

Supplementary Information

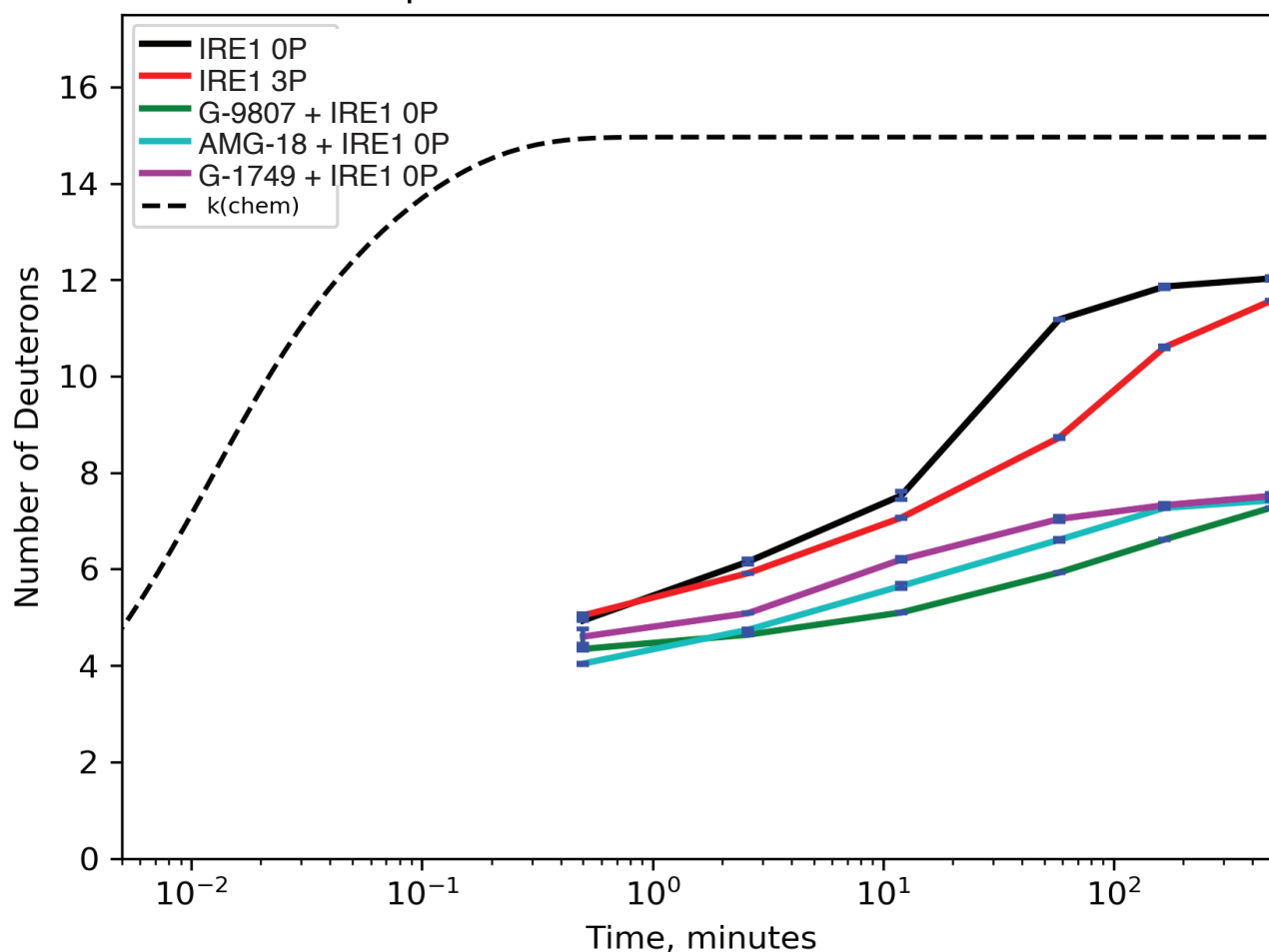
Hydrogen-Deuterium exchange (HX-MS) deuteration plots

Note: human IRE1 residue numbering is significantly offset from the sequential numbering used in the peptide plots and tables.

For reference, residue 16 in HX data is equivalent to residue 562 in the PDB files referenced in the main text. (See Figure S1A)

