Supplementary Data

Statistical modeling of gene expression profiles

The log-fold change in gene expression was modeled by the following equation (32):

$$y_n(t) = \sum_m X_{nm} b_{nm} c_m(t) + \varepsilon_{nt}$$

Here, $y_n(t)$ is the log-fold change for the n-th gene at time t; X_{nm} is a binary matrix encoding the structure of the regulatory network (obtained typically from the literature); b_{nm} is the unknown rate constant for activation/repression; $c_m(t)$ is the (log) fold-change in transcription factor (TF) activity; and ε_{nt} is an error term. Standard statistical inference techniques can then be employed using TFInfer (3), which is an implementation of the probabilistic model (32). This enables estimates of the changes in the activity of regulators from an analysis of the behavior of their targets.

TFInfer does not know *a priori* the sign of the TF–gene interactions, which means that the multiplying one or more of the inferred TF profiles by -1 does not result in a worse solution according to the inference scheme in TFInfer. Only after the results have been generated, can this be corrected by comparing the inferred signs with information from databases on TF activity and flipping TF profiles where necessary, as well as the signs of its interactions.

Significance testing for differences in TF activity

To test for significant differences in TF activity between two different conditions, we modified the model above to include data from the two conditions: that is,

$$y_{nr}(t) = \sum_m X_{nm} b_{nm} c_{mr}(t) + \varepsilon_{nrt}$$

where the added index, r, indexes the experimental conditions; the baseline expression μ_n and coefficients b_{mn} are assumed to be common to both conditions. Then, for a given m, we assume that $c_{m1}(t) = c_{m2}(t)$ for all timepoints t.

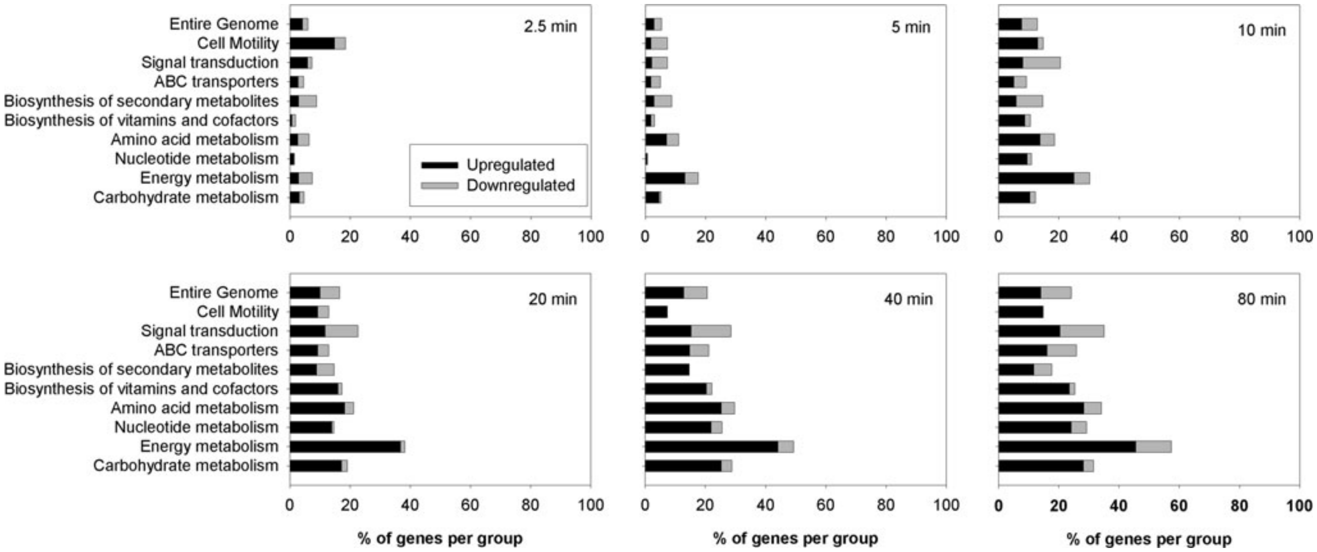
The inferred contribution of all TFs to the expression of all genes in the regulon of the given TF is then subtracted, leaving residuals,

$$y'_{nr}(t) = y_{nr}(t) - \sum_m X_{nm} b_{nm} c_{mr}(t)$$

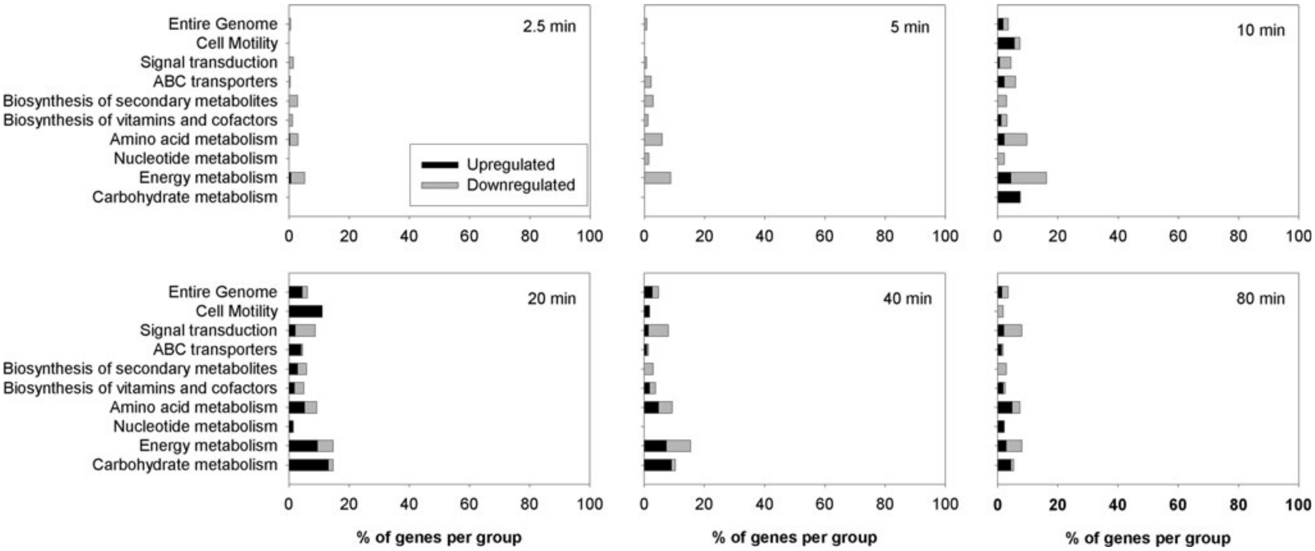
which represents the normally distributed contribution of noise under the null hypothesis. The distribution of the differences of the residuals is in turn normally distributed. Thus, the distribution of

