

Supplementary Material

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TABLES

Strain (ploidy)	Medium	Airflow (mL/min)	Reactor volume (mL)	Stirring speed (RPM)	pH	Dilution rate (hr ⁻¹)	CDC period (hours)	YMC period (hours)	References
LBGH1022 (diploid)	SD+1.0% glucose	550	3900	900	5.5	0.05	13.8	6.5	(Küenzi and Fiechter, 1969)
LBGH1022 (diploid)	SD+7.0% glucose	6375	2550	900	5.5	0.185	3.7	2.5	(Kaspar von Meyenburg, 1969)
LBGH1022 (diploid)	SD+1.0% glucose	3000	4000	Vary(DO clamp)	5.5	0.2	3.5	2.2	(Parulekar <i>et al.</i> , 1986)
S288C (haploid)	YP+0.5% glucose	1000	350	100-500	Free	0.066 - 0.170	4.6 - 10.5	5.0 - 13.0	(Porro <i>et al.</i> , 1988)
Fleischmann (diploid)	SD+1.0% glucose	3000	1000	Vary(DO clamp)	5.5	0.145	4.8	3.5	(Chen and McDonald, 1990)
S288C (haploid)	YP+0.5% glucose	1000	350	200-300	Free	0.07	10.0	15.0	(Martegani <i>et al.</i> , 1990)
IFO0233 (diploid)	YP+2% glucose	200	1350	700	4.0	0.08	8.7	0.66	(Satroudinov <i>et al.</i> , 1992)
IFO0233 (diploid)	YP+2.2% glucose	150-1000	1200	800	4.0	0.08	8.7	0.66	(Keulers <i>et al.</i> , 1996a)
IFO0233 (diploid)	YP+1.5% ethanol	180	1200	800	4.0	0.085	8.1	0.66	(Keulers <i>et al.</i> , 1996b)
IFO0233 (diploid)	SD+2.2% glucose	200	1000	750	3.4	0.050-0.125	5.6-13.9	0.38 - 1.10	(Murray and Marks, 2001)
IFO0233 (diploid)	SD+2.2% glucose	200	1000	750	3.4	0.09	7.7	0.8	(Murray <i>et al.</i> , 2003)
CBS7336 (diploid)	SD+3.0% glucose	833	500		5.0	0.1	6.9	4.0	(Müller <i>et al.</i> , 2003)
IFO0233 (diploid)	SD+2.2% glucose	150	750	750	3.4	0.09	7.7	0.8	(Klevecz <i>et al.</i> , 2004)
CEN.PK (diploid)	SD+1.0% glucose	1000	1000	400	3.4	0.09	7.7	5.0	(Tu <i>et al.</i> , 2005)
S288C (haploid)	YP+1.0% glucose	1000	500	420	5.0	0.1	6.9	4.5	(Xu and Tsurugi, 2006)
CEN.PK (haploid)	SD+1.0% glucose	1000	1000	400	3.4	0.09	7.7	4.5	(Chen <i>et al.</i> , 2007)
CEN.PK (haploid)	YP+1.0% glucose	900	850	550	3.4	0.085	8.1	3.8	(Robertson <i>et al.</i> , 2008)
DBY12007 (diploid)	SD+0.08% glucose		300	400	Free	0.05-0.14	5.0 - 13.9	1.0 - 4.0	(Slavov and Botstein, 2011)
DBY12007 (diploid)	SD+100mM ethanol		500	400	Free			4.2	(Slavov <i>et al.</i> , 2011)

Table S1: Strains, ploidy, medium, and chemostat settings across the yeast metabolic cycle literature. Growth medium is categorized either as SD (synthetic defined) or YP (yeast extract and peptone). Constant pH was maintained via automatic addition of NaOH unless otherwise stated ("Free"). Constant pO₂ was maintained by automatic adjustment of impeller stirring speed ("Vary"). Unknown parameters were left blank.

