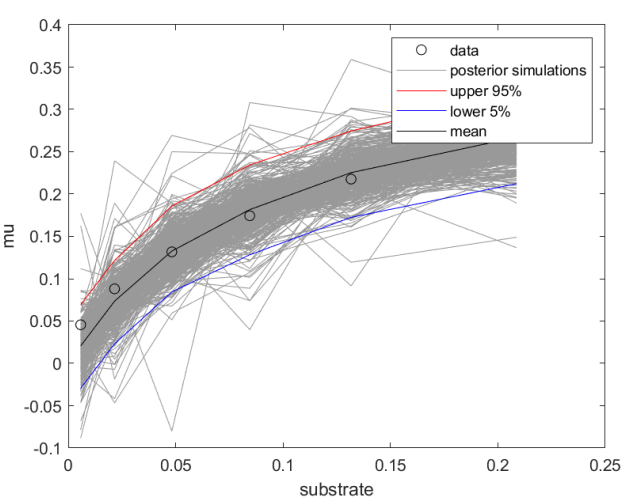
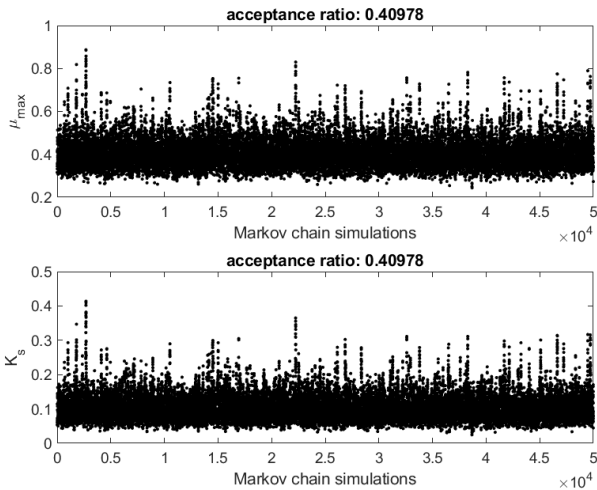


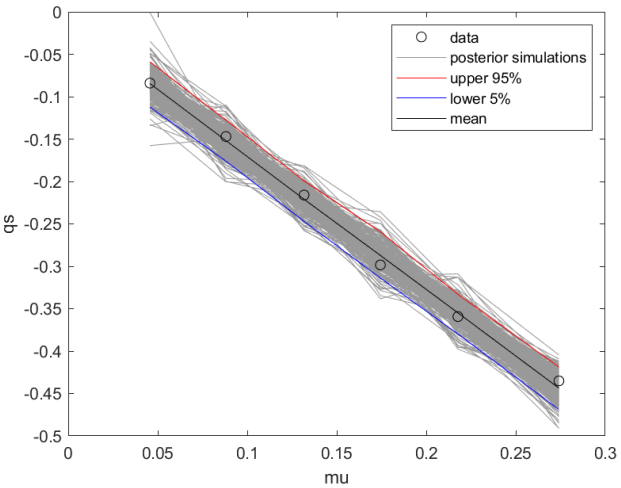
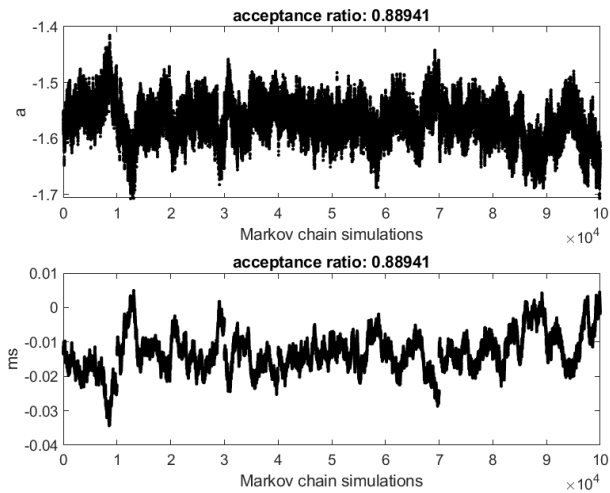
Supplementary File S1

MCMC chains, simulations, and correlation matrices.
Monod kinetics for maximum growth rate and affinity constant.



