

Digital alternatives to DDH

“ *Investigators are encouraged to propose new [...] genomic methods [...] provided [...] a sufficient degree of congruence between the technique used and DNA:DNA reassociation.*

— Stackebrandt et al. 2002

most likely consequence if not fulfilled:

⇒ inconsistencies in microbial taxonomy

GGDC: a digital DDH alternative



GGDC

Genome-to-Genome Distance Calculator



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[GGDC 1.0](#)

[GGDC 2.0](#)

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Calculate distances and DDH estimates with GGDC 2.0

GGDC 2.0 is an updated and enhanced version with improved DDH-prediction models and additional features such as confidence-interval estimation. To the best of our knowledge, it is the only digital DDH method that provides this feature. Of all genome-based methods we are aware of, GGDC 2.0 yields the highest correspondence to wet-lab DDH (without sharing DDH's drawbacks). Details are described in our [BMC Bioinformatics study](#).

Hint: If you need advice on the following form fields, you can simply hover your mouse pointer over the "Help" areas.

Form

1st step: Choose the alignment method for finding intergenomic matches

GGDC 2.0 BLAST+

Calculate confidence interval for DDH prediction based on bootstrap replicates

[Help](#)

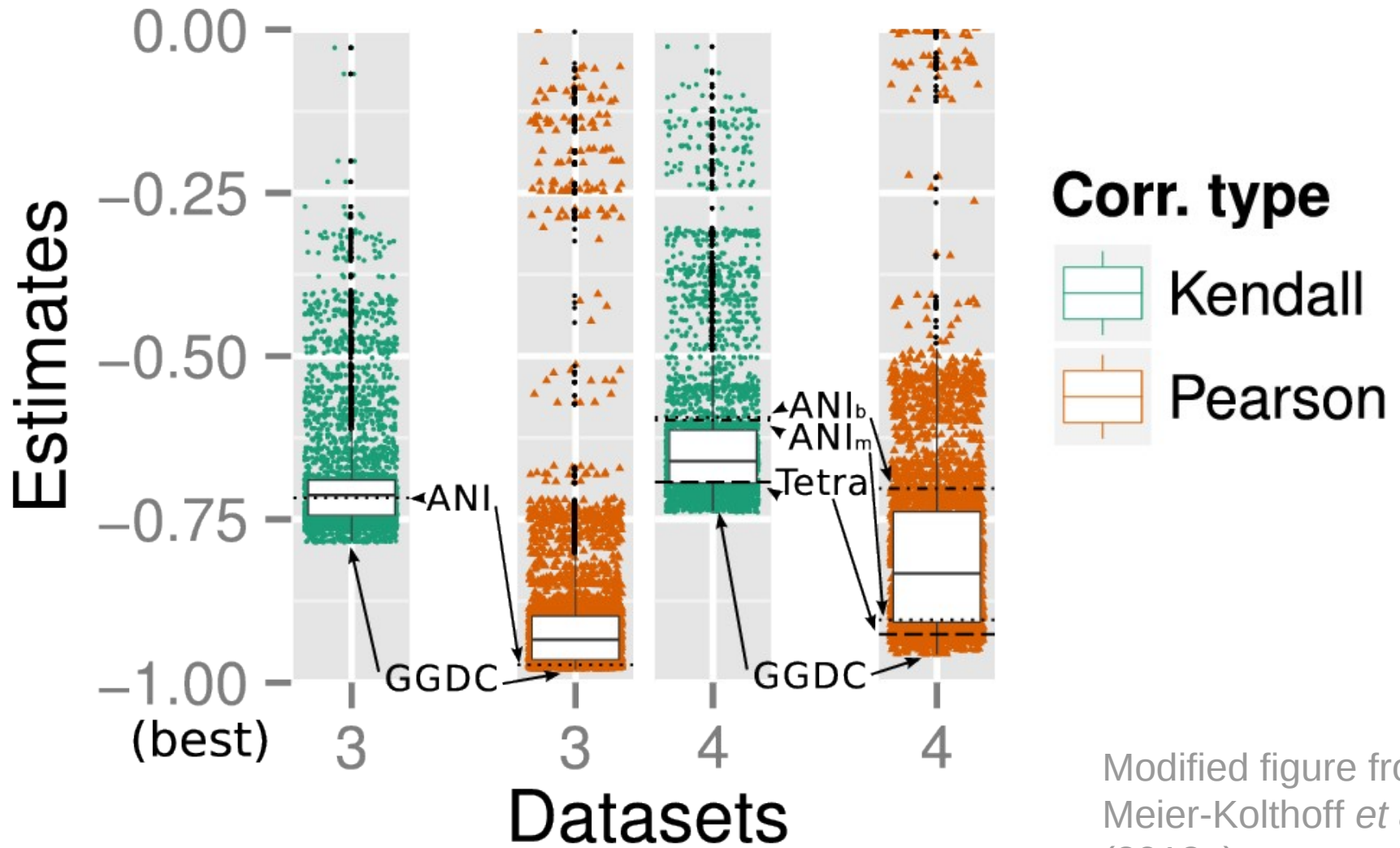
2nd step: Choose the query genome

<http://ggdc.dsmz.de>

The GGDC builds upon the GBDP approach

- GBDP established ten years ago (Henz *et al.*, 2004)
- originally devised for assessing genome-based phylogenies
- one of the most accurate phylogenomic methods (Patil and McHardy, 2013)

GGDC yields highest correspondence to wet-lab DDH

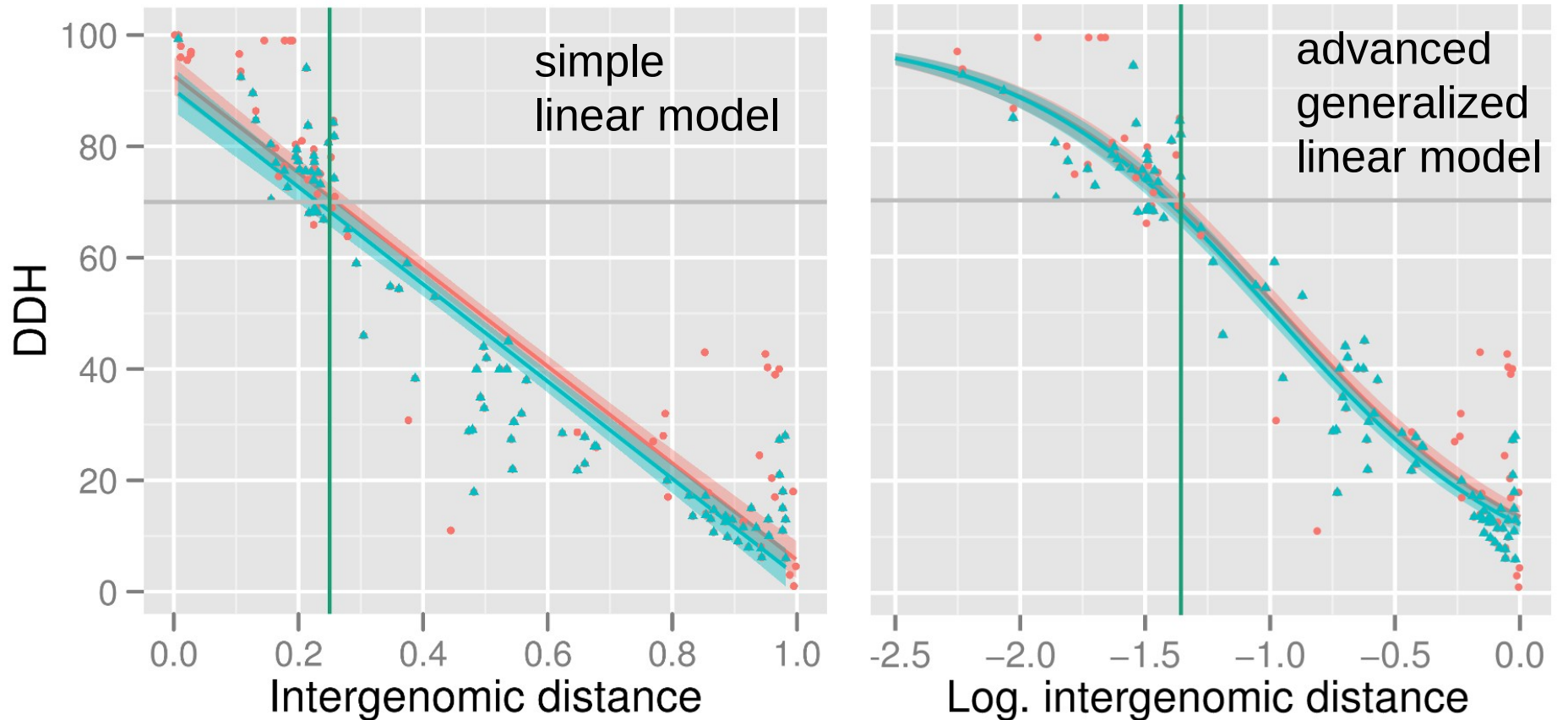


Modified figure from
Meier-Kolthoff *et al.*
(2013a)