$$\frac{1}{2\sigma^2} \sum_n \sum_t \left(y'_{n1}(t) - y'_{n2}(t)\right)^2$$

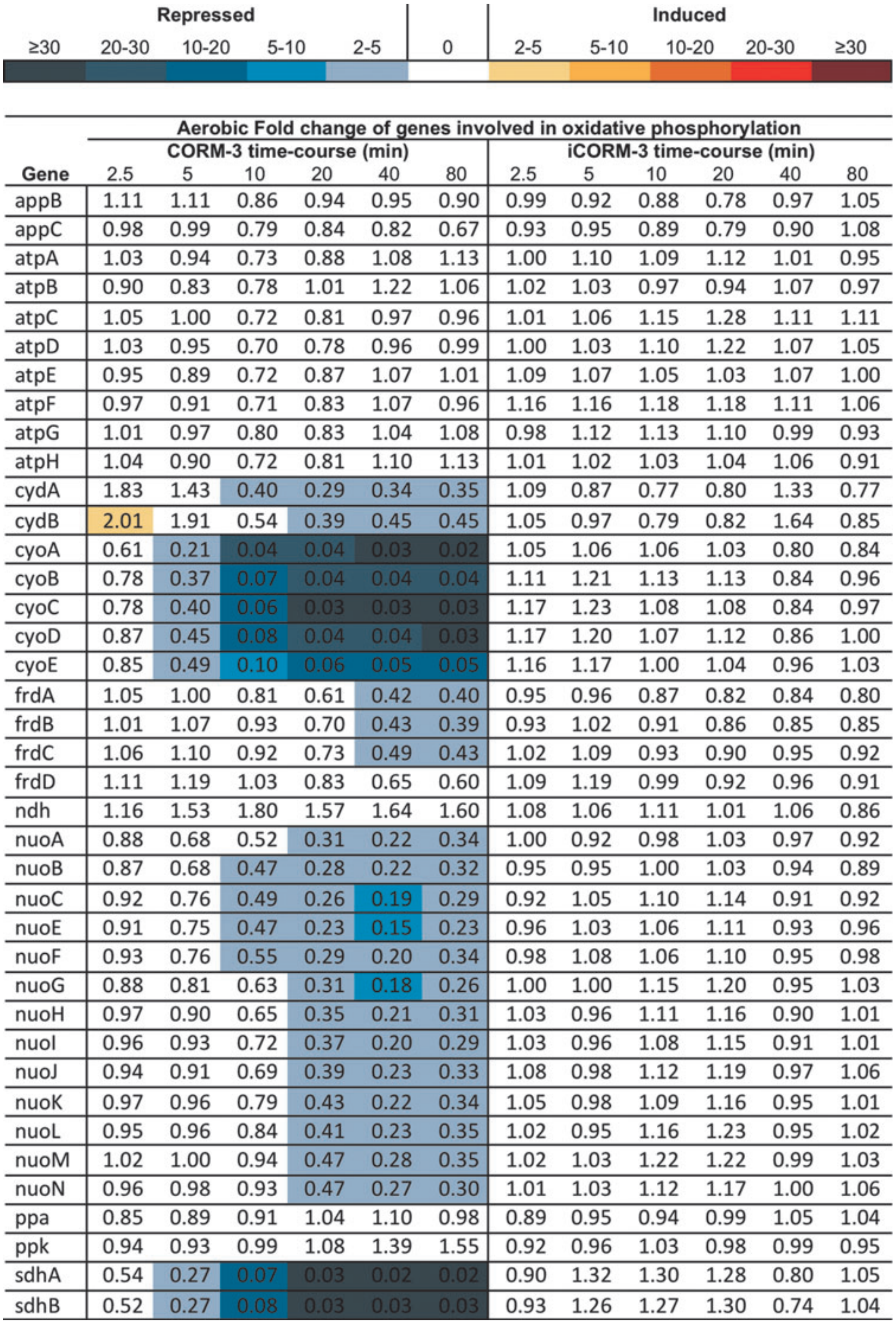
is chi-squared with degrees of freedom equal to the size of the regulon of the TF in question multiplied by the number of timepoints, where σ^2 is the variance of the noise term ε_{nrt}. This gives a null distribution against which we can check the sums of the squares of the differences of the residuals from the data. The above procedure is repeated for all genes m to give a p-value for each TF in the network.



SUPPLEMENTARY FIG. S1. Expression changes of genes belonging to functional groups in response to Ru(CO)$_3$Cl(Glycinate) (CORM-3) exposure under anaerobic conditions. Wild-type *Escherichia coli* cells were grown anaerobically in continuous culture and a defined minimal medium before addition of 40 μM CORM-3. Samples were taken at 0, 2.5, 5, 10, 20, 40, and 80 min after addition of the compound and analyzed transcriptomically. The bars show the percentage of genes belonging to each group that were altered at each time point. Black bars indicate upregulation, and gray bars indicate downregulation.

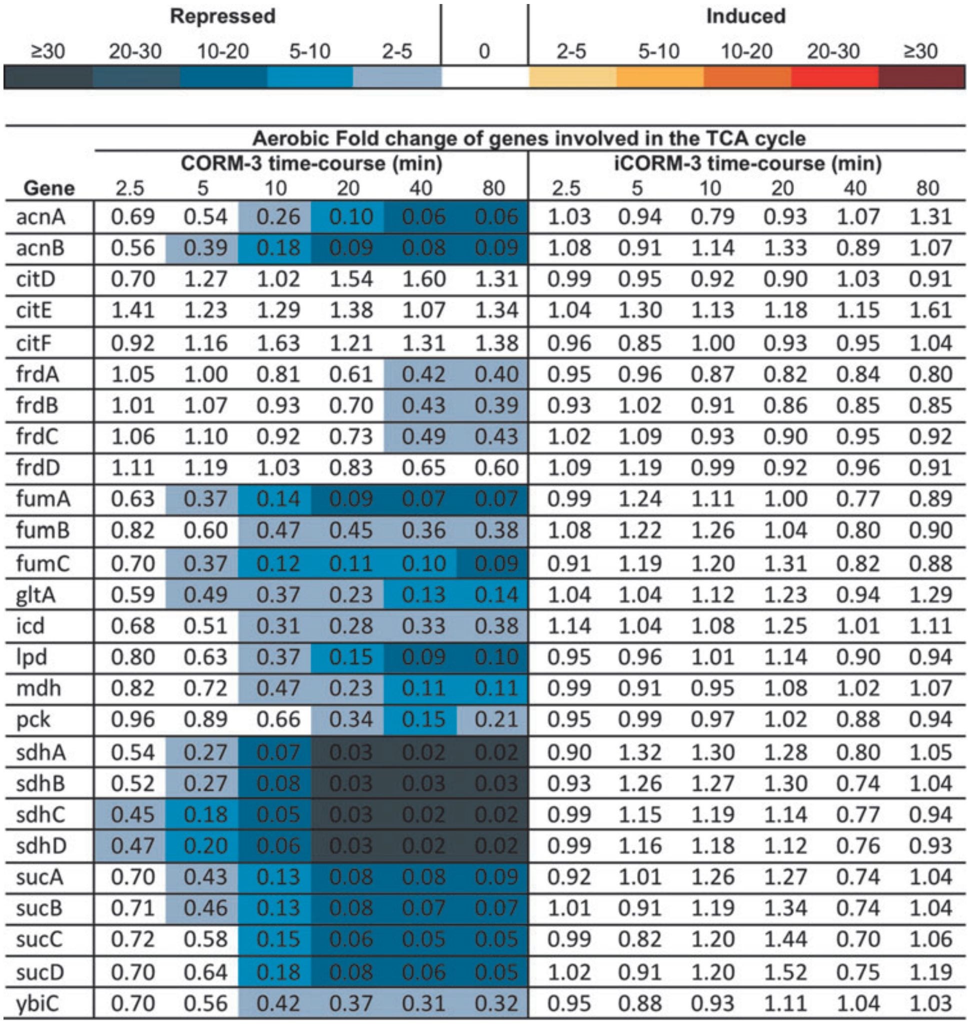


SUPPLEMENTARY FIG. S2. Expression changes of genes belonging to functional groups in response to inactivated CORM-3 (iCORM-3) exposure under anaerobic conditions. Wild-type *E. coli* cells were grown anaerobically in continuous culture and a defined minimal medium before addition of 40 μM iCORM-3. Samples were taken at 0, 2.5, 5, 10, 20, 40, and 80 min after addition of the compound and analyzed transcriptomically. The bars show the percentage of genes belonging to each group that were altered at each time point. Black bars indicate upregulation, and gray bars indicate downregulation.



