# The *las* and *rhl* Quorum Sensing Systems in *Pseudomonas aeruginosa* Form a Multi-Signal Reciprocal Network Which Can Tune Reactivity to Variations in Physical and Social Environments

## Supporting Information

### Structured Literature Search

The PubMed database of the US National Institutes of Health was queried on 20 July 2021 using the query [PubMed Search ("review"[Title/Abstract] OR "review"[Publication Type]) AND "quorum sensing"[Title] AND "pseudomonas aeruginosa"[Title/Abstract]](https://pubmed.ncbi.nlm.nih.gov/?term=%28%22review%22%5BTitle%2FAbstract%5D+OR+%22review%22%5BPublication+Type%5D%29+AND+%22quorum+sensing%22%5BTitle%5D+AND+%22pseudomonas+aeruginosa%22%5BTitle%2FAbstract%5D&sort=), resulting in 76 results with publication dates from 1996 to 2021. Papers that incluced a daigram of the gene transcription networks for the *las* and *rhl* quorum sensing systems were further analyzed to show the interactions present on those diagrams. Tables S.1 and S.2 show the results. Of the papers analyzed, all show the *las* system positively activating the *rhl* system, and none show the *rhl* system postively activating the *las* system.

| Paper | PMID | →*lasI* | →*lasR* | →*rhlI* | →*rhlR* | →elastase |
| --- | --- | --- | --- | --- | --- | --- |
| (García-Reyes, Soberón-Chávez, and Cocotl-Yanez 2020) | [31794380](https://pubmed.ncbi.nlm.nih.gov/31794380/) | ● | ○ | ● | ● | ● |
| (Rutherford and Bassler 2012) | [23125205](https://pubmed.ncbi.nlm.nih.gov/23125205/) | ● | ○ | ● | ● |  |
| (Proctor, McCarron, and Ternan 2020) | [31971503](https://pubmed.ncbi.nlm.nih.gov/31971503/) | ● | ○ | ○ | ● |  |
| (Jakobsen et al. 2013) | [23841636](https://pubmed.ncbi.nlm.nih.gov/23841636/) | ● | ○ | ● | ● |  |
| (Soukarieh et al. 2018) | [29999316](https://pubmed.ncbi.nlm.nih.gov/29999316/) | ● | ● | ● | ● |  |
| (Tateda 2005) | [15926474](https://pubmed.ncbi.nlm.nih.gov/15926474/) | ● | ○ | ● | ○ | ● |
| (Williams et al. 2007) | [19249239](https://pubmed.ncbi.nlm.nih.gov/19249239/) | ○ | ○ | ● | ● |  |
| (Heurlier, Dénervaud, and Haas 2006) | [16503417](https://pubmed.ncbi.nlm.nih.gov/16503417/) | ● | ○ | ● | ○ |  |
| (Le Berre et al. 2006) | [16631332](https://pubmed.ncbi.nlm.nih.gov/16631332/) | ○ | ○ | ● | ● |  |
| (Juhas, Eberl, and Tümmler 2005) | [15816912](https://pubmed.ncbi.nlm.nih.gov/15816912/) | ● | ● | ● | ● | ● |
| (Donabedian 2003) | [12799145](https://pubmed.ncbi.nlm.nih.gov/12799145/) | ● | ○ | ● | ● | ● |
| (Reuter, Steinbach, and Helms 2016) | [26819549](https://pubmed.ncbi.nlm.nih.gov/26819549/) | ● | ○ | ○ | ● | ● |
| (Yong and Zhong 2013) | [22767136](https://pubmed.ncbi.nlm.nih.gov/22767136/) | ● | ○ | ● | ● | ● |
| (Welsh and Blackwell 2016) | [27268906](https://pubmed.ncbi.nlm.nih.gov/27268906/) |  |  | ● | ● | ● |
| (De Sordi and Mühlschlegel 2009) | [19845041](https://pubmed.ncbi.nlm.nih.gov/19845041/) | ● | ○ | ● | ○ |  |
| (Winzer and Williams 2001) | [11437336](https://pubmed.ncbi.nlm.nih.gov/11437336/) | ● | ○ | ○ | ● | ● |
| (Schuster et al. 2013) | [23682605](https://pubmed.ncbi.nlm.nih.gov/23682605/) | ● | ○ | ● | ● |  |
| (Papaioannou, Utari, and Quax 2013) | [24065108](https://pubmed.ncbi.nlm.nih.gov/24065108/) | ● | ● | ○ | ● | ● |
| (Roy, Adams, and Bentley 2011) | [22112397](https://pubmed.ncbi.nlm.nih.gov/22112397/) | ● | ○ | ● | ● |  |