Strains	T_{max} (mins)	κ (mins)	b (mins)	m
CEN.PK	9.45 ± 4.84 $\times 10^2$	1.72 ± 1.33 $\times 10^3$	9.75 ± 0.79 $\times 10^1$	-2.61 ± 0.97 $\times 10^{-2}$
DBY12007	3.12 ± 0.61 $\times 10^2$	6.49 ± 2.83 $\times 10^2$	6.78 ± 0.23 $\times 10^1$	-2.10 ± 0.28 $\times 10^{-2}$

	T_{max}/κ	b (mins)	m
YPS670 (oak)	$(5.18 \pm 0.32) \times 10^{-1}$	7.28 ± 0.76 $\times 10^1$	-3.41 ± 1.48 $\times 10^{-2}$
YJM128 (lung)	$(3.06 \pm 0.33) \times 10^{-1}$	4.59 ± 0.69 $\times 10^1$	1.61 ± 1.40 $\times 10^{-2}$

Table S2: Best-fit parameters of the mixed model to YMC and HOC across strains. The mixed model is a hyperbolic model (T_{max} , κ) fit to T_{ymc} [left] and a linear model (b , m) fit to T_{hoc} [right] where $T_{ioc} = T_{ymc} - T_{hoc}$. For wild isolates YJM128 and YPS670, the best mixed model fit was indistinguishable from a best linear fit, where $b=0$ and $m = T_{max}/\kappa$ for T_{ymc} ; see Figure S3.