	Aerobic Fold change of genes involved in oxidative phosphorylation											
	CORM-3 time-course (min)						iCORM-3 time-course (min)					
Gene	2.5	5	10	20	40	80	2.5	5	10	20	40	80
appB	1.11	1.11	0.86	0.94	0.95	0.90	0.99	0.92	0.88	0.78	0.97	1.05
appC	0.98	0.99	0.79	0.84	0.82	0.67	0.93	0.95	0.89	0.79	0.90	1.08
atpA	1.03	0.94	0.73	0.88	1.08	1.13	1.00	1.10	1.09	1.12	1.01	0.95
atpB	0.90	0.83	0.78	1.01	1.22	1.06	1.02	1.03	0.97	0.94	1.07	0.97
atpC	1.05	1.00	0.72	0.81	0.97	0.96	1.01	1.06	1.15	1.28	1.11	1.11
atpD	1.03	0.95	0.70	0.78	0.96	0.99	1.00	1.03	1.10	1.22	1.07	1.05
atpE	0.95	0.89	0.72	0.87	1.07	1.01	1.09	1.07	1.05	1.03	1.07	1.00
atpF	0.97	0.91	0.71	0.83	1.07	0.96	1.16	1.16	1.18	1.18	1.11	1.06
atpG	1.01	0.97	0.80	0.83	1.04	1.08	0.98	1.12	1.13	1.10	0.99	0.93
atpH	1.04	0.90	0.72	0.81	1.10	1.13	1.01	1.02	1.03	1.04	1.06	0.91
cydA	1.83	1.43	0.40	0.29	0.34	0.35	1.09	0.87	0.77	0.80	1.33	0.77
cydB	2.01	1.91	0.54	0.39	0.45	0.45	1.05	0.97	0.79	0.82	1.64	0.85
cyoA	0.61	0.21	0.04	0.04	0.03	0.02	1.05	1.06	1.06	1.03	0.80	0.84
cyoB	0.78	0.37	0.07	0.04	0.04	0.04	1.11	1.21	1.13	1.13	0.84	0.96
cyoC	0.78	0.40	0.06	0.03	0.03	0.03	1.17	1.23	1.08	1.08	0.84	0.97
cyoD	0.87	0.45	0.08	0.04	0.04	0.03	1.17	1.20	1.07	1.12	0.86	1.00
cyoE	0.85	0.49	0.10	0.06	0.05	0.05	1.16	1.17	1.00	1.04	0.96	1.03
frdA	1.05	1.00	0.81	0.61	0.42	0.40	0.95	0.96	0.87	0.82	0.84	0.80
frdB	1.01	1.07	0.93	0.70	0.43	0.39	0.93	1.02	0.91	0.86	0.85	0.85
frdC	1.06	1.10	0.92	0.73	0.49	0.43	1.02	1.09	0.93	0.90	0.95	0.92
frdD	1.11	1.19	1.03	0.83	0.65	0.60	1.09	1.19	0.99	0.92	0.96	0.91
ndh	1.16	1.53	1.80	1.57	1.64	1.60	1.08	1.06	1.11	1.01	1.06	0.86
nuoA	0.88	0.68	0.52	0.31	0.22	0.34	1.00	0.92	0.98	1.03	0.97	0.92
nuoB	0.87	0.68	0.47	0.28	0.22	0.32	0.95	0.95	1.00	1.03	0.94	0.89
nuoC	0.92	0.76	0.49	0.26	0.19	0.29	0.92	1.05	1.10	1.14	0.91	0.92
nuoE	0.91	0.75	0.47	0.23	0.15	0.23	0.96	1.03	1.06	1.11	0.93	0.96
nuoF	0.93	0.76	0.55	0.29	0.20	0.34	0.98	1.08	1.06	1.10	0.95	0.98
nuoG	0.88	0.81	0.63	0.31	0.18	0.26	1.00	1.00	1.15	1.20	0.95	1.03
nuoH	0.97	0.90	0.65	0.35	0.21	0.31	1.03	0.96	1.11	1.16	0.90	1.01
nuoI	0.96	0.93	0.72	0.37	0.20	0.29	1.03	0.96	1.08	1.15	0.91	1.01
nuoJ	0.94	0.91	0.69	0.39	0.23	0.33	1.08	0.98	1.12	1.19	0.97	1.06
nuoK	0.97	0.96	0.79	0.43	0.22	0.34	1.05	0.98	1.09	1.16	0.95	1.01
nuoL	0.95	0.96	0.84	0.41	0.23	0.35	1.02	0.95	1.16	1.23	0.95	1.02
nuoM	1.02	1.00	0.94	0.47	0.28	0.35	1.02	1.03	1.22	1.22	0.99	1.03
nuoN	0.96	0.98	0.93	0.47	0.27	0.30	1.01	1.03	1.12	1.17	1.00	1.06
ppa	0.85	0.89	0.91	1.04	1.10	0.98	0.89	0.95	0.94	0.99	1.05	1.04
ppk	0.94	0.93	0.99	1.08	1.39	1.55	0.92	0.96	1.03	0.98	0.99	0.95
sdhA	0.54	0.27	0.07	0.03	0.02	0.02	0.90	1.32	1.30	1.28	0.80	1.05
sdhB	0.52	0.27	0.08	0.03	0.03	0.03	0.93	1.26	1.27	1.30	0.74	1.04

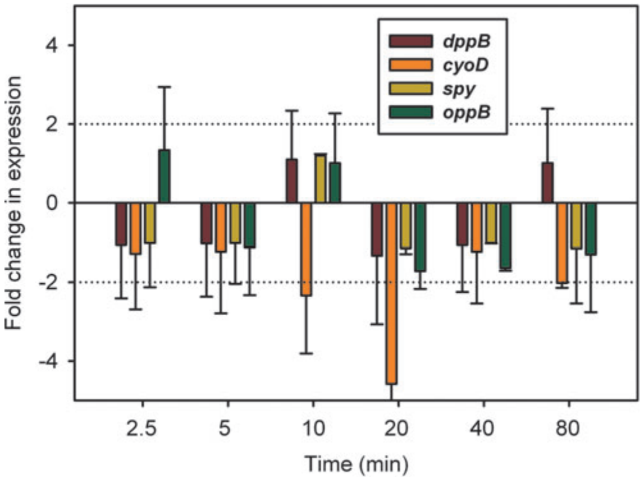
SUPPLEMENTARY FIG. S3. Differential expression of genes involved in oxidative phosphorylation after aerobic exposure to iCORM-3. The color-scale bar shows mean fold changes in individual genes of *E. coli* grown aerobically in Evans medium after the addition of 40 μM CORM-3 or iCORM-3.