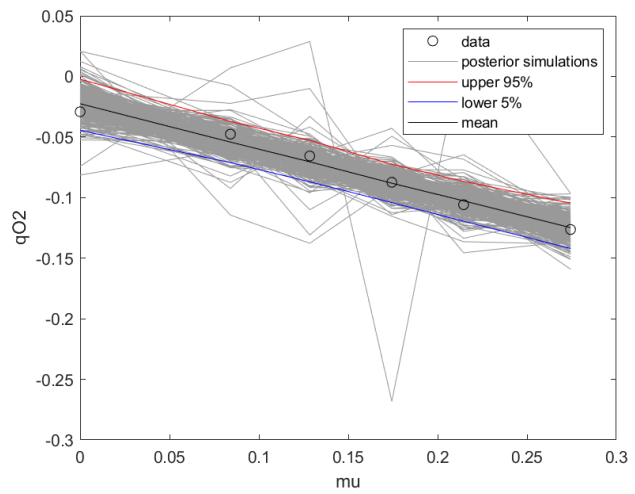
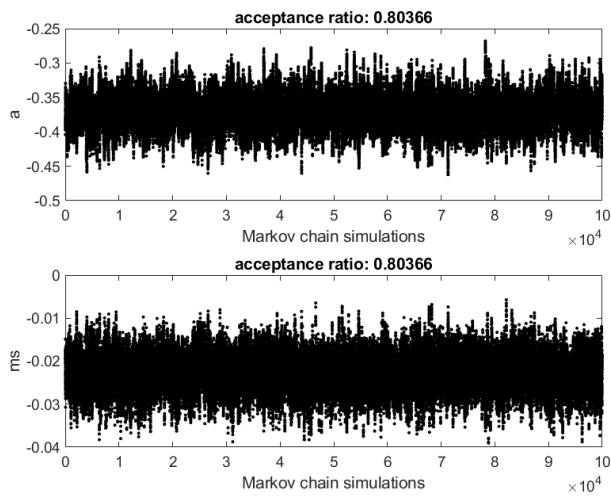
Correlation matrix parameter estimation		
	μ_{\max}	K_s
μ_{\max}	1.0000	-
K_s	0.9694	1.0000

Herbert–Pirt distribution for substrate yield and maintenance coefficient.



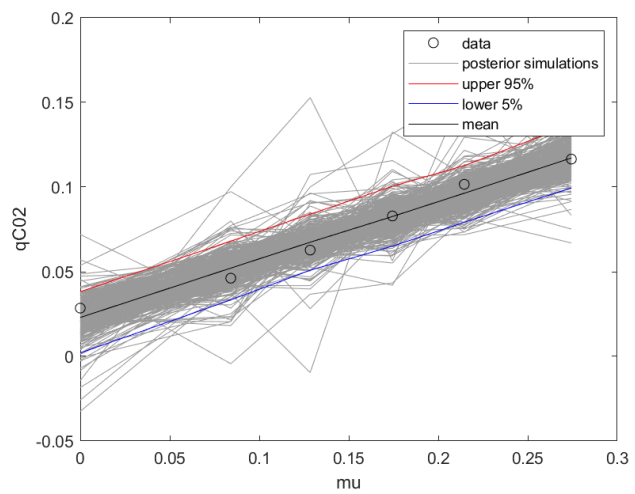
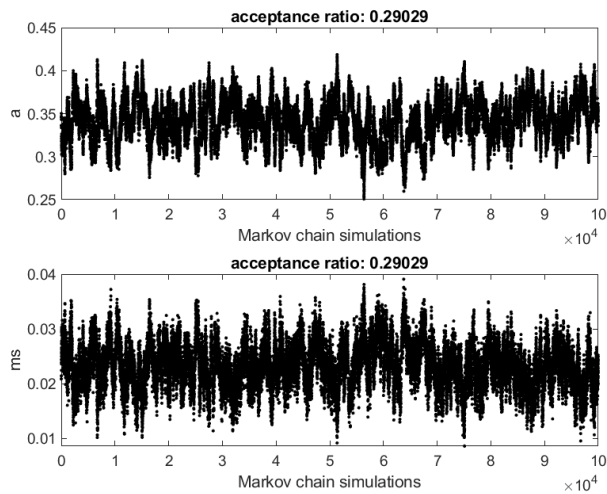
Correlation matrix parameter estimation		
	qs	ms
qs	1.0000	-
ms	-0.8792	1.0000

Herbert–Pirt distribution for O₂ yield and maintenance coefficient.



