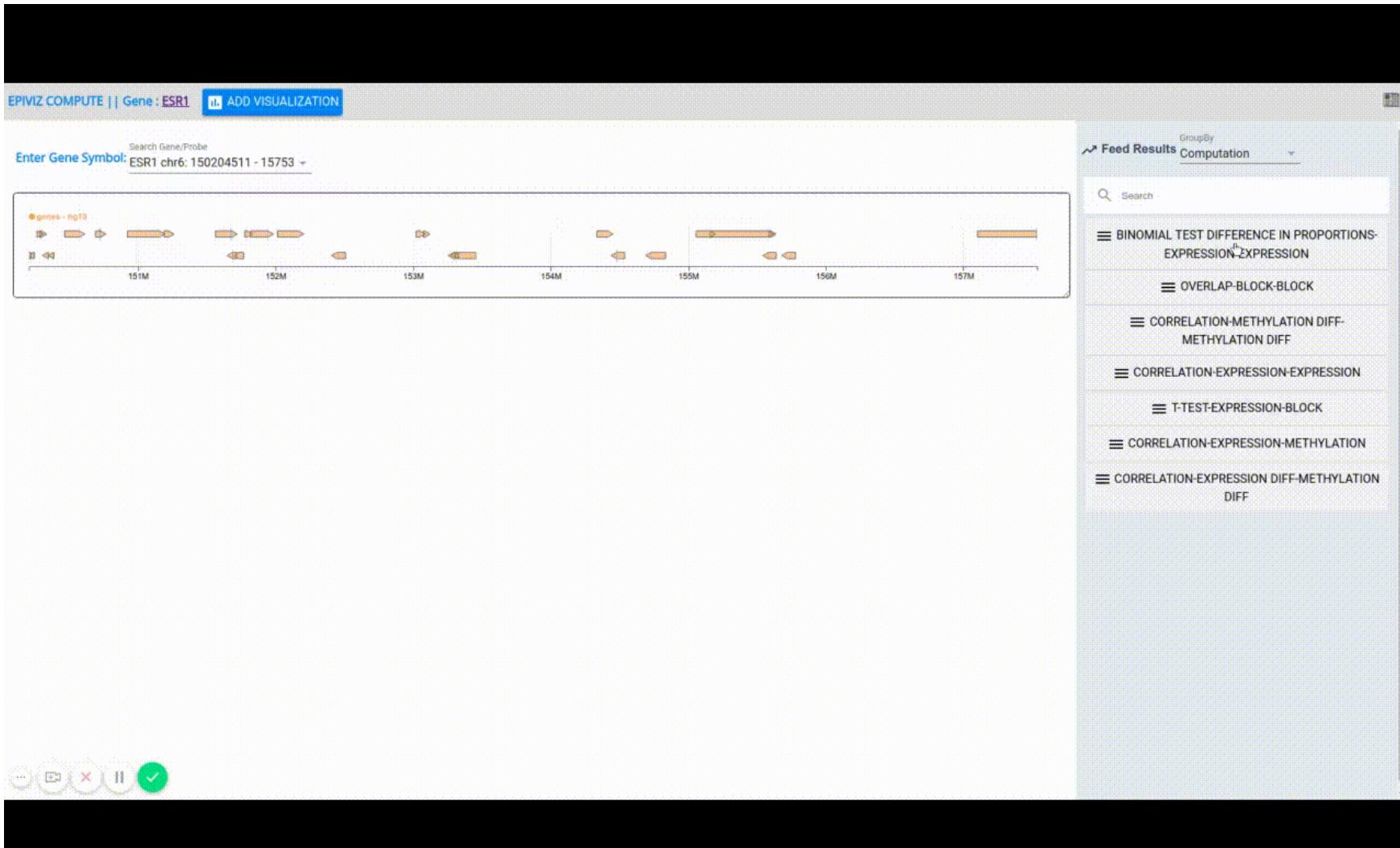
One idea: statistically guided visual exploration via *proactive computation*

Analysis runs in background
(proactive computation)

"Interesting results" presented to user, guides exploration of data underlying result.