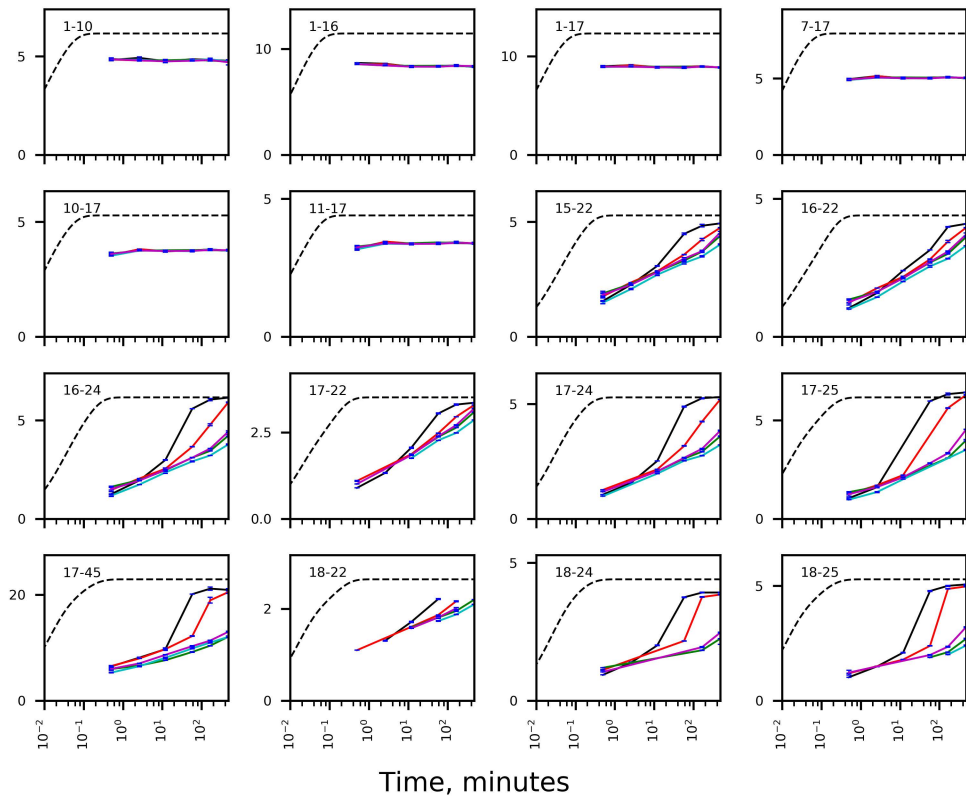
Legend for plot colors:

26-44cs0 with 17 HX Sites.
Sequence: CPKDVLGHGAEGTIVYRGM



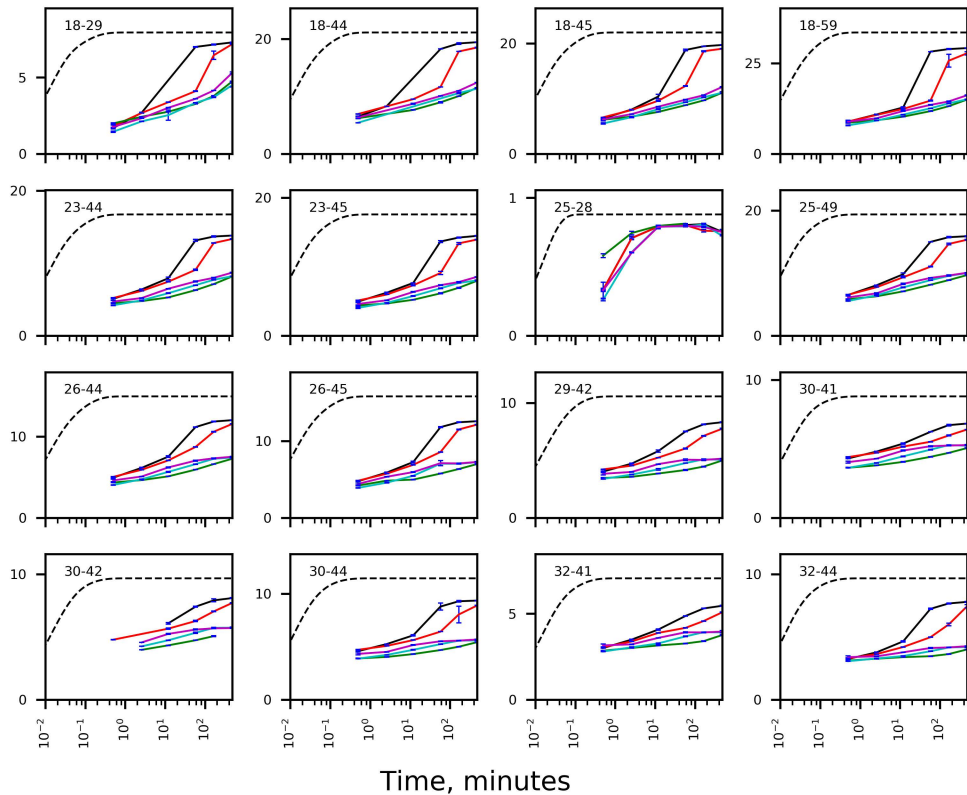
IRE1 Uptake Traces

Number of Deuterons



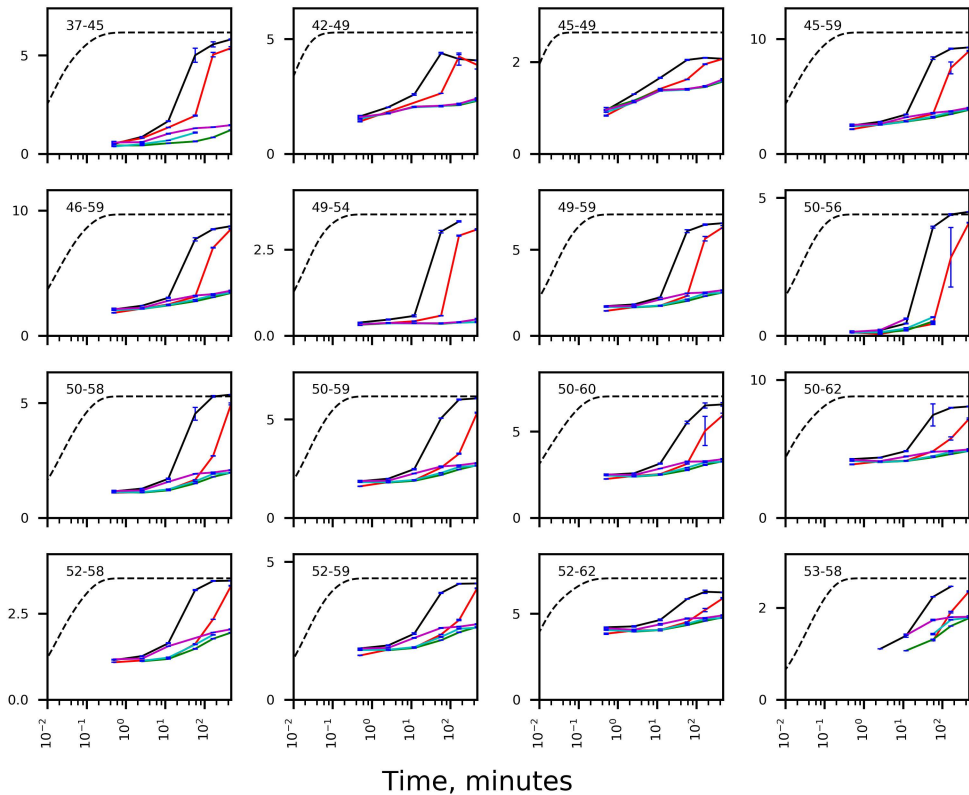
IRE1 Uptake Traces

Number of Deuterons



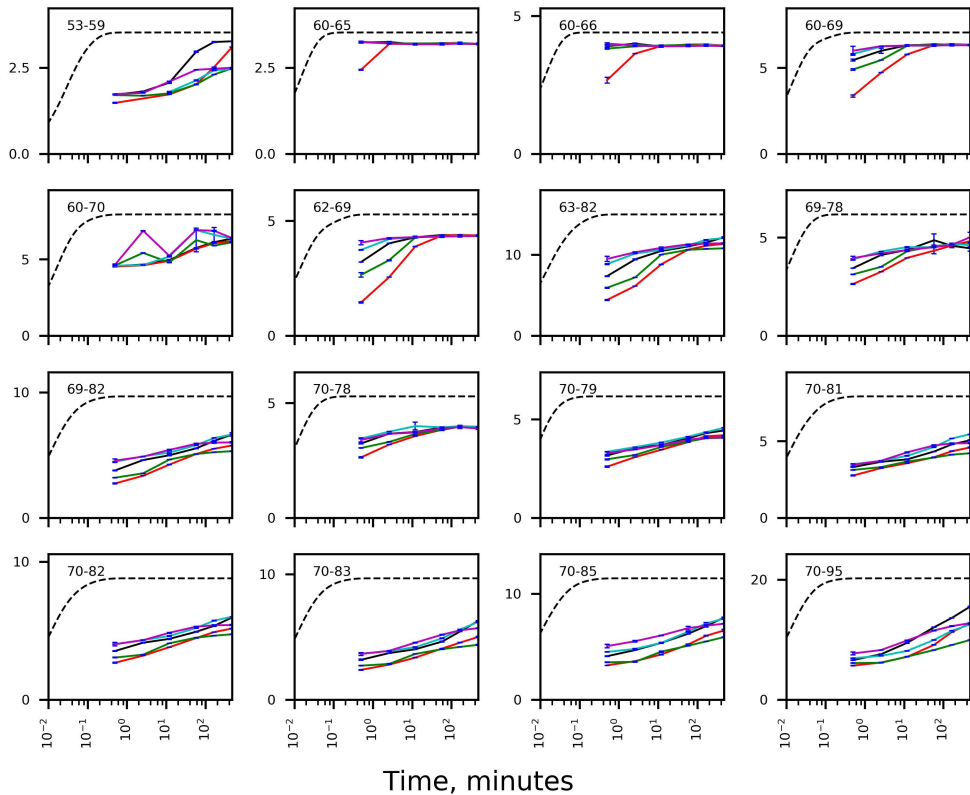
IRE1 Uptake Traces

Number of