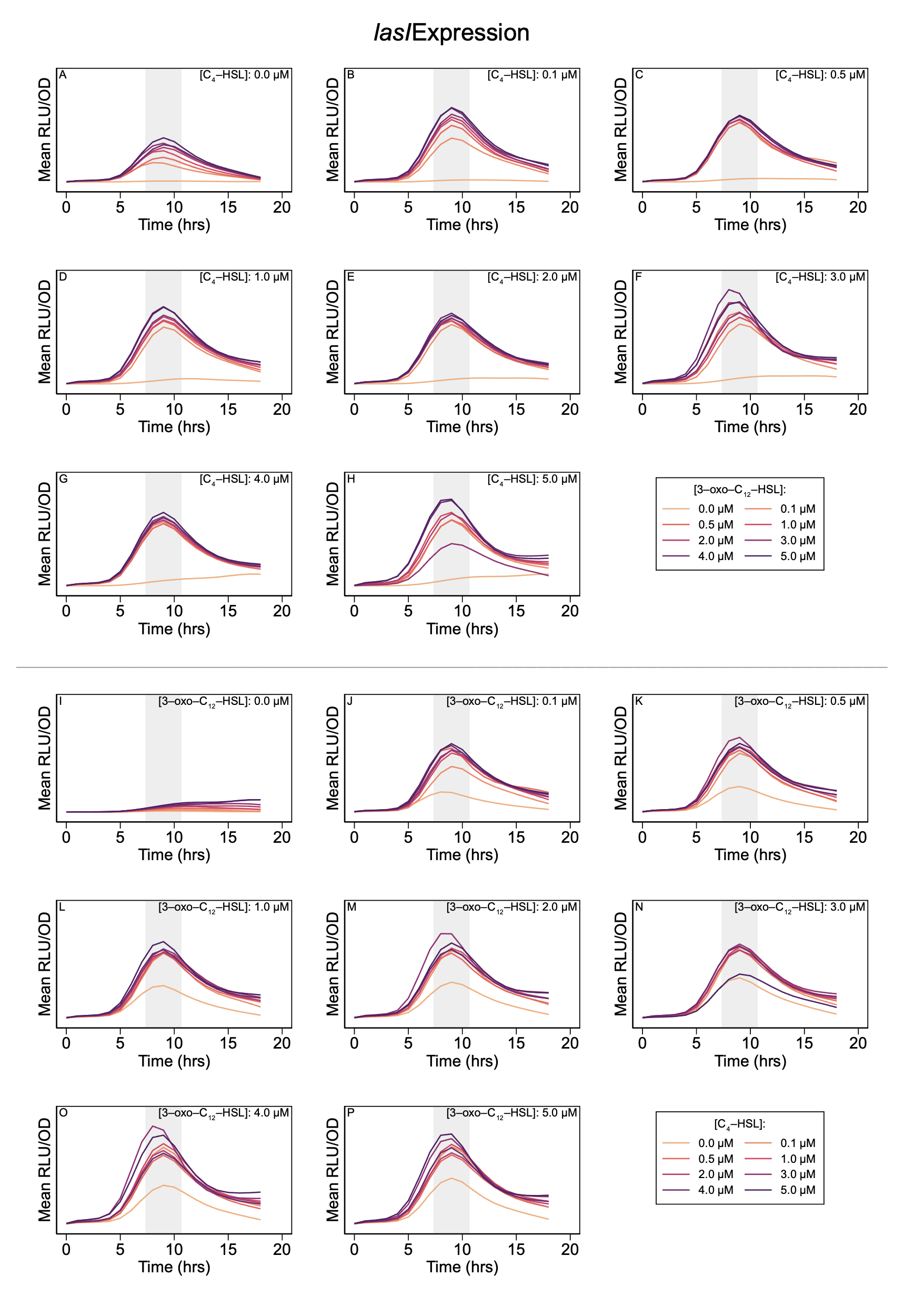
**Table S.1.** Activation of QS genes by LasR/3‑oxo‑C12‑HSL in review of published literature. Solid dots indicate positive activation in the paper’s diagram of gene transcription, while hollow dots indicate that the diagram shows no effect. No diagrams indicated repression. Note that some papers made no attempt to indicate particular interactions; several, for example, concentrated strictly on the QS genes themselves and did not show the effect on downstream genes such as those for elastase.