Statistically guided visualization

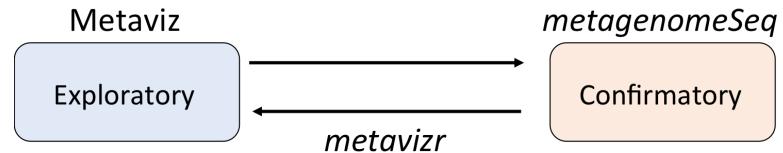


Interactive Data Analysis

In general, how do we support interactive data analysis?

Workflow construction: keep pieces small, we like to do that for *reusability*, now let's do it for *data reflection*.

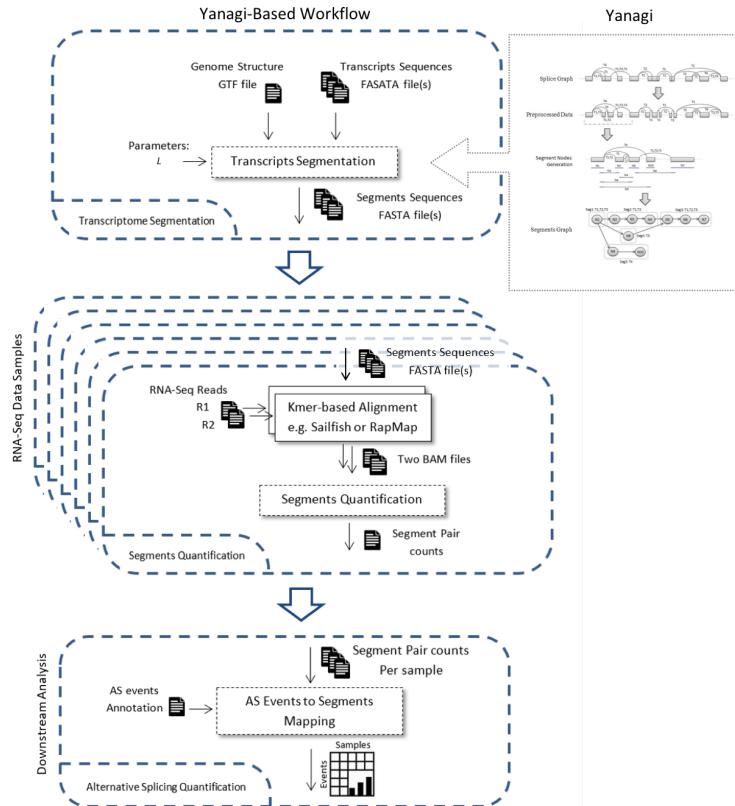
What is the "sufficient statistic" my tool produces that a user can interact with?



Interactive Data Analysis

One example: segment-based analysis of RNA-seq data

Transcript quantification as sufficient statistic?