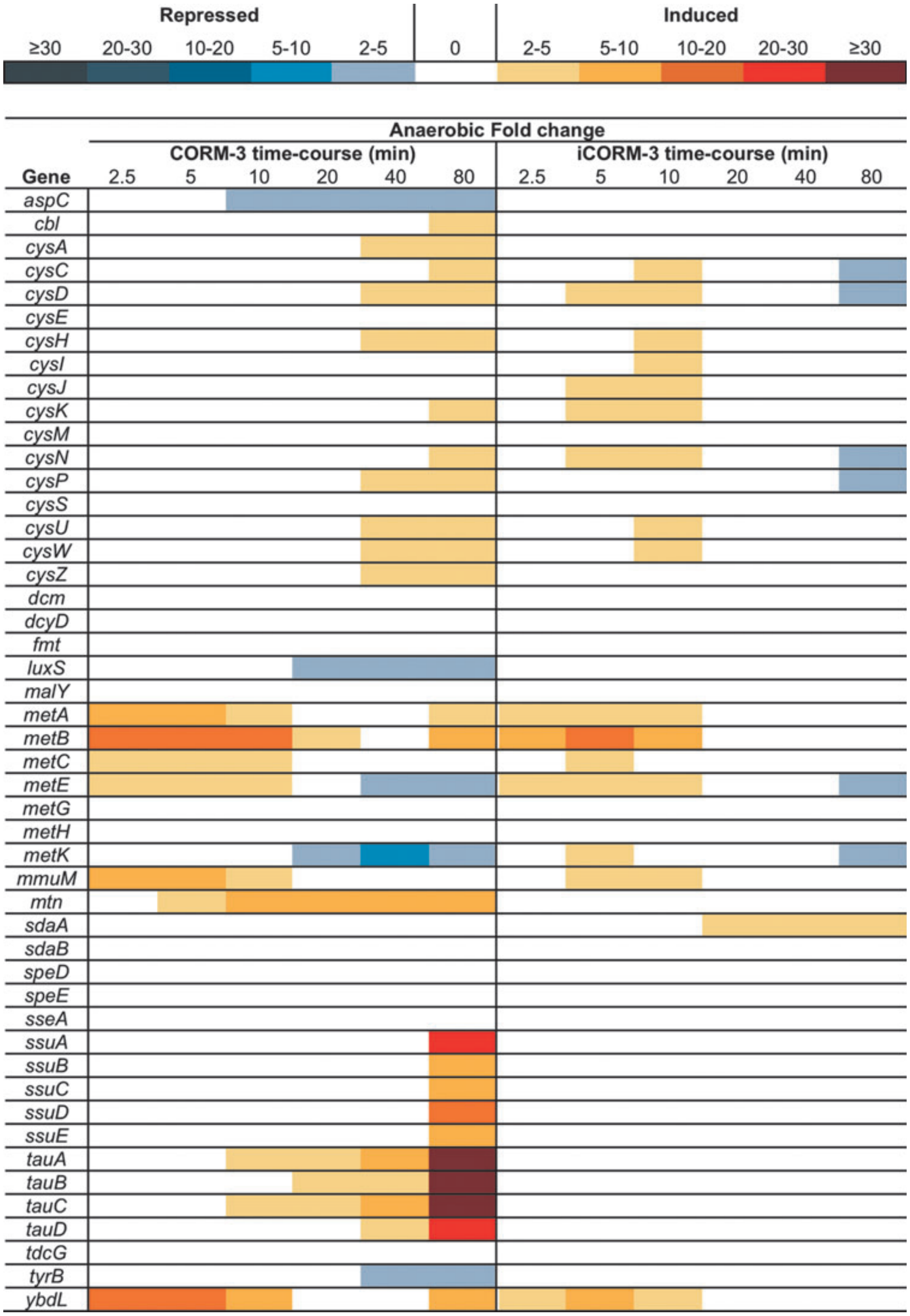
Repressed						Induced				
≥30	20-30	10-20	5-10	2-5	0	2-5	5-10	10-20	20-30	≥30

	Aerobic Fold change of genes involved in the TCA cycle											
	CORM-3 time-course (min)						iCORM-3 time-course (min)					
Gene	2.5	5	10	20	40	80	2.5	5	10	20	40	80
acnA	0.69	0.54	0.26	0.10	0.06	0.06	1.03	0.94	0.79	0.93	1.07	1.31
acnB	0.56	0.39	0.18	0.09	0.08	0.09	1.08	0.91	1.14	1.33	0.89	1.07
citD	0.70	1.27	1.02	1.54	1.60	1.31	0.99	0.95	0.92	0.90	1.03	0.91
citE	1.41	1.23	1.29	1.38	1.07	1.34	1.04	1.30	1.13	1.18	1.15	1.61
citF	0.92	1.16	1.63	1.21	1.31	1.38	0.96	0.85	1.00	0.93	0.95	1.04
frdA	1.05	1.00	0.81	0.61	0.42	0.40	0.95	0.96	0.87	0.82	0.84	0.80
frdB	1.01	1.07	0.93	0.70	0.43	0.39	0.93	1.02	0.91	0.86	0.85	0.85
frdC	1.06	1.10	0.92	0.73	0.49	0.43	1.02	1.09	0.93	0.90	0.95	0.92
frdD	1.11	1.19	1.03	0.83	0.65	0.60	1.09	1.19	0.99	0.92	0.96	0.91
fumA	0.63	0.37	0.14	0.09	0.07	0.07	0.99	1.24	1.11	1.00	0.77	0.89
fumB	0.82	0.60	0.47	0.45	0.36	0.38	1.08	1.22	1.26	1.04	0.80	0.90
fumC	0.70	0.37	0.12	0.11	0.10	0.09	0.91	1.19	1.20	1.31	0.82	0.88
gltA	0.59	0.49	0.37	0.23	0.13	0.14	1.04	1.04	1.12	1.23	0.94	1.29
icd	0.68	0.51	0.31	0.28	0.33	0.38	1.14	1.04	1.08	1.25	1.01	1.11
lpd	0.80	0.63	0.37	0.15	0.09	0.10	0.95	0.96	1.01	1.14	0.90	0.94
mdh	0.82	0.72	0.47	0.23	0.11	0.11	0.99	0.91	0.95	1.08	1.02	1.07
pck	0.96	0.89	0.66	0.34	0.15	0.21	0.95	0.99	0.97	1.02	0.88	0.94
sdhA	0.54	0.27	0.07	0.03	0.02	0.02	0.90	1.32	1.30	1.28	0.80	1.05
sdhB	0.52	0.27	0.08	0.03	0.03	0.03	0.93	1.26	1.27	1.30	0.74	1.04
sdhC	0.45	0.18	0.05	0.03	0.02	0.02	0.99	1.15	1.19	1.14	0.77	0.94
sdhD	0.47	0.20	0.06	0.03	0.02	0.02	0.99	1.16	1.18	1.12	0.76	0.93
sucA	0.70	0.43	0.13	0.08	0.08	0.09	0.92	1.01	1.26	1.27	0.74	1.04
sucB	0.71	0.46	0.13	0.08	0.07	0.07	1.01	0.91	1.19	1.34	0.74	1.04
sucC	0.72	0.58	0.15	0.06	0.05	0.05	0.99	0.82	1.20	1.44	0.70	1.06
sucD	0.70	0.64	0.18	0.08	0.06	0.05	1.02	0.91	1.20	1.52	0.75	1.19
ybiC	0.70	0.56	0.42	0.37	0.31	0.32	0.95	0.88	0.93	1.11	1.04	1.03

SUPPLEMENTARY FIG. S4. Differential expression of genes involved in the tricarboxylic (TCA) cycle after aerobic exposure to iCORM-3. The color-scale bar shows mean fold changes in individual genes of *E. coli* grown aerobically in Evans medium after the addition of 40 μM CORM-3 or iCORM-3.



SUPPLEMENTARY FIG. S5. Differential expression of genes after exposure to CO gas. *E. coli* cultures grown continuously in Evans medium were exposed to $50\,\mathrm{ml}\cdot\mathrm{min}^{-1}$ CO gas. Cell samples were extracted immediately before and at several times after turning on the CO gas flow. RNA extracted from the samples was processed for real time PCR analysis of the changes in expression level of the genes *dppB*, *cyoD*, *spy*, and *oppB*. Gene expression changes of less than twofold were deemed insignificant. $N = 2$ biological repeats ± standard error of the mean.