| Paper | PMID | →*lasI* | →*lasR* | →*rhlI* | →*rhlR* | →elastase |
| --- | --- | --- | --- | --- | --- | --- |
| (García-Reyes, Soberón-Chávez, and Cocotl-Yanez 2020) | [31794380](https://pubmed.ncbi.nlm.nih.gov/31794380/) | ○ | ○ | ○ | ○ | ● |
| (Rutherford and Bassler 2012) | [23125205](https://pubmed.ncbi.nlm.nih.gov/23125205/) | ○ | ○ | ● | ○ |  |
| (Proctor, McCarron, and Ternan 2020) | [31971503](https://pubmed.ncbi.nlm.nih.gov/31971503/) | ○ | ○ | ● | ○ |  |
| (Jakobsen et al. 2013) | [23841636](https://pubmed.ncbi.nlm.nih.gov/23841636/) | ○ | ○ | ● | ○ |  |
| (Soukarieh et al. 2018) | [29999316](https://pubmed.ncbi.nlm.nih.gov/29999316/) | ○ | ○ | ○ | ○ |  |
| (Tateda 2005) | [15926474](https://pubmed.ncbi.nlm.nih.gov/15926474/) | ○ | ○ | ● | ○ | ● |
| (Williams et al. 2007) | [19249239](https://pubmed.ncbi.nlm.nih.gov/19249239/) | ○ | ○ | ○ | ○ |  |
| (Heurlier, Dénervaud, and Haas 2006) | [16503417](https://pubmed.ncbi.nlm.nih.gov/16503417/) | ○ | ○ | ● | ○ |  |
| (Le Berre et al. 2006) | [16631332](https://pubmed.ncbi.nlm.nih.gov/16631332/) | ○ | ○ | ○ | ○ |  |
| (Juhas, Eberl, and Tümmler 2005) | [15816912](https://pubmed.ncbi.nlm.nih.gov/15816912/) | ○ | ○ | ● | ● | ● |
| (Donabedian 2003) | [12799145](https://pubmed.ncbi.nlm.nih.gov/12799145/) | ○ | ○ | ○ | ○ | ● |
| (Reuter, Steinbach, and Helms 2016) | [26819549](https://pubmed.ncbi.nlm.nih.gov/26819549/) | ○ | ○ | ○ | ○ | ● |
| (Yong and Zhong 2013) | [22767136](https://pubmed.ncbi.nlm.nih.gov/22767136/) | ○ | ○ | ● | ○ | ● |
| (Welsh and Blackwell 2016) | [27268906](https://pubmed.ncbi.nlm.nih.gov/27268906/) | ○ | ○ |  |  | ○ |
| (De Sordi and Mühlschlegel 2009) | [19845041](https://pubmed.ncbi.nlm.nih.gov/19845041/) | ○ | ○ | ● | ○ |  |
| (Winzer and Williams 2001) | [11437336](https://pubmed.ncbi.nlm.nih.gov/11437336/) | ○ | ○ | ● | ○ | ● |
| (Schuster et al. 2013) | [23682605](https://pubmed.ncbi.nlm.nih.gov/23682605/) | ○ | ○ | ● | ○ |  |
| (Papaioannou, Utari, and Quax 2013) | [24065108](https://pubmed.ncbi.nlm.nih.gov/24065108/) | ○ | ○ | ● | ○ | ● |
| (Roy, Adams, and Bentley 2011) | [22112397](https://pubmed.ncbi.nlm.nih.gov/22112397/) | ○ | ○ | ○ | ○ |  |