FIGURES

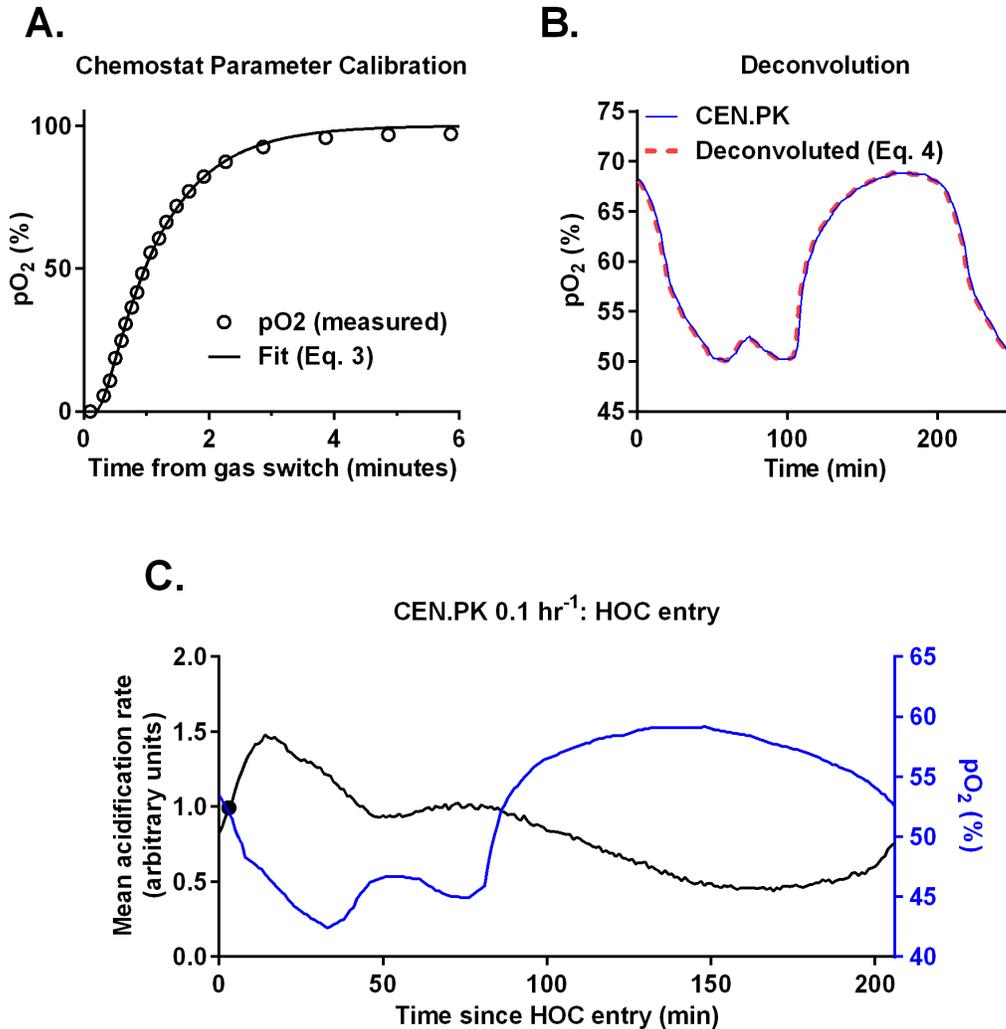


Figure S1: Calibration of pO₂ and definition of HOC. (A) Probe pO₂ reached equilibrium within minutes upon switching the chemostat from nitrogen gas to room air at t=0 mins. These data were fit to Eq. 3 to estimate $k = 1.09 \text{ mins}^{-1}$, $\tau_r = 0.149 \text{ mins}$, and $t_0 = 0.181 \text{ minutes}$. (B) Using these parameters, we de-convolved the measured pO₂ trace (blue) to instantaneous equilibrium pO₂ levels (dashed red) using Eq. 4. The de-convolved data is nearly identical to the original data, where the primary difference is ~ 1 minute time shift. (C) We defined entry into HOC as the time at which decreasing pO₂ reached 65% of the full peak-to-trough. This definition of entry into HOC was coincident with the acidification rate reaching 50% of peak-to-trough levels. Chemostat acidification is co-incident with the catabolism of storage carbohydrates, fermentation of the excess glucose, secretion of ethanol and acetate, and acidification of the medium. For consistency, we defined entry into LOC as the time at which increasing pO₂ had risen to 65% of the full peak-to-trough.