SUPPLEMENTARY FIG. S6. Differential expression of genes involved in sulfate transport and metabolism. The color-scale bar shows mean fold changes in individual genes of *E. coli* grown anaerobically in Evans medium after the addition of 40 μM CORM-3 or iCORM-3.

Supplementary Table S1A. Mean Activity Profiles for All Transcription Factors Under Exposure to CORM-3 in Aerobic Growth Conditions

	Time (min)						
Transcription factor name	*0*	*2.5*	*5*	*10*	*20*	*40*	*80*
AraC	−0.0375	−0.1158	−0.1976	−0.1709	0.1032	0.3430	0.3194
ArcA	−0.0078	−0.3785	−1.0034	−1.5690	−1.4358	−1.4530	−1.5768
CpxR	0.0102	1.2877	2.0750	2.8660	2.9912	3.1667	3.1944
CRP	−0.0011	−0.3191	−0.6597	−1.3364	−1.6404	−1.9034	−1.8769
CusR	−0.0408	−2.0635	−2.5208	−2.3905	−1.7917	−1.3532	−1.0940
DgsA	−0.0038	−0.0488	−0.1101	−0.2967	−0.8353	−1.4055	−1.0270
EvgA	−0.0141	−0.1191	−0.4179	−0.9093	−0.9348	−0.9164	−0.7216
Fis	−0.0134	−0.2268	−0.4658	−0.7798	−0.8546	−0.8832	−0.8767
FlhDC	0.0043	0.1122	0.3088	0.6095	0.9657	1.5041	1.8917
FNR	0.0049	0.0634	0.1465	0.3038	0.3897	0.5156	0.5370
FruR	−0.0149	−0.0795	0.0508	0.4359	0.7075	0.8480	0.8158
Fur	0.0299	0.1702	0.2304	0.2836	0.4117	0.5155	0.5758
GadE	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
GadWX	−0.0090	−0.2137	−0.3089	−0.6237	−1.1218	−1.7434	−2.5133
GalR	−0.0510	−0.0786	−0.1270	−0.1910	−0.2548	−0.3022	−0.3325
GalS	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
GcvA	−0.0270	−2.1923	−2.5217	−2.5920	−2.5053	−0.5966	−0.4368
GlcC	−0.0691	−0.5447	−0.9962	−1.4801	−1.6028	−1.5984	−1.7161
HNS	−0.0103	−0.1771	−0.3647	−0.6842	−0.8975	−1.0229	−1.0366
IclR	−0.1002	−0.3720	−0.7172	−1.1589	−1.4212	−1.3820	−1.5543
IHF	−0.0020	−0.0893	−0.0528	0.1120	0.5889	1.2222	1.0637
IscR	0.0079	0.1751	0.4817	0.9980	1.2128	1.3772	1.2905
Lrp	0.0039	0.1255	0.2635	0.6298	1.0200	1.3419	1.3948
MalT	−0.0005	−0.0107	−0.0364	−0.0868	−0.9450	−1.8497	−1.7347
MarA	−0.0282	−0.1847	−0.4897	−0.9625	−1.1151	−1.2072	−1.2609
MhpR	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
ModE	0.0026	0.0139	0.0821	0.1902	0.3555	0.4738	0.3944
Nac	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
NarL	0.0046	0.0374	0.0261	−0.0350	−0.2347	−0.4194	−0.4280
NarP	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
NtrC	−0.0064	−0.0126	−0.0724	−0.9549	−2.4091	−3.0001	−2.8697
OmpR	0.0649	0.3120	0.6075	0.9476	0.9066	0.7141	0.6702
PdhR	−0.0056	−0.0144	0.1893	1.1883	2.1385	2.4406	2.3022
PhoP	−0.0405	−0.6730	−1.1429	−1.5569	−1.7711	−1.7381	−1.4890
RstA	0.0049	0.0070	−0.0212	−0.1537	−0.4565	−1.2126	−2.1338
YdeO	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

CORM-3, Ru(CO)$_3$Cl(glycinate).

Supplementary Table S1B. Errors (Two Standard Deviations) for All Transcription Factors Exposed to CORM-3 Under Aerobic Growth Conditions

	Time (min)						
Transcription factor name	*0*	*2.5*	*5*	*10*	*20*	*40*	*80*
AraC	0.2503	0.2256	0.2238	0.2237	0.2238	0.2256	0.2503
ArcA	0.1059	0.1049	0.1049	0.1049	0.1049	0.1049	0.1059
CpxR	0.1089	0.1085	0.1085	0.1085	0.1085	0.1085	0.1089
CRP	0.0478	0.0476	0.0476	0.0476	0.0476	0.0476	0.0478
CusR	0.2315	0.2299	0.2299	0.2299	0.2299	0.2299	0.2315
DgsA	0.2408	0.2326	0.2326	0.2326	0.2326	0.2326	0.2408
EvgA	0.1998	0.1904	0.1903	0.1903	0.1903	0.1904	0.1998
Fis	0.0940	0.0916	0.0916	0.0916	0.0916	0.0916	0.0940
FlhDC	0.1431	0.1407	0.1407	0.1407	0.1407	0.1407	0.1431
FNR	0.0764	0.0740	0.0740	0.0740	0.0740	0.0740	0.0764
FruR	0.1448	0.1386	0.1385	0.1385	0.1385	0.1386	0.1448
Fur	0.1221	0.1138	0.1136	0.1136	0.1136	0.1138	0.1221
GadE	0.1916	0.1700	0.1678	0.1675	0.1678	0.1700	0.1916
GadWX	0.1986	0.1955	0.1955	0.1955	0.1955	0.1955	0.1986
GalR	0.2757	0.2396	0.2303	0.2285	0.2303	0.2396	0.2757
GalS	0.2914	0.2534	0.2424	0.2402	0.2424	0.2534	0.2914
GcvA	0.2246	0.2238	0.2238	0.2238	0.2238	0.2238	0.2246
GlcC	0.2762	0.2630	0.2628	0.2628	0.2628	0.2630	0.2762
HNS	0.0949	0.0926	0.0926	0.0926	0.0926	0.0926	0.0949
IclR	0.3830	0.3515	0.3498	0.3498	0.3498	0.3515	0.3830
IHF	0.0620	0.0618	0.0618	0.0618	0.0618	0.0618	0.0620
IscR	0.1507	0.1466	0.1466	0.1466	0.1466	0.1466	0.1507
Lrp	0.1291	0.1262	0.1262	0.1262	0.1262	0.1262	0.1291
MalT	0.2429	0.2384	0.2384	0.2384	0.2384	0.2384	0.2429
MarA	0.2192	0.2074	0.2072	0.2072	0.2072	0.2074	0.2192
MhpR	0.2914	0.2534	0.2424	0.2402	0.2424	0.2534	0.2914
ModE	0.1147	0.1076	0.1074	0.1074	0.1074	0.1076	0.1147
Nac	0.4046	0.3600	0.3396	0.3338	0.3396	0.3600	0.4046
NarL	0.0995	0.0946	0.0946	0.0946	0.0946	0.0946	0.0995
NarP	0.1300	0.1204	0.1201	0.1201	0.1201	0.1204	0.1300
NtrC	0.2192	0.2171	0.2171	0.2171	0.2171	0.2171	0.2192
OmpR	0.2604	0.2413	0.2406	0.2406	0.2406	0.2413	0.2604
PdhR	0.2183	0.2152	0.2152	0.2152	0.2152	0.2152	0.2183
PhoP	0.2023	0.1972	0.1972	0.1972	0.1972	0.1972	0.2023
RstA	0.3045	0.2965	0.2965	0.2965	0.2965	0.2965	0.3045
YdeO	0.4046	0.3600	0.3396	0.3338	0.3396	0.3600	0.4046