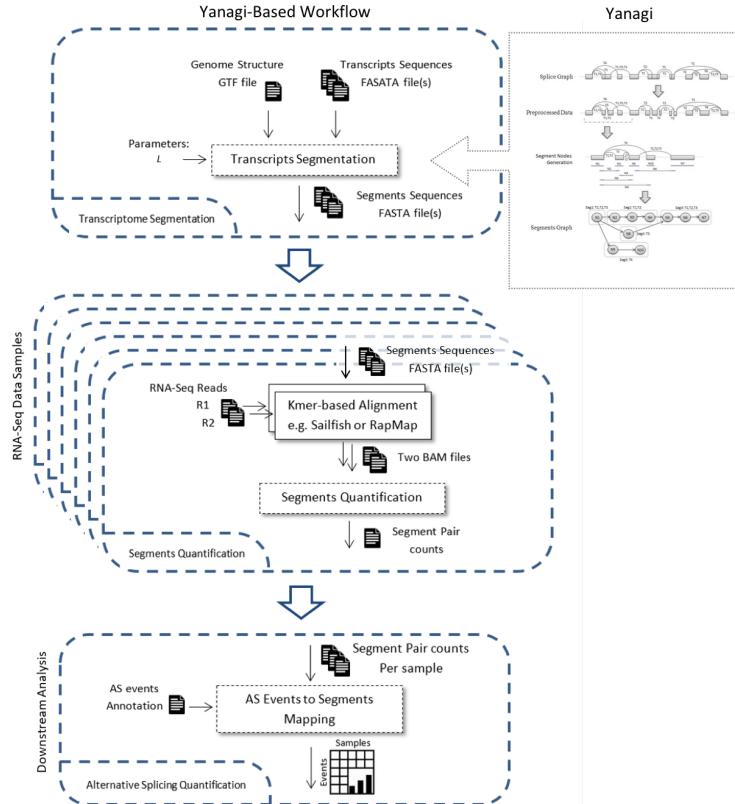


Interactive Data Analysis

One example: segment-based analysis of RNA-seq data

No. There is (pseudo)-counting, and there is quantification.

Can we produce a "sufficient statistic" we can interact with *before* quantification.