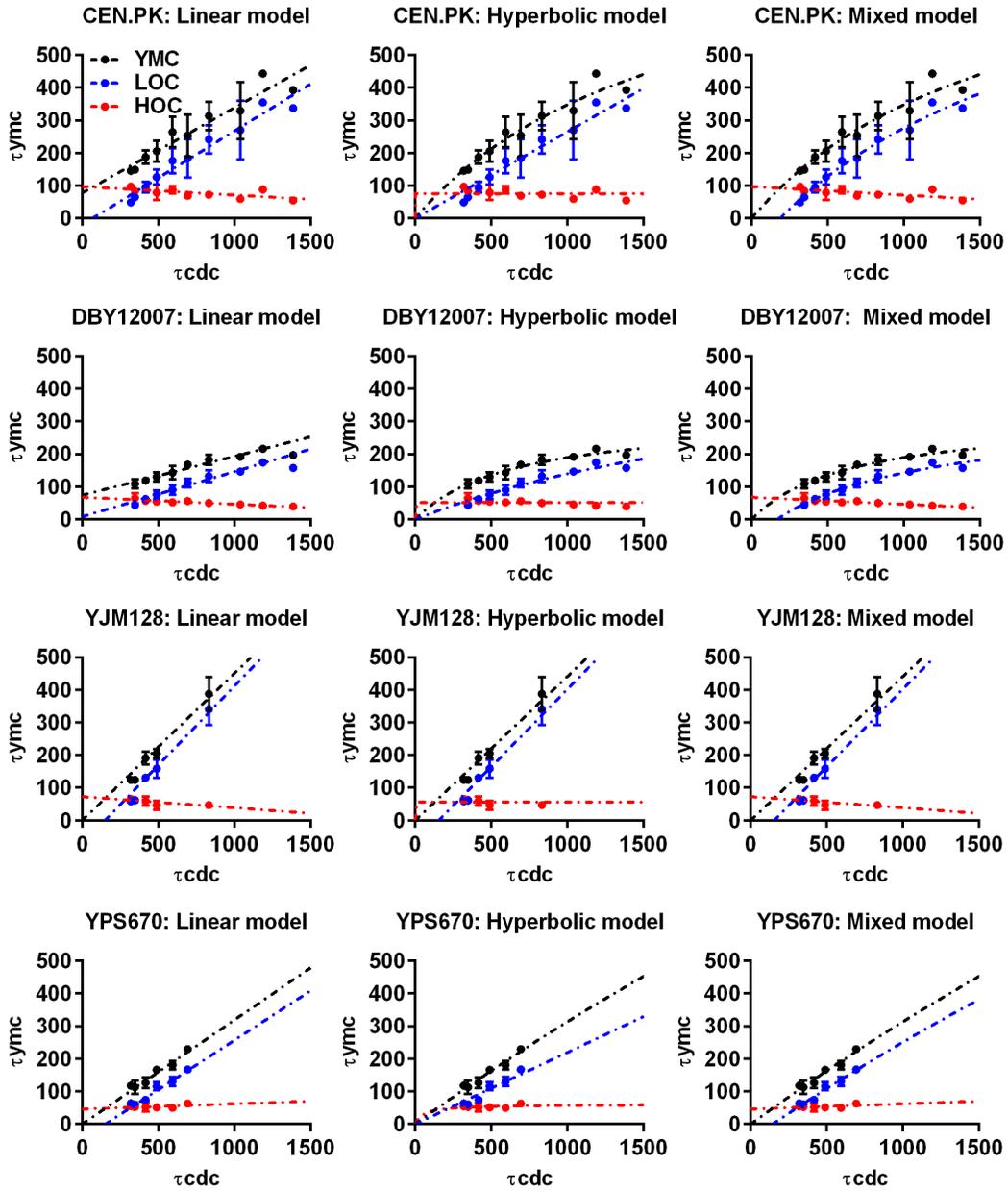


Figure S2: Best-fit of linear, hyperbolic, and mixed models to YMC data. Plots of τ_{ymc} (black dots), τ_{hoc} (red dots), and τ_{loc} (blue dots) as a function of CDC period (τ_{cdc}) for CEN.PK, DBY12007, YJM128 (lung), and YPS670 (oak). For clarity, we plotted the average and standard deviation of time-series averages of biological replicates at identical dilution rates. Linear, hyperbolic, and mixed models (dashed lines) were fit to τ_{ymc} , τ_{loc} , and τ_{hoc} for each strain. Linear models (Eq. 8) were limited to positive τ -intercepts ($b > 0$) to avoid the unphysical notion of a negative τ_{ymc} . Hyperbolic models (Eq. 9) were unconstrained. Mixed models utilized the hyperbolic fit to τ_{ymc} , the linear fit to τ_{hoc} , and the difference between them for τ_{loc} .