Supplementary Table S2A. Mean Activity Profiles for All Transcription Factors Under Exposure to iCORM-3 in Aerobic Growth Conditions

	Time (min)						
Transcription factor name	*0*	*2.5*	*5*	*10*	*20*	*40*	*80*
AraC	0.0344	0.0632	0.1993	0.2964	0.4324	0.5317	0.5219
ArcA	−0.0072	0.1140	0.3571	0.5702	0.5041	−0.6695	0.0362
CpxR	−0.0230	−0.4315	−0.7029	−0.9524	−1.1929	−1.2993	−1.4339
CRP	0.0107	0.2972	0.5886	0.6042	0.3863	0.0881	0.0613
CusR	0.0064	0.0767	0.2624	0.3074	0.3611	1.4230	1.8673
DgsA	−0.1435	−0.2629	−0.3002	−0.2902	−0.3160	−0.3940	−0.4306
EvgA	0.0175	0.3860	−0.0482	0.3331	0.2202	−0.6825	−0.9338
Fis	−0.0211	−0.1571	−0.2828	−0.3788	−0.4435	−0.6537	−0.3597
FlhDC	0.0060	0.1454	−0.3799	−0.7532	−0.8838	−0.4385	−0.0049
FNR	0.0153	0.1756	0.0932	0.2786	0.4304	0.3981	0.6080
FruR	0.0578	0.2268	0.3003	0.3521	0.2162	0.0718	−0.0129
Fur	−0.0129	−0.2449	0.1054	−0.3225	−0.2586	−0.5001	−0.2467
GadE	0.0326	0.4645	0.7897	1.0726	1.4276	1.1069	0.8841
GadWX	0.0733	0.1772	0.3387	0.4754	0.6446	0.6882	0.6489
GalR	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
GalS	−0.1210	−0.1950	−0.2629	−0.3462	−0.4927	−0.5994	−0.6277
GcvA	−0.0140	−3.3009	−3.6403	−3.7035	−0.5600	0.0223	0.1042
GlcC	−0.2607	−0.3854	−0.3865	−0.3652	−0.3756	−0.3812	−0.3369
HNS	0.0436	0.3612	0.4940	0.6300	0.5620	0.3667	0.1630
IclR	0.2348	0.2790	0.3174	0.3403	0.3254	0.3500	0.3892
IHF	−0.0011	0.1786	−0.3810	−0.8515	−0.8548	0.0025	0.1747
IscR	−0.0309	−0.3973	−0.5041	−0.8090	−1.0483	−0.6137	−0.7131
Lrp	0.0037	0.2689	1.2866	1.3686	0.3871	−0.1614	−0.0636
MalT	−0.0676	−0.4361	−0.7291	−0.6845	−1.0627	−0.7701	−0.5687
MarA	−0.0235	−0.1145	−0.3028	−0.4290	−0.4911	−0.0812	−0.0153
MhpR	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
ModE	0.0017	0.0140	−0.0252	−0.0993	−0.1277	−0.1953	−0.2680
Nac	−0.0178	−0.5754	−1.2341	−2.1660	−2.6450	−1.3003	0.1590
NarL	−0.0143	−0.0794	−0.0628	−0.1152	−0.1734	−0.2046	−0.2520
NarP	−0.0161	−0.5332	−1.0383	−0.4148	−0.1167	0.2095	0.4814
NtrC	−0.0038	−0.9136	−1.4144	−0.4231	0.7601	1.0157	0.7029
OmpR	0.0267	0.1823	0.4082	0.3388	−0.0197	−0.3517	−0.6866
PdhR	0.0870	0.1628	0.1965	0.1444	0.1261	0.1780	0.2037
PhoP	−0.0597	−0.1407	−0.3275	−0.4131	−0.5052	−0.5485	−0.5512
RstA	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
YdeO	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

iCORM-3, inactivated CORM-3.

Supplementary Table S2B. Errors (Two Standard Deviations) for All Transcription Factors Exposed to iCORM-3 Under Aerobic Growth Conditions

	Time (min)						
Transcription factor name	*0*	*2.5*	*5*	*10*	*20*	*40*	*80*
AraC	0.2360	0.2060	0.2005	0.1997	0.2005	0.2060	0.2360
ArcA	0.1154	0.1149	0.1148	0.1148	0.1148	0.1149	0.1154
CpxR	0.1327	0.1291	0.1291	0.1291	0.1291	0.1291	0.1327
CRP	0.0513	0.0505	0.0505	0.0505	0.0505	0.0505	0.0513
CusR	0.3191	0.3091	0.3090	0.3090	0.3090	0.3091	0.3191
DgsA	0.2336	0.2040	0.1987	0.1980	0.1987	0.2040	0.2336
EvgA	0.2326	0.2282	0.2282	0.2282	0.2282	0.2282	0.2326
Fis	0.1012	0.0960	0.0959	0.0959	0.0959	0.0960	0.1012
FlhDC	0.1648	0.1619	0.1619	0.1619	0.1619	0.1619	0.1648
FNR	0.0832	0.0801	0.0801	0.0801	0.0801	0.0801	0.0832
FruR	0.1455	0.1331	0.1325	0.1325	0.1325	0.1331	0.1455
Fur	0.1410	0.1378	0.1378	0.1378	0.1378	0.1378	0.1410
GadE	0.2160	0.2083	0.2083	0.2083	0.2083	0.2083	0.2160
GadWX	0.1967	0.1741	0.1715	0.1713	0.1715	0.1741	0.1967
GalR	0.3074	0.2676	0.2550	0.2522	0.2550	0.2676	0.3074
GalS	0.2611	0.2270	0.2192	0.2178	0.2192	0.2270	0.2611
GcvA	0.1801	0.1799	0.1799	0.1799	0.1799	0.1799	0.1801
GlcC	0.2889	0.2511	0.2404	0.2383	0.2404	0.2511	0.2889
HNS	0.0975	0.0928	0.0928	0.0928	0.0928	0.0928	0.0975
IclR	0.3963	0.3518	0.3319	0.3263	0.3319	0.3518	0.3963
IHF	0.0686	0.0685	0.0685	0.0685	0.0685	0.0685	0.0686
IscR	0.1681	0.1631	0.1630	0.1630	0.1630	0.1631	0.1681
Lrp	0.1537	0.1529	0.1529	0.1529	0.1529	0.1529	0.1537
MalT	0.2780	0.2616	0.2613	0.2612	0.2613	0.2616	0.2780
MarA	0.2435	0.2244	0.2236	0.2236	0.2236	0.2244	0.2435
MhpR	0.3074	0.2676	0.2550	0.2522	0.2550	0.2676	0.3074
ModE	0.1284	0.1191	0.1188	0.1188	0.1188	0.1191	0.1284
Nac	0.3395	0.3363	0.3363	0.3363	0.3363	0.3363	0.3395
NarL	0.1122	0.1055	0.1054	0.1054	0.1054	0.1055	0.1122
NarP	0.1480	0.1464	0.1464	0.1464	0.1464	0.1464	0.1480
NtrC	0.3916	0.3852	0.3852	0.3852	0.3852	0.3852	0.3916
OmpR	0.2978	0.2774	0.2768	0.2768	0.2768	0.2774	0.2978
PdhR	0.2395	0.2089	0.2031	0.2023	0.2031	0.2089	0.2395
PhoP	0.1992	0.1761	0.1734	0.1731	0.1734	0.1761	0.1992
RstA	0.3331	0.2911	0.2760	0.2723	0.2760	0.2911	0.3331
YdeO	0.4221	0.3775	0.3564	0.3502	0.3564	0.3775	0.4221