Pitfalls in predicting digital DDH

- statistical uncertainty associated to any such model-based approach (ANI¹, GGDC², JSpecies³)
- but digital DDH at the 70% threshold can hardly be judged without knowledge of statistical deviation
- GGDC reports such confidence intervals to its users

Empirical data indicate non-linear relationship



Modified figure from
Meier-Kolthoff *et al.* (2013a)

- data show better fit to model
- DDH predictions more accurate
- used in GGDC 2.0

Direct comparability with wet-lab DDH is important

- microbiologists are used to the established DDH scale and thresholds
- digital DDH alternatives often operate on a scale of their own (drawback)
- GGDC predicts digital DDH on the well-known DDH scale

Phylogenetic reliability assesse

- GBDP is also used in phylogenomics!
 - can calculate pairwise distance replicates (e.g., via bootstrapping)
- ⇒ assessment of branch support essential for any serious tree analysis!

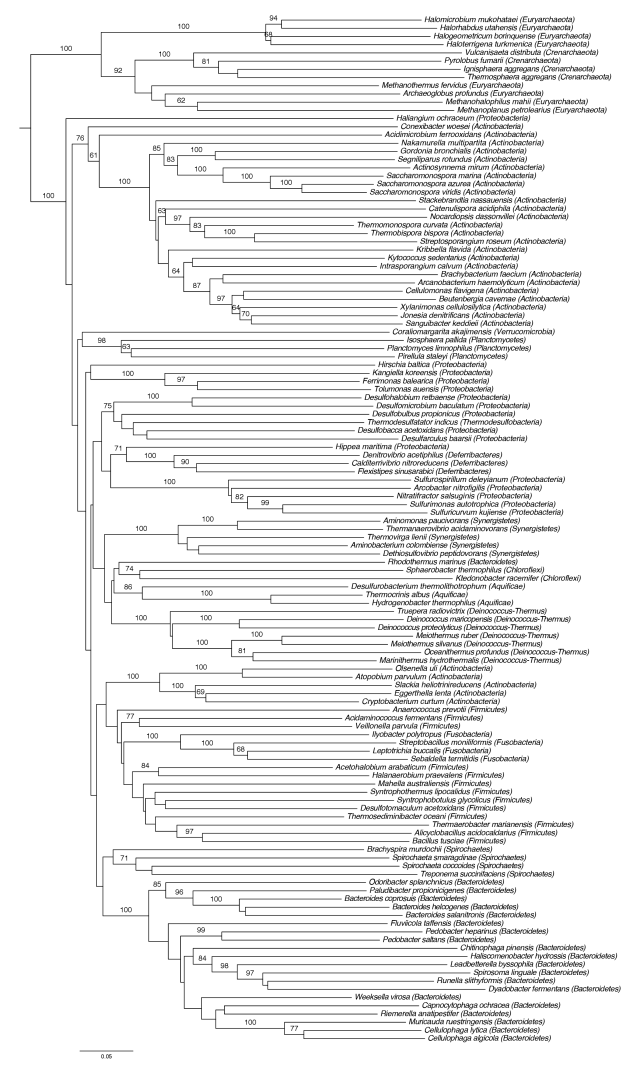


Figure: Genome-based GED tree

Summary

	SpecI (Mende et al. 2013)	ANI, JSpecies	GGDC
correlation with wet-lab DDH is main criterion	✗	✓	✓
highest correlation obtained	✗	✗	✓
uncertainty in empirical model	✓	✓	✓
uncertainty displayed	✗	✗	✓
data suggest non-linear model	✗	✓	✓
non-linear model used	✗	✗	✓
comparability with wet-lab DDH useful	✓	✓	✓
results on same scale as wet-lab DDH	✗	✗	✓
phylogenetic reliability assessed	✓	✗	✓