Correlation matrix parameter estimation		
	q _{O2}	m _{O2}
q _{O2}	1.0000	-
m _{O2}	-0.8533	1.0000

Herbert–Pirt distribution for CO₂ yield and maintenance coefficient.



Correlation matrix parameter estimation		
	q _{CO2}	m _{CO2}
q _{CO2}	1.0000	-
m _{CO2}	-0.8487	1.0000

Supplementary File S2

Repeated parameter estimation, including multiple DO values.

The parameter estimation was repeated, including all values from the chemostats (6 dissolved oxygen values across 3 growth rates). This yielded the results in Table S1 (“estimation with all additional values”).

Table S1. Results from parameter estimations.

		Original Values—Manu-script			Estimation with All Addi-tional Values			Estimation with Additional Values—DO Limitation Omitted		
Parameters		Mean	STDEV	MC error	Mean	STDEV	MC error	Mean	STDEV	MC error
Monod	μ_{\max} (h ⁻¹)	0.3988	0.0670	0.0003	0.1617	0.0197	0.0001	0.2810	0.0184	0.0001
	K_s (g L ⁻¹)	0.1013	0.0387	0.0002	0.0180	0.0120	0.0001	0.0430	0.0081	0.0000
q^s	a_s (mol mol ⁻¹)	-1.5902	0.0434	0.0002	-1.3655	0.1690	0.0006	-1.3788	0.1281	0.0005
	m_s (mol mol ⁻¹ h ⁻¹)	-0.0145	0.0075	0.0000	-0.0227	0.0193	0.0001	-0.0012	0.0195	0.0001
q_{O_2}	a_{O_2} (mol mol ⁻¹)	-0.3706	0.0244	0.0001	-0.2680	0.0635	0.0002	-0.2796	0.0592	0.0002
	m_{O_2} (mol mol ⁻¹ h ⁻¹)	-0.0229	0.0042	0.0000	-0.0039	0.0092	0.0000	-0.0080	0.0091	0.0000
q_{CO_2}	a_{CO_2} (mol mol ⁻¹)	0.3898	0.0262	0.0001	0.2875	0.0635	0.0002	0.2939	0.0493	0.0002
	m_{CO_2} (mol mol ⁻¹)	0.0269	0.0045	0.0000	0.0037	0.0091	0.0000	0.0090	0.0493	0.0000

These results show that when all chemostat values were incorporated into the estimation, each parameter was affected. Most notably, the maximum growth rate dropped quite significantly. Meanwhile, the standard deviation for the estimated maintenance coefficients also became larger. However, as *Yarrowia lipolytica* is a strictly aerobic organism, it is reasonable to assume that there is a severely-reduced-to-no substrate uptake or growth under anaerobic conditions. These values do not, therefore, provide any additional information for the parameter estimation and instead bias the dataset. This is also depicted in Figure S1, where all data points are plotted and the oxygen-limited chemostat is underlined in red (DO = 0.5% for $\mu = 0.05, 0.1$, and 0.2).