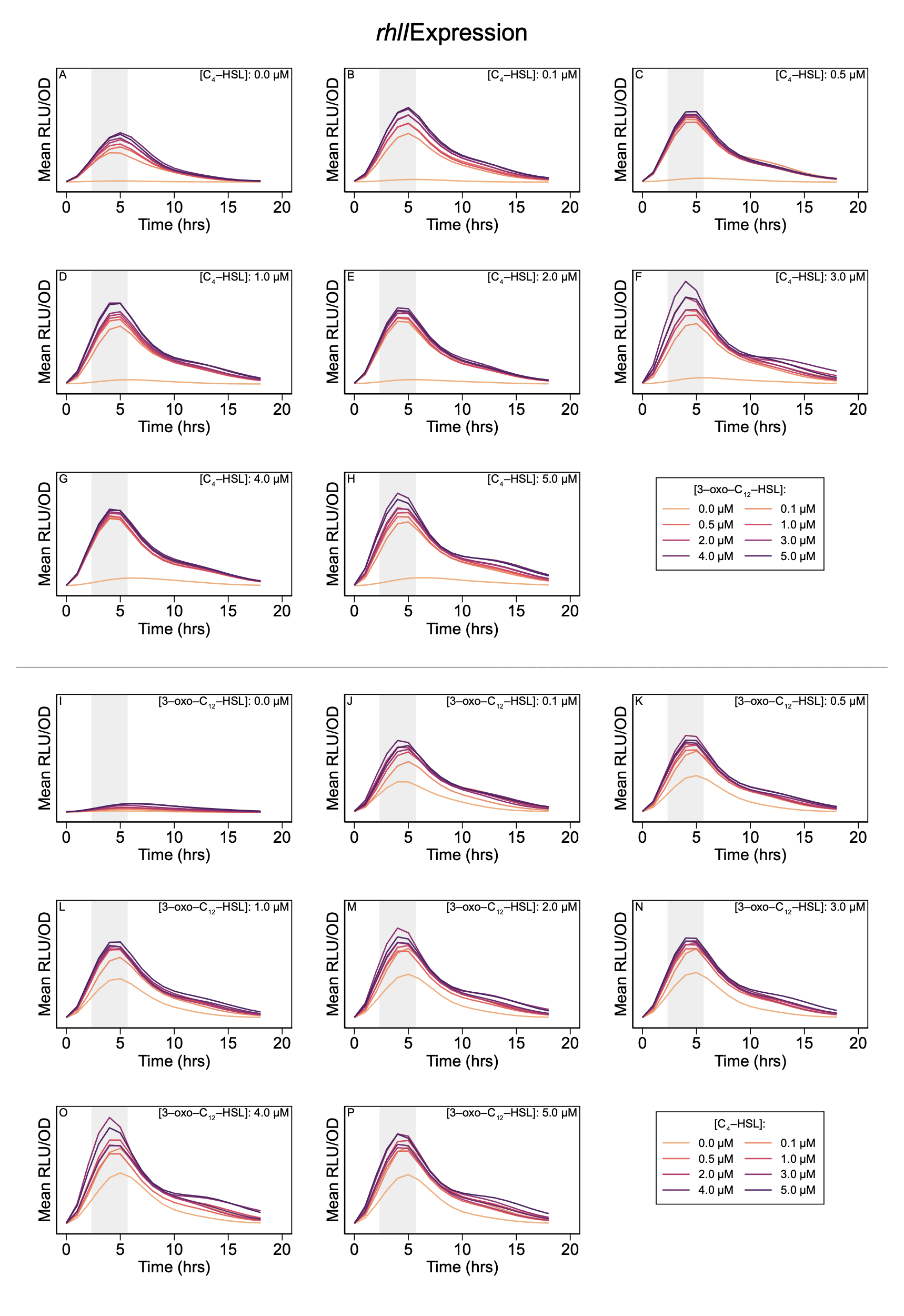
**Table S.2.** Activation of QS genes by RhlR/C4‑HSL in review of published literature. Same notation as previous table.

