### S1 Supporting Information

**a. System specifications and environment setup.**

The ICOR model was built and trained on a testing system with specifications below. The benchmarking for optimization run-time was conducted on this machine as well.

- Intel® Core™ i7-10700 Processor @ 2.90 GHz
- 32 gigabytes, 2933-MHz RAM
- 3,500/3,200 MB/s read/write SSD
- NVIDIA Turing™ GeForce RTX™ 2060 (6GB VRAM)

The software specifications on which the ICOR tool was built are specified below, along with the environment setup for the benchmarking tests.

- Microsoft Windows 10
- MATLAB 9.10 R2021a
- Python 3.9 (64-bit)

**b. Codon Adaptation Index Formulae**

\[
\text{CAI} = \left( \prod_{i=1}^{L} \frac{1}{L} \right) \]

where \(L\) is the number of codons in the sequence and \(w\) is calculated by:

\[
w_i = \frac{RSCU_i}{RSCU_{max}}
\]

where \(RSCU_{max}\) is the highest codon usage frequency for a synonymous codon in a set of highly expressed genes and where \(RSCU_i\) is the codon usage frequency for synonymous codon \(i\).