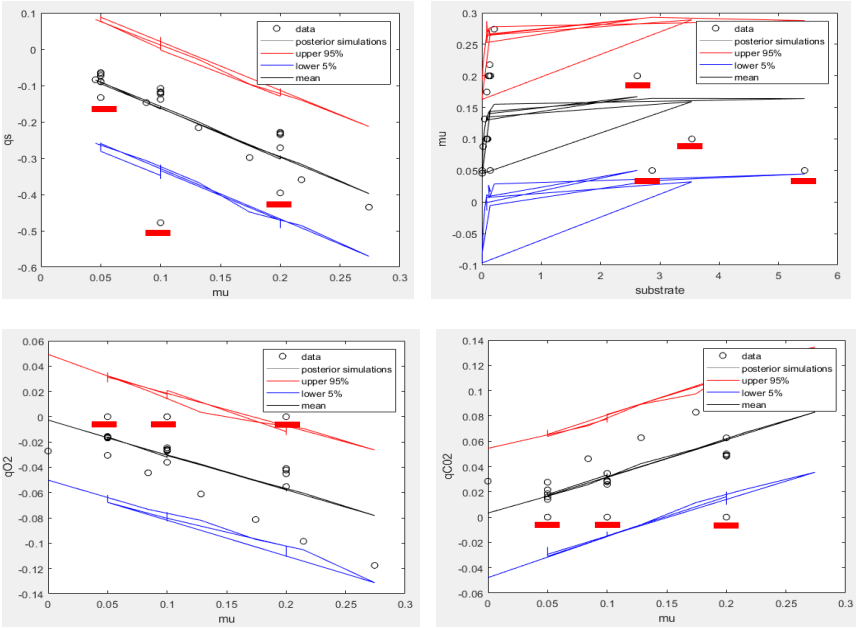


Figure S1. Parameter estimation for all chemostat data, including varying dissolved oxygen concentrations across growth rates. Red underlined data points indicate data from samples under oxygen-limited conditions, where cell washout was observed.

When excluding these oxygen-limited conditions (but keeping the other additional chemostat data), we can see that the estimated values slightly changed with a reduced standard deviation (Table S1 estimation with additional values—DO limitation omitted) and a better fit, which shows in the plotted data points (Figure S2).

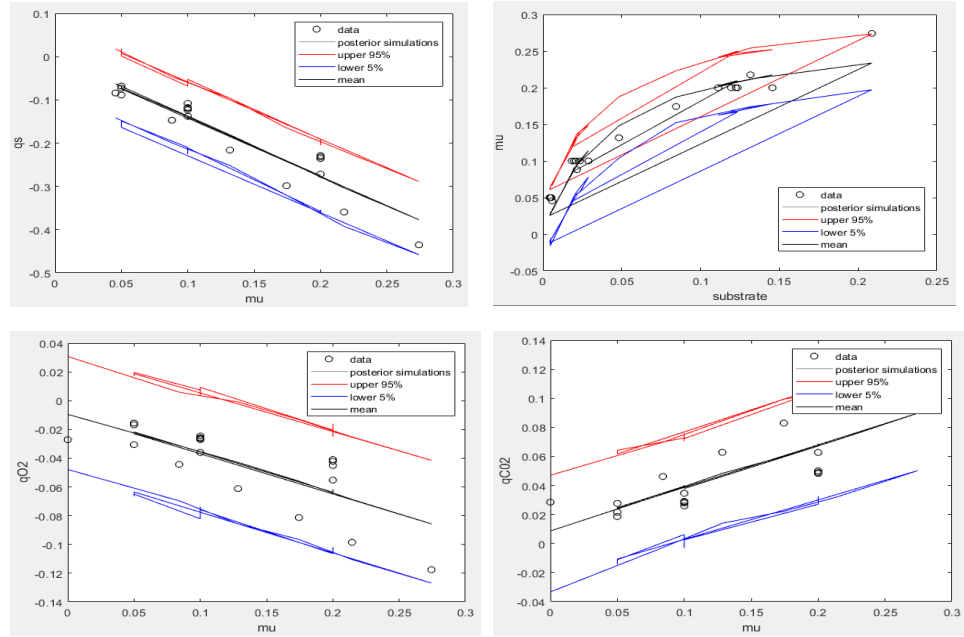


Figure S2. Parameter estimation for all available chemostat data, excluding those data points in which oxygen limitation was imposed and cell washout was observed.

This yielded us a parameter estimation that takes into account a broader range of dissolved oxygen concentrations, with values from 2.5 up to 50%. These parameters were then inputted into the compartmental model, of which the results are depicted in Figure S3.