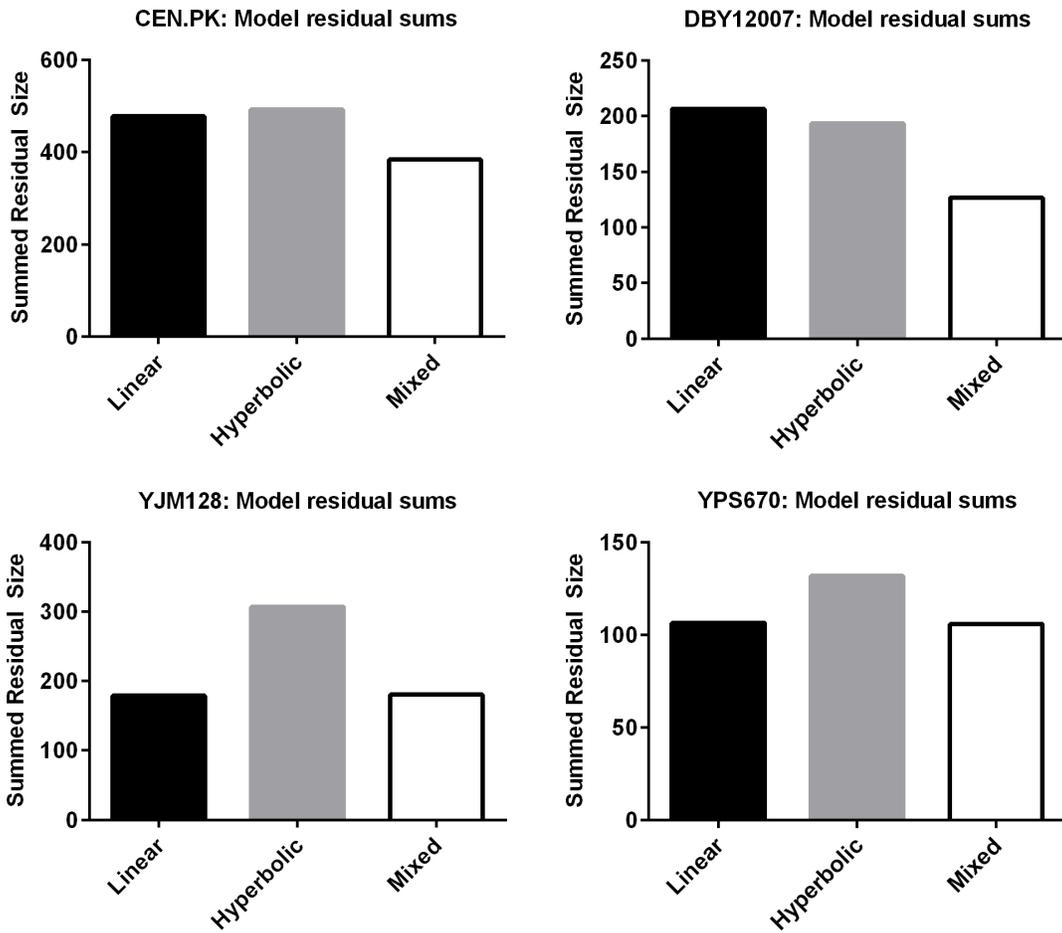


Figure S3: Residuals of best-fit linear, hyperbolic, and mixed models. Residual sums for each strain and model indicate that the mixed model was optimal for laboratory strains CEN.PK and DBY12007. All linear and all hyperbolic models were indistinguishable for wild isolates YJM128 (lung) and YPS670 (oak). Thus, we used the mixed model for all strains.

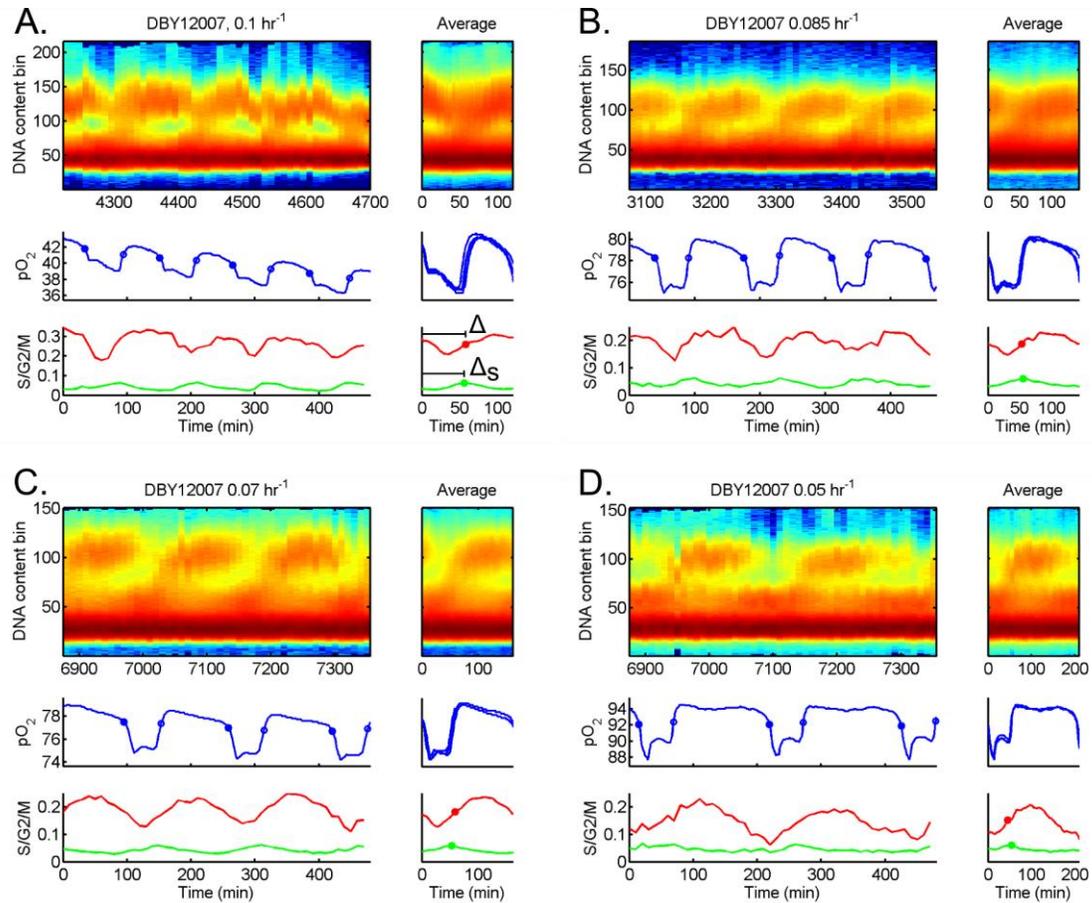


Figure S4: Timing of DNA replication relative to HOC in strain DBY12007 across growth rates. Additional cell cycle analysis for strain DBY12007 at different dilution rates: (A) 0.1 hr^{-1} , (B) 0.085 hr^{-1} , (C) 0.07 hr^{-1} , (D) 0.05 hr^{-1} . Data displayed as in Figure 5.