### Data Analysis

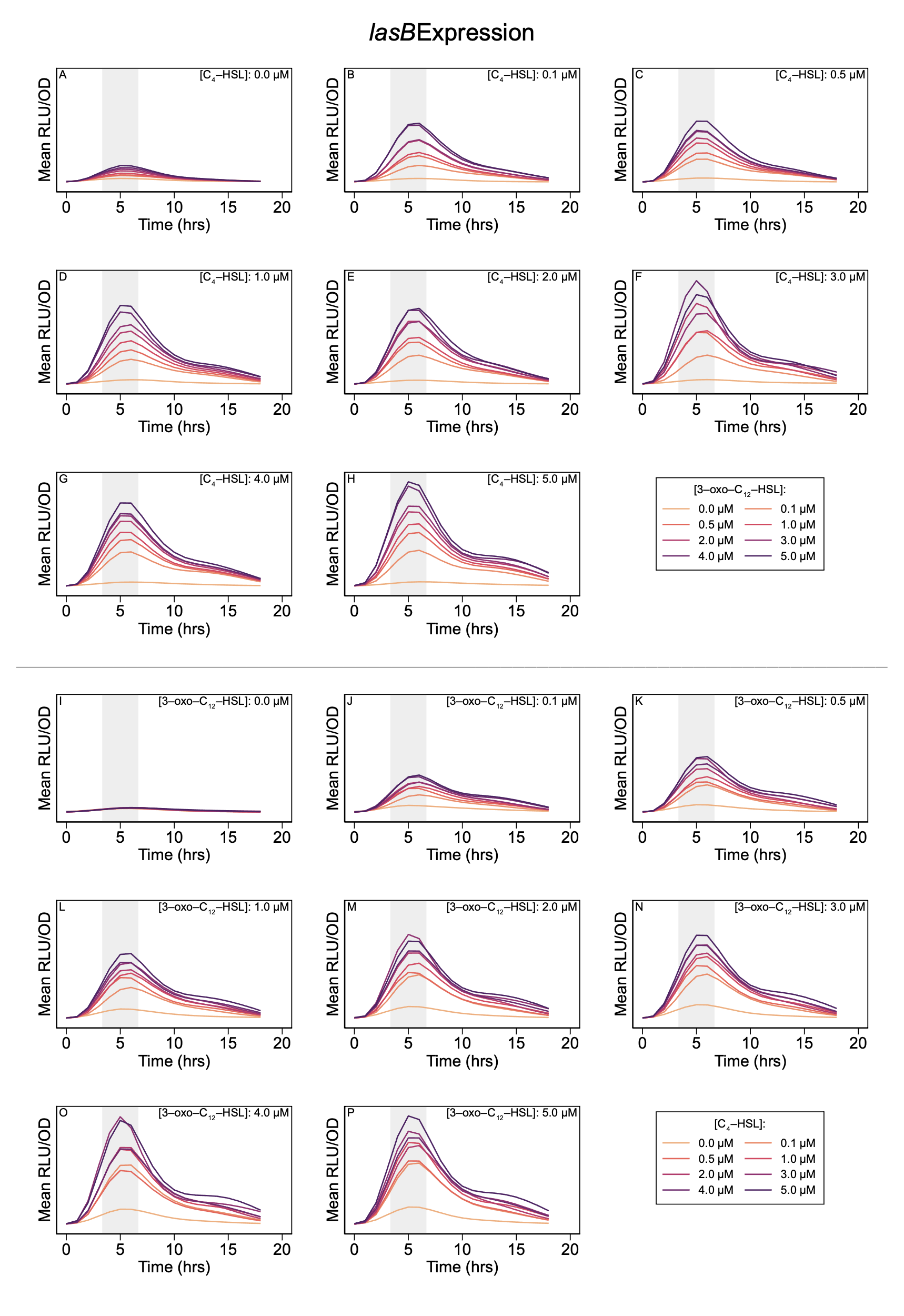
Gene expression data for *lasI,* *rhlI,* and *lasB* was collected every hour for a 24-hour period. Observations used for analysis were limited to a two-hour window that contained the peak expression level for each gene. Figures S.1, S.2, and S.3 show the full time course of expression levels and highlight the intervals used for analysis. Those windows were 8–10 hours, 3–5 hours, and 4–6 hours for *lasI,* *rhlI,* and *lasB,* respectively.



**Figure S.1. Expression level of lasI over time course of experiment.** Shaded regions highlight peak expression and indicate two-hour period used in analysis.