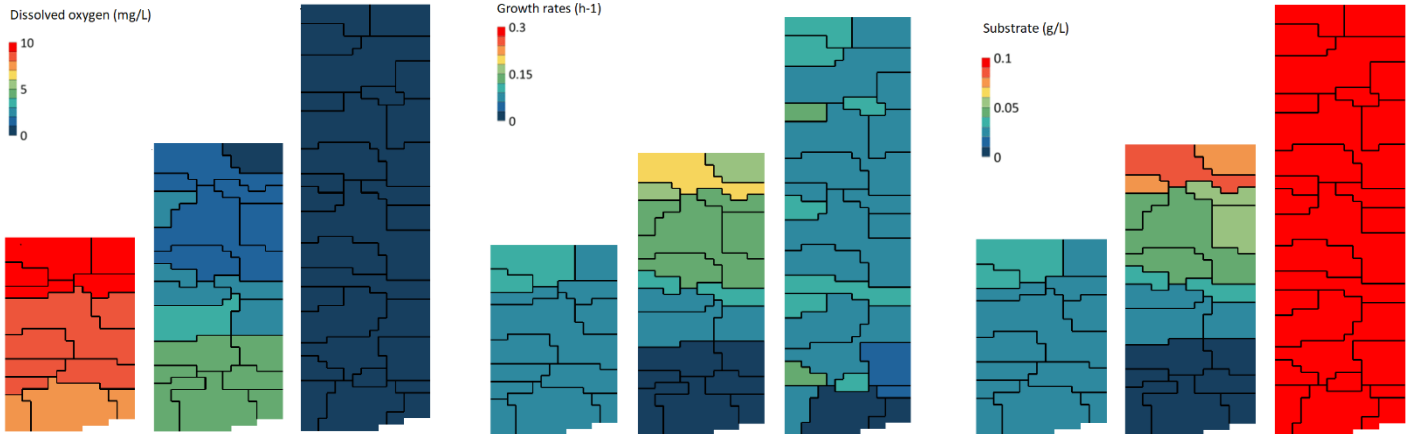


Figure S3. Results of the compartmental model on new estimated parameters. From left to right, the dissolved oxygen concentration, growth rate, and substrate concentrations are depicted for the varying volumes.

These outcomes of the compartmental model are very similar to the ones presented in the manuscript, with full oxidative conditions at volumes of 45 and 60 m³, whereas the 90 m³ bioreactor ran into a 77% oxygen limitation.

Supplementary File S3

Highly weighted genes in PCA

Principal Component 1		
Gene Name	Suggested Function	Loading
YALI1_B12489g	Triacylglycerol lipase	Positive
YALI1_A06530g	Uncharacterized protein	Positive
YALI1_E30815g	Alkane monooxygenase	Positive
YALI1_A09064g	Uncharacterized transmembrane transporter	Positive
YALI1_D07831g	CAP domain-containing protein	Positive
YALI1_C21946g	Uncharacterized transmembrane transporter	Positive
YALI1_C21946g	Uncharacterized transmembrane transporter	Positive
YALI1_C08523g	General substrate transporter	Positive
YALI1_F38013g	Uncharacterized protein	Positive
YALI1_D04128g	Uncharacterized protein	Positive
YALI1_C16961g	Transmembrane amino acid transporter	Negative
YALI1_B09211g	Keto reductase domain-containing protein	Negative
YALI1_B28454g	4-hydroxyphenylpyruvate dioxygenase	Negative
YALI1_A03688g	Uncharacterized protein	Negative
YALI1_A04006g	Uncharacterized protein	Negative
YALI1_B28394g	D-galacturonate reductase	Negative
YALI1_A15624g	Transmembrane transporter	Negative
YALI1_A13508g	Uncharacterized protein	Negative
YALI1_E28300g	Phosphate transporter	Negative
YALI1_D06233	Uncharacterized protein	Negative
Principal component 2		
Gene name	Suggested function	Loading
YALI1_A21203g	Elongation factor	Positive
YALI1_A09553g	Thiamine thiazole synthase	Positive
YALI1_E17326g	Formate dehydrogenase	Positive
YALI1_F02592g	Beta-glucosidase	Positive
YALI1_F26167g	ADP/ATP translocase	Positive
YALI1_B10525g	Epimerase domain-containing protein	Positive
YALI1_D30899g	Uncharacterized protein	Positive
YALI1_B08461g	High-affinity glucose transporter	Positive
YALI1_A00148g	Uncharacterized protein	Positive
YALI1_A06099g	Cerevisin (protease)	Positive
YALI1_E14619g	Amidase signature domain-containing protein	Negative
YALI1_D15568g	Uncharacterized protein	Negative
YALI1_E08620g	Urea amidolyase	Negative
YALI1_B23522g	Uncharacterized protein	Negative
YALI1_B14544g	Ferric reductase NAD binding domain	Negative
YALI1_E29481g	Glycosidase	Negative
YALI1_C15610g	Uncharacterized protein	Negative
YALI1_C21924g	Uncharacterized protein	Negative
YALI1_D19721g	Globin-like protein	Negative
YALI1_F04314g	Kinase-like domain-containing protein	Negative