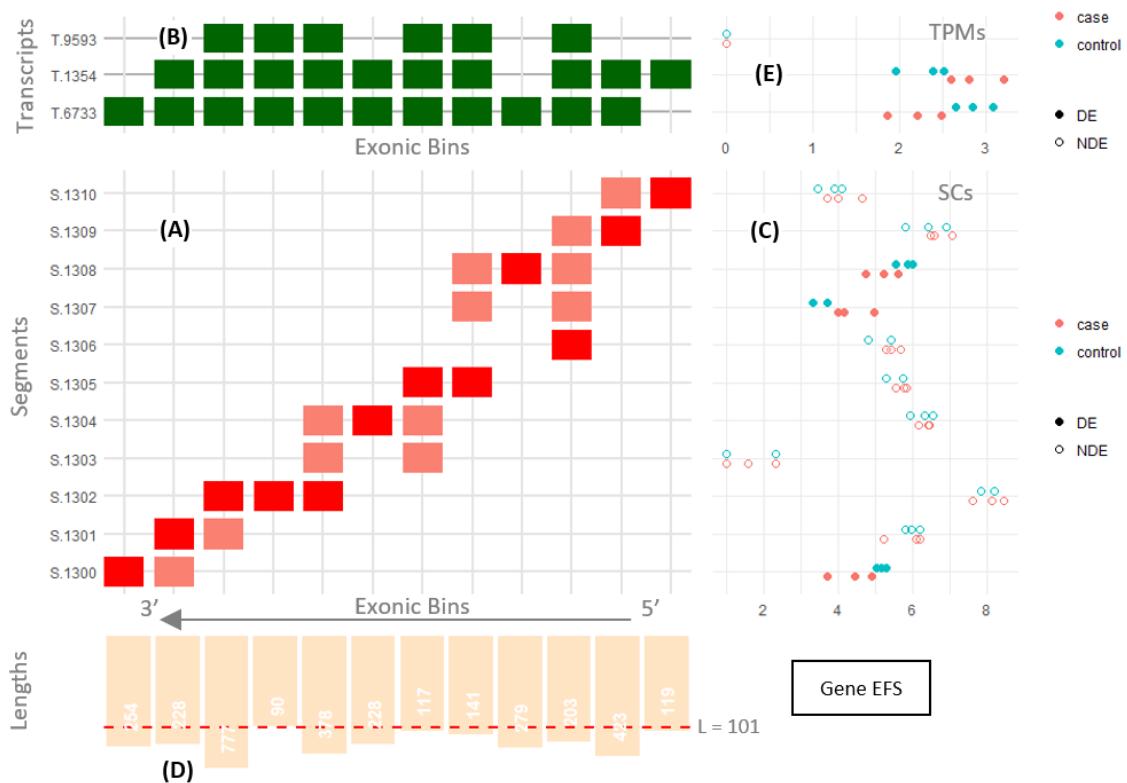


Interactive Data Analysis

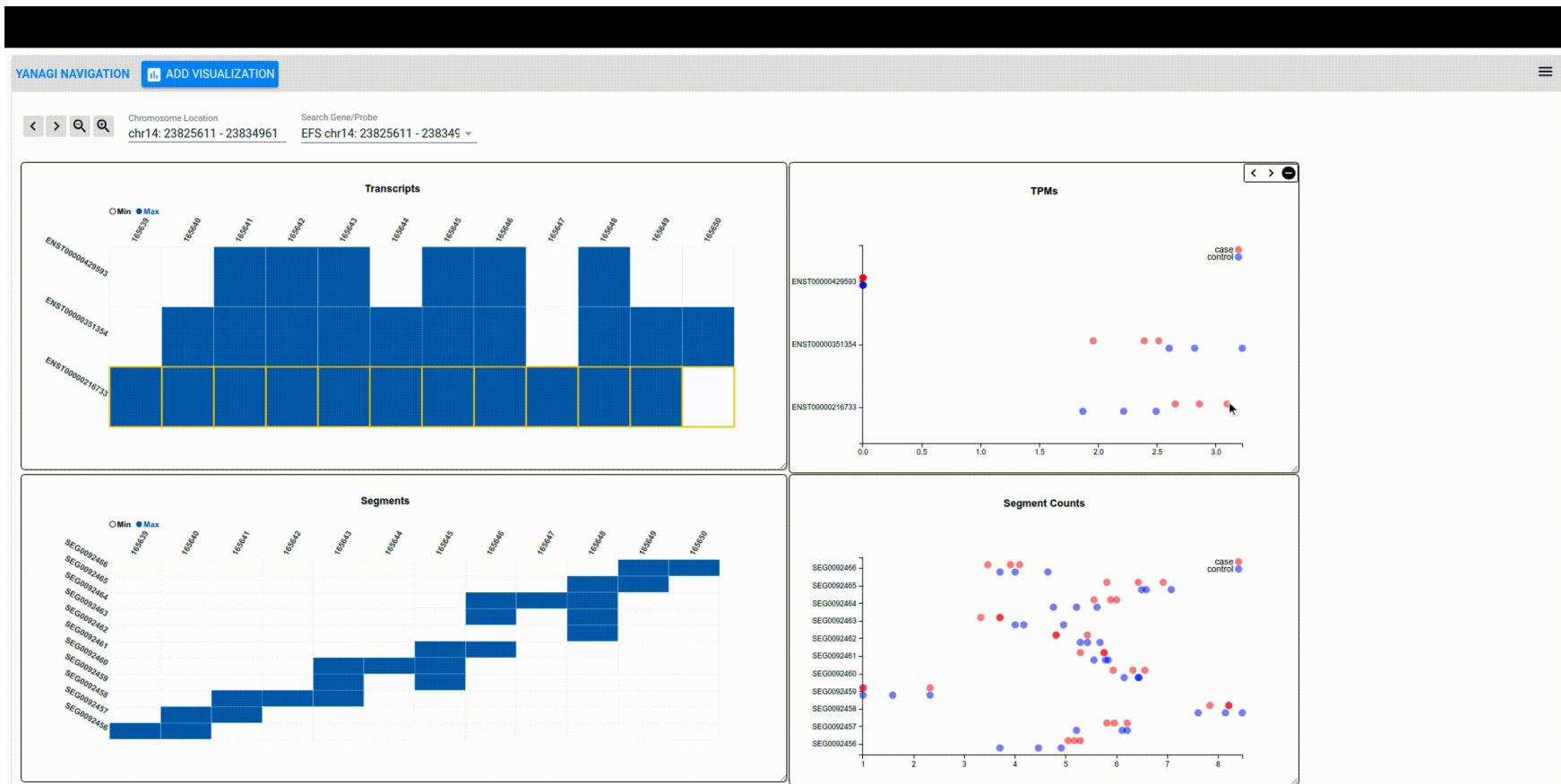
One example: segment-based analysis of RNA-seq data

Segment-counts as the "sufficient statistic"

Gunady et al. Yanagi (2018) biorxiv



Interactive Data Analysis



Summary

Exploration of hierarchical features (FacetZoom)

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Design for longitudinal experimental structure (SparklineMatrix)

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Interact with data and statistical model via visualization
(metavizr)

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Exploration of hierarchical features (FacetZoom)

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Interact with data and statistical model via visualization
(metavizr)

Design your tools with data reflection, build IDA tools around that

Acknowledgements

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More info

<http://epiviz.org>

<http://www.hcbravo.org>