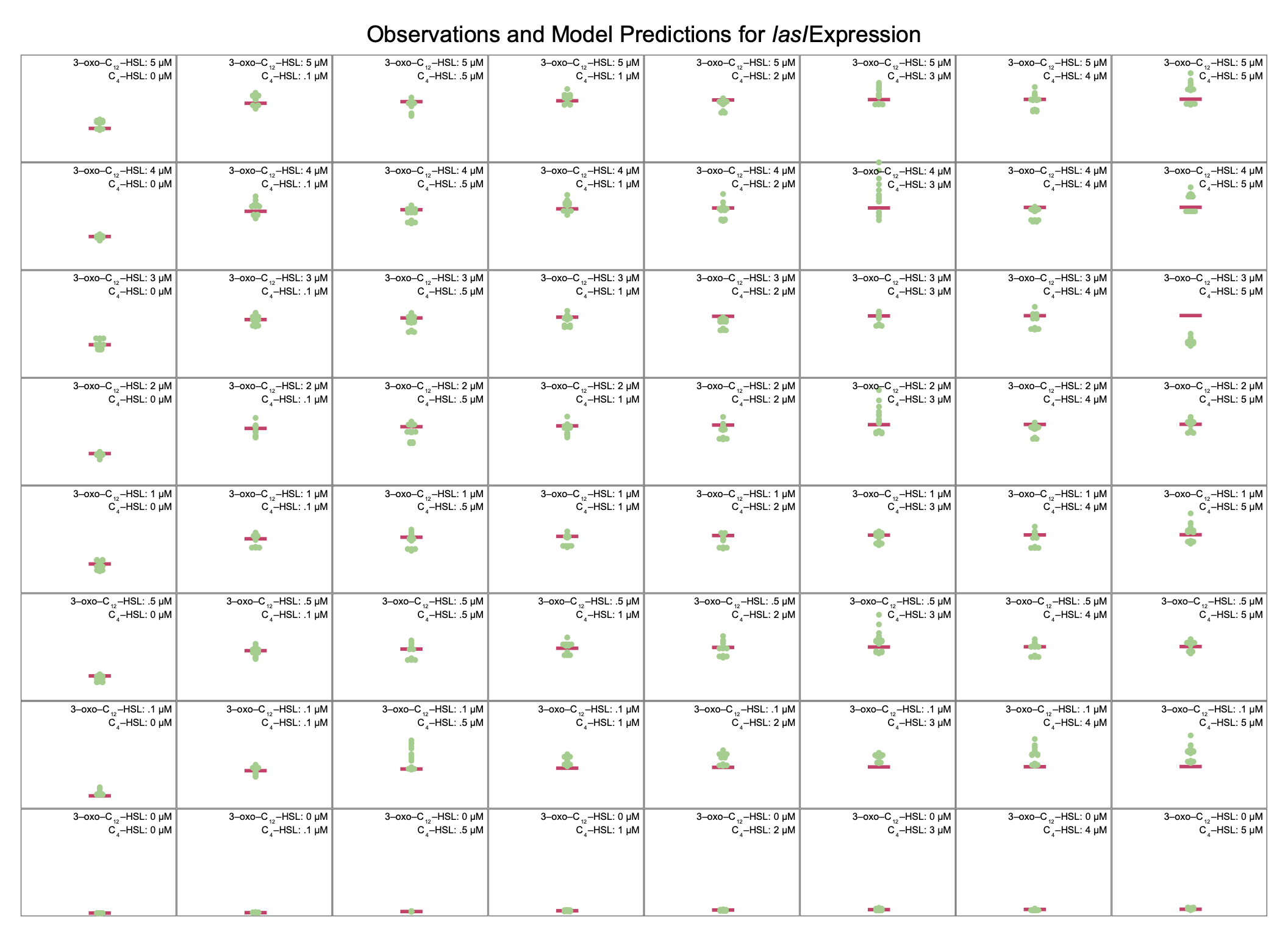
**Figure S.2. Expression level of rhlI over time course of experiment.** Shaded regions highlight peak expression and indicate two-hour period used in analysis.