Supplementary Table S3A. Mean Activity Profiles for All Transcription Factors Under Exposure to CORM-3 in Anaerobic Growth Conditions

	Time (min)						
Transcription factor name	*0*	*2.5*	*5*	*10*	*20*	*40*	*80*
AraC	−0.1195	−0.1996	−0.2069	−0.1595	−0.1454	−0.1284	−0.1492
ArcA	−0.0223	−0.5382	−0.8849	−0.9845	−1.1432	−1.1255	−1.1140
CpxR	0.0118	0.9581	1.6374	2.4311	2.5704	2.6952	2.7699
CRP	0.0042	0.1074	0.1634	0.5571	0.9701	1.3153	1.3621
CusR	−0.0754	−0.3038	−0.5924	−0.6059	−0.4338	−0.1932	0.1863
DgsA	0.1157	0.4586	0.5844	0.5006	0.2508	0.1759	0.2031
EvgA	−0.0594	−0.3082	−0.5346	−0.8814	−0.9401	−1.0109	−1.1680
Fis	−0.0213	−0.6754	−0.7676	−0.8417	−1.0117	−1.0222	−1.3811
FlhDC	0.0157	0.2338	−0.3496	−0.6626	−0.6120	−0.7020	−0.6438
FNR	0.0063	0.0775	0.1511	0.3508	0.4930	0.5981	0.7197
FruR	0.0020	−0.0239	−0.1465	−0.3739	−0.6219	−0.8499	−0.9730
Fur	0.0085	0.0504	0.1296	0.2735	0.4851	0.5549	0.7397
GadE	−0.0063	−0.0687	−0.2030	−0.5672	−0.9969	−1.5148	−1.9828
GadWX	0.0023	0.0138	−0.0354	−0.3704	−1.0026	−2.1600	−3.0373
GalR	−0.0259	−0.0337	−0.0608	−0.1183	−0.1712	−0.2067	−0.2251
GalS	0.0887	0.3938	0.1385	0.0162	−0.2544	−0.6204	−0.8161
GcvA	−0.0543	−0.7826	−1.7596	−1.9600	−1.7925	−1.3422	−0.5754
GlcC	−0.0198	−0.0315	−0.1716	−0.2387	−0.3170	−0.4088	−0.4685
HNS	0.0135	0.4189	0.4658	1.2526	0.8943	1.2034	1.1448
IclR	0.1658	0.4285	0.8863	1.0226	0.9863	0.9328	0.8672
IHF	0.0001	0.0071	0.0618	0.2143	0.6099	1.0273	1.5104
IscR	0.0094	0.1124	0.4003	0.6994	1.0224	1.2949	1.6212
Lrp	0.0068	0.1683	0.4369	0.7852	1.1287	1.4510	1.6708
MalT	−0.0054	−0.0657	−0.8681	−1.7825	−2.3454	−2.5155	−1.7087
MarA	0.0502	0.2313	0.3871	0.5950	0.7654	1.0269	1.2051
MhpR	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
ModE	−0.0203	−0.1098	−0.2232	−0.3622	−0.4008	−0.3721	−0.3904
Nac	0.0326	0.3643	0.7945	1.2086	1.7668	2.4719	2.6480
NarL	0.0130	0.0902	0.1098	0.1684	0.2257	0.2991	0.3698
NarP	0.0066	0.1997	−0.0225	−0.4145	0.1706	−0.0059	−0.1305
NtrC	0.0109	0.2405	1.1031	1.1248	1.4888	2.4608	2.5381
OmpR	0.0066	0.1350	−0.1468	−1.2851	−2.0410	−1.8885	−1.6229
PdhR	−0.0700	−0.6581	−0.8081	−0.9407	−0.5634	−0.2415	0.1010
PhoP	0.0221	0.3045	0.8328	1.1882	1.3902	1.7917	2.0414
RstA	0.0089	0.0645	0.0157	−0.2900	−0.7608	−1.2604	−1.9800
YdeO	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

Supplementary Table S3B. Errors (Two Standard Deviations) for All Transcription Factors Exposed to CORM-3 Under Anaerobic Growth Conditions

	Time (min)						
Transcription factor name	*0*	*2.5*	*5*	*10*	*20*	*40*	*80*
AraC	0.2567	0.2233	0.2159	0.2146	0.2159	0.2233	0.2567
ArcA	0.1065	0.1047	0.1047	0.1047	0.1047	0.1047	0.1065
CpxR	0.1189	0.1183	0.1183	0.1183	0.1183	0.1183	0.1189
CRP	0.0524	0.0521	0.0521	0.0521	0.0521	0.0521	0.0524
CusR	0.3272	0.3007	0.2995	0.2994	0.2995	0.3007	0.3272
DgsA	0.2441	0.2237	0.2227	0.2227	0.2227	0.2237	0.2441
EvgA	0.2269	0.2112	0.2107	0.2107	0.2107	0.2112	0.2269
Fis	0.1022	0.1010	0.1010	0.1010	0.1010	0.1010	0.1022
FlhDC	0.1636	0.1589	0.1589	0.1589	0.1589	0.1589	0.1636
FNR	0.0797	0.0770	0.0770	0.0770	0.0770	0.0770	0.0797
FruR	0.1468	0.1393	0.1392	0.1392	0.1392	0.1393	0.1468
Fur	0.1304	0.1223	0.1221	0.1221	0.1221	0.1223	0.1304
GadE	0.2002	0.1951	0.1951	0.1951	0.1951	0.1951	0.2002
GadWX	0.1997	0.1980	0.1979	0.1979	0.1979	0.1980	0.1997
GalR	0.2907	0.2527	0.2418	0.2396	0.2418	0.2527	0.2907
GalS	0.3225	0.2984	0.2975	0.2974	0.2975	0.2984	0.3225
GcvA	0.3608	0.3514	0.3514	0.3514	0.3514	0.3514	0.3608
GlcC	0.2605	0.2265	0.2187	0.2174	0.2187	0.2265	0.2605
HNS	0.1088	0.1079	0.1079	0.1079	0.1079	0.1079	0.1088
IclR	0.4364	0.3907	0.3860	0.3855	0.3860	0.3907	0.4364
IHF	0.0674	0.0670	0.0670	0.0670	0.0670	0.0670	0.0674
IscR	0.1564	0.1519	0.1519	0.1519	0.1519	0.1519	0.1564
Lrp	0.1361	0.1331	0.1331	0.1331	0.1331	0.1331	0.1361
MalT	0.2362	0.2330	0.2330	0.2330	0.2330	0.2330	0.2362
MarA	0.2246	0.2079	0.2074	0.2073	0.2074	0.2079	0.2246
MhpR	0.3601	0.3166	0.2991	0.2946	0.2991	0.3166	0.3601
ModE	0.1217	0.1135	0.1133	0.1133	0.1133	0.1135	0.1217
Nac	0.2994	0.2892	0.2892	0.2892	0.2892	0.2892	0.2994
NarL	0.1069	0.1010	0.1009	0.1009	0.1009	0.1010	0.1069
NarP	0.1394	0.1369	0.1369	0.1369	0.1369	0.1369	0.1394
NtrC	0.2556	0.2507	0.2507	0.2507	0.2507	0.2507	0.2556
OmpR	0.2617	0.2572	0.2572	0.2572	0.2572	0.2572	0.2617
PdhR	0.2607	0.2503	0.2502	0.2502	0.2502	0.2503	0.2607
PhoP	0.2062	0.2001	0.2000	0.2000	0.2000	0.2001	0.2062
RstA	0.3215	0.3090	0.3088	0.3088	0.3088	0.3090	0.3215
YdeO	0.4135	0.3689	0.3481	0.3421	0.3481	0.3689	0.4135