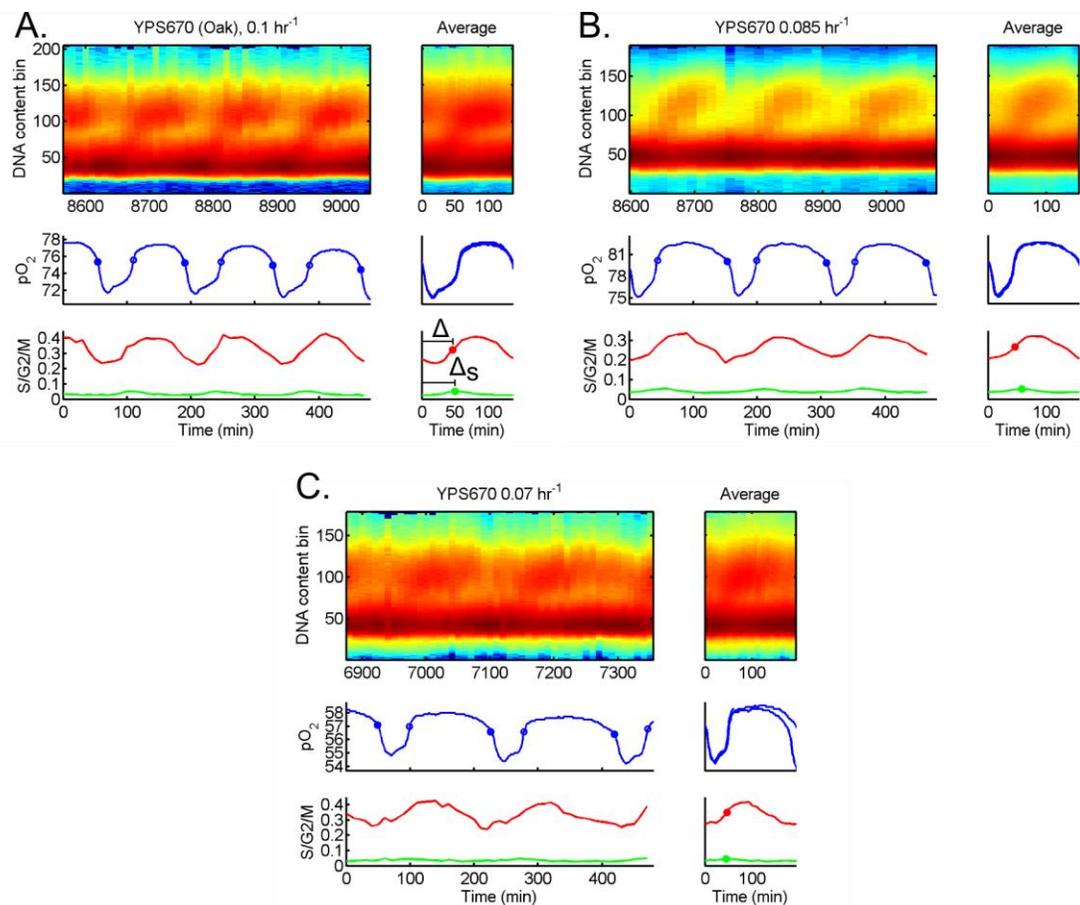


Figure S5: Timing of DNA replication relative to HOC in strain YPS670 across growth rates. Additional cell cycle analysis for strain YPS670 at different dilution rates: (A) 0.1 hr⁻¹, (B) 0.085 hr⁻¹, (C) 0.07 hr⁻¹. Data displayed as in Figure 5.