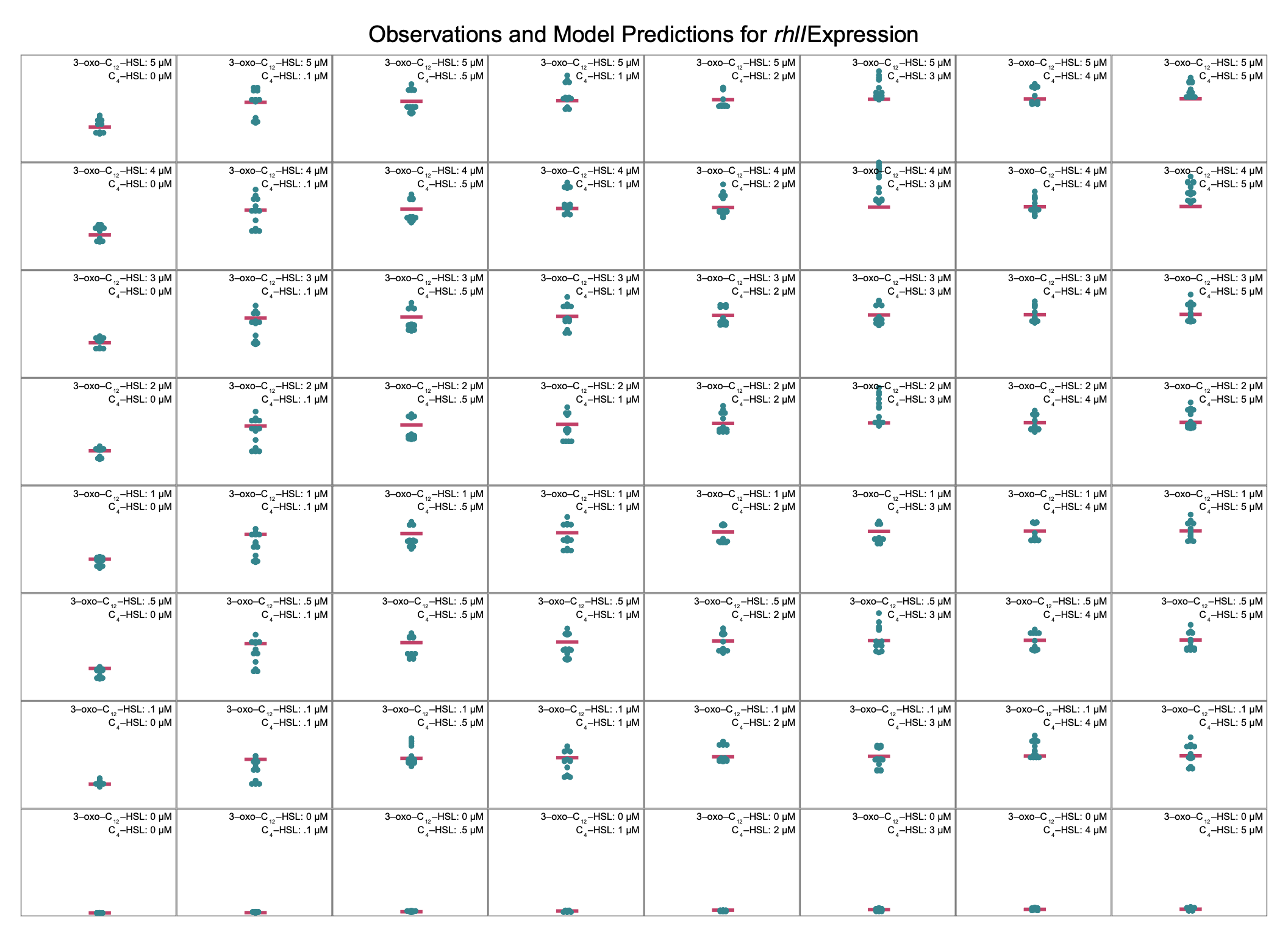
**Figure S.3. Expression level of lasB over time course of experiment.** Shaded regions highlight peak expression and indicate two-hour period used in analysis.