Supplementary Table S4A. Mean Activity Profiles for All Transcription Factors Under Exposure to iCORM-3 in Anaerobic Growth Conditions

	Time (min)						
Transcription factor name	*0*	*2.5*	*5*	*10*	*20*	*40*	*80*
AraC	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
ArcA	−0.0099	−0.2795	−0.0946	−0.5280	−1.0861	−1.4489	−1.6155
CpxR	0.0000	−0.0634	−0.2704	−0.7054	−1.8295	−3.1800	−3.0599
CRP	−0.0016	−0.2537	−0.4625	−1.2335	−1.8434	−1.1522	−0.5620
CusR	0.0939	0.4395	0.0252	−0.3989	−0.6497	−0.5834	−0.4532
DgsA	0.0079	0.3595	0.7266	1.6838	2.8290	2.4081	1.1063
EvgA	−0.0006	−0.2922	−0.1697	0.4488	2.3979	0.0395	0.1936
Fis	−0.0003	0.0430	−0.3168	−0.6995	−0.9879	−0.8087	−0.6400
FlhDC	0.0022	0.0687	−0.1782	−0.6035	−0.8232	0.1062	0.0493
FNR	0.0110	0.0959	−0.0741	−0.1983	−0.3396	−0.3887	−0.3838
FruR	0.0114	0.2537	0.4867	0.9642	1.2185	0.8321	0.2319
Fur	−0.0357	−0.4292	−0.1730	−0.0490	−0.2613	−0.3714	−0.2643
GadE	0.0025	0.0074	0.0729	0.1501	0.2865	0.4412	0.4807
GadWX	−0.0150	−0.3249	−0.4738	−0.7354	−1.5400	−2.2786	−1.8780
GalR	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
GalS	−0.1249	−0.1997	−0.2864	−0.4234	−0.5328	−0.6261	−0.6463
GcvA	−0.0367	−1.8353	−2.9792	−2.5143	−2.0607	−1.7648	−0.3492
GlcC	0.3152	0.4891	0.5409	0.5809	0.6274	0.6192	0.5609
HNS	−0.0104	−0.3021	−0.4481	−0.8683	−1.2594	−1.5159	−1.0975
IclR	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
IHF	0.0124	0.2095	0.2805	0.5244	0.6334	0.8407	0.7168
IscR	0.0105	0.2995	0.6267	0.9882	1.6714	1.8624	1.4837
Lrp	0.0038	0.1585	0.5461	0.9155	1.4136	0.9458	0.0107
MalT	−0.0283	−0.4761	−0.8421	−1.7604	−1.4214	−0.9717	−0.4010
MarA	0.0214	0.0409	0.1176	0.2192	0.3255	0.3840	0.3777
MhpR	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
ModE	0.0143	0.0639	0.0795	0.0509	0.0466	0.0692	0.0601
Nac	0.0667	0.7813	0.8032	1.7379	1.5138	1.1428	−0.1322
NarL	0.0263	0.1698	0.2962	0.4117	0.5059	0.4796	0.2865
NarP	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
NtrC	−0.0173	−1.9391	−1.2967	−3.0441	−2.2130	−1.2538	0.2144
OmpR	−0.0119	−0.0443	0.3053	0.5870	0.7269	0.5574	0.4878
PdhR	−0.0654	−0.6780	−1.0235	−1.6388	−1.8800	−1.7024	−1.6209
PhoP	0.0002	0.0038	0.4563	1.0008	1.6259	2.2132	2.7256
RstA	0.0068	0.1673	−0.1592	−0.1371	0.1674	1.1822	2.5124
YdeO	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

Supplementary Table S4B. Errors (Two Standard Deviations) for All Transcription Factors Exposed to iCORM-3 Under Anaerobic Growth Conditions

	Time (min)						
Transcription factor name	*0*	*2.5*	*5*	*10*	*20*	*40*	*80*
AraC	0.2783	0.2418	0.2322	0.2304	0.2322	0.2418	0.2783
ArcA	0.1185	0.1171	0.1171	0.1171	0.1171	0.1171	0.1185
CpxR	0.1306	0.1301	0.1301	0.1301	0.1301	0.1301	0.1306
CRP	0.0555	0.0555	0.0555	0.0555	0.0555	0.0555	0.0555
CusR	0.3657	0.3397	0.3388	0.3388	0.3388	0.3397	0.3657
DgsA	0.2417	0.2398	0.2398	0.2398	0.2398	0.2398	0.2417
EvgA	0.2443	0.2443	0.2443	0.2443	0.2443	0.2443	0.2443
Fis	0.1085	0.1067	0.1067	0.1067	0.1067	0.1067	0.1085
FlhDC	0.1742	0.1718	0.1718	0.1718	0.1718	0.1718	0.1742
FNR	0.0877	0.0842	0.0841	0.0841	0.0841	0.0842	0.0877
FruR	0.1693	0.1664	0.1664	0.1664	0.1664	0.1664	0.1693
Fur	0.1454	0.1401	0.1401	0.1401	0.1401	0.1401	0.1454
GadE	0.1969	0.1743	0.1717	0.1715	0.1717	0.1743	0.1969
GadWX	0.2380	0.2333	0.2333	0.2333	0.2333	0.2333	0.2380
GalR	0.3148	0.2743	0.2610	0.2579	0.2610	0.2743	0.3148
GalS	0.2665	0.2317	0.2233	0.2218	0.2233	0.2317	0.2665
GcvA	0.2729	0.2709	0.2709	0.2709	0.2709	0.2709	0.2729
GlcC	0.2751	0.2391	0.2299	0.2281	0.2299	0.2391	0.2751
HNS	0.1196	0.1179	0.1179	0.1179	0.1179	0.1179	0.1196
IclR	0.4304	0.3860	0.3645	0.3582	0.3645	0.3860	0.4304
IHF	0.0696	0.0677	0.0677	0.0677	0.0677	0.0677	0.0696
IscR	0.1738	0.1706	0.1706	0.1706	0.1706	0.1706	0.1738
Lrp	0.1703	0.1684	0.1684	0.1684	0.1684	0.1684	0.1703
MalT	0.2993	0.2925	0.2925	0.2925	0.2925	0.2925	0.2993
MarA	0.2286	0.1999	0.1951	0.1944	0.1951	0.1999	0.2286
MhpR	0.3148	0.2743	0.2610	0.2579	0.2610	0.2743	0.3148
ModE	0.1344	0.1240	0.1237	0.1237	0.1237	0.1240	0.1344
Nac	0.4993	0.4866	0.4865	0.4865	0.4865	0.4866	0.4993
NarL	0.1128	0.1060	0.1059	0.1059	0.1059	0.1060	0.1128
NarP	0.1469	0.1342	0.1336	0.1336	0.1336	0.1342	0.1469
NtrC	0.2395	0.2389	0.2389	0.2389	0.2389	0.2389	0.2395
OmpR	0.2967	0.2703	0.2688	0.2687	0.2688	0.2703	0.2967
PdhR	0.2628	0.2535	0.2534	0.2534	0.2534	0.2535	0.2628
PhoP	0.2142	0.2105	0.2105	0.2105	0.2105	0.2105	0.2142
RstA	0.3358	0.3313	0.3312	0.3312	0.3312	0.3313	0.3358
YdeO	0.4304	0.3860	0.3645	0.3582	0.3645	0.3860	0.4304