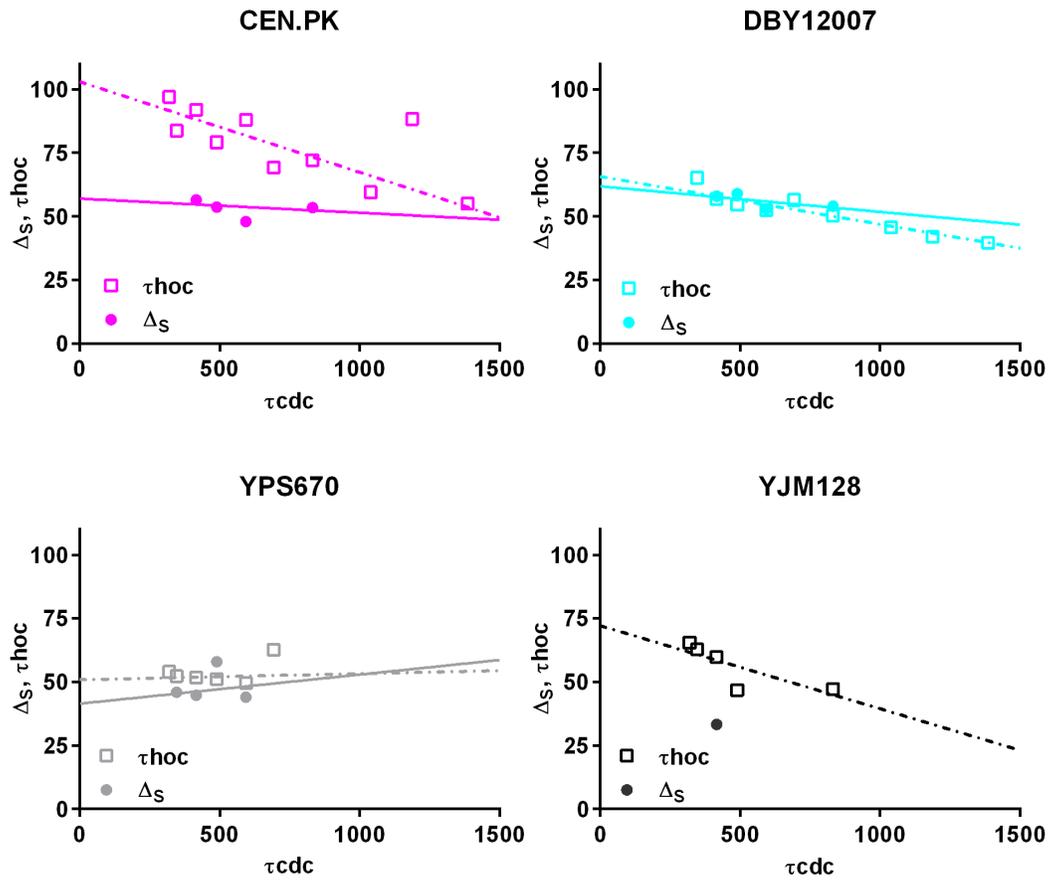


Figure S6: Relative timing of DNA replication and HOC across strains and growth rates. Mean Δ_S (solid circles) and τ_{hoc} (open squares) as a function of τ_{cdc} for each strain. Linear regression of Δ_S (solid line) and τ_{hoc} (dashed line) data shows that DNA replication can occur during HOC ($\Delta_S < \tau_{hoc}$) or LOC ($\Delta_S > \tau_{hoc}$) depending on the strain and the growth rate.

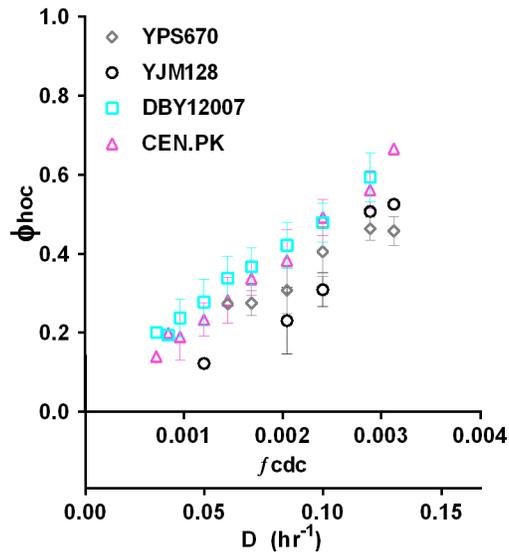


Figure S7: Fraction of time spent in high oxygen consumption phase (Φ_{hoc}) across strains and growth rate. We could collapse timescale differences between strains by plotting the fraction of time during a YMC that is spent in HOC ($\Phi_{hoc} = T_{hoc}/T_{ymc}$) as a function of growth rate (f_{cdc}). All strains exhibited a similar linear increase in Φ_{hoc} as a function of growth rate.

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