### Multi-Signal Models

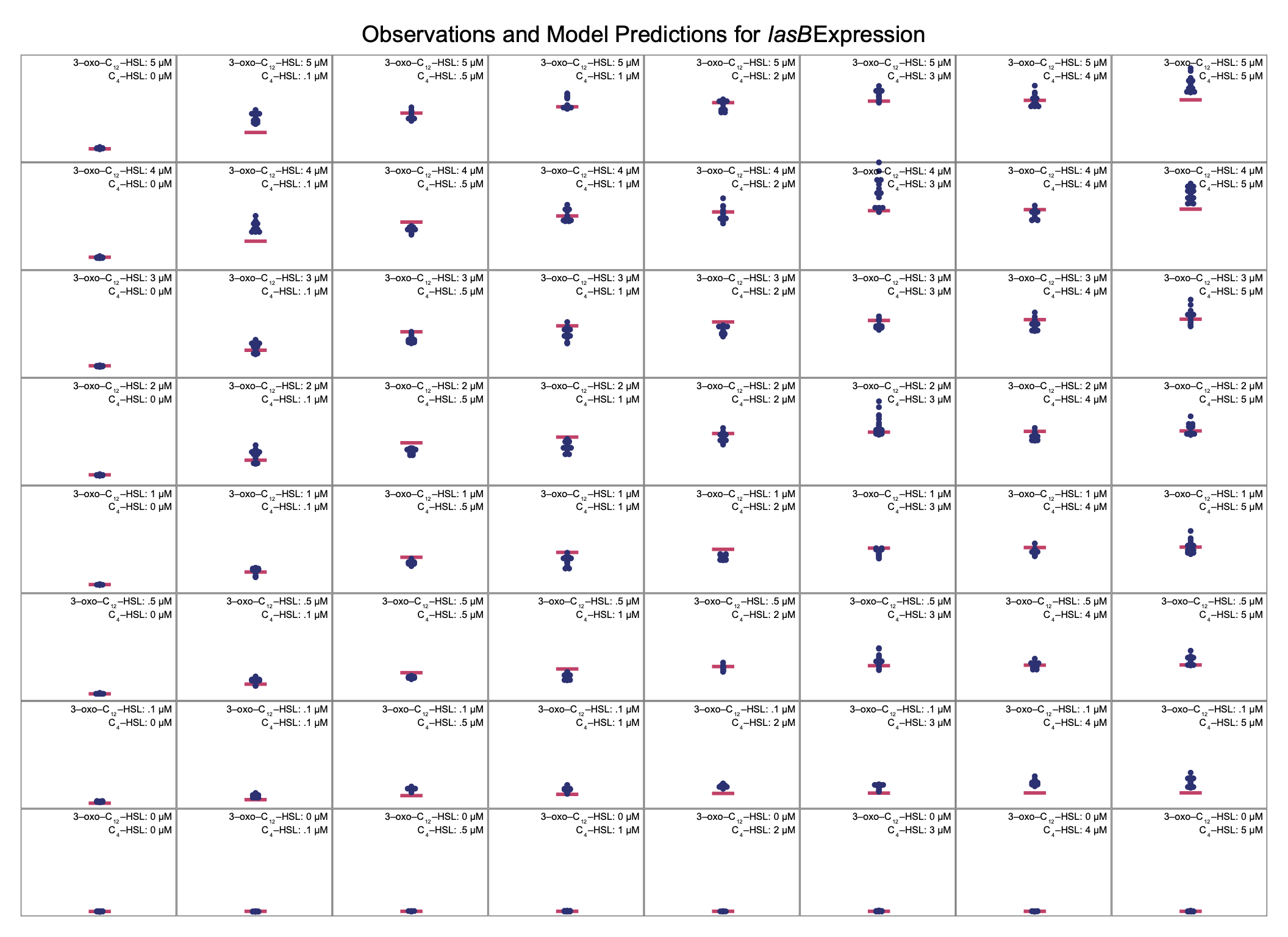
Figure 7 in the main text summarizes the predictions of the multi-signal models for *lasI* and *rhlI* expression. The following figures provide a more detailed comparison of the model predictions for all three genes.



**Figure S.4. Multi-signal model for lasI expression.** Panels compare model predictions to observations for all combinations of signal concentrations. Horizontal bars indicate model predictions, while plotted points show observed values.



**Figure S.5. Multi-signal model for rhlI expression.** Panels compare model predictions to observations for all combinations of signal concentrations. Horizontal bars indicate model predictions, while plotted points show observed values.



**Figure S.6. Multi-signal model for lasB expression.** Panels compare model predictions to observations for all combinations of signal concentrations. Horizontal bars indicate model predictions, while plotted points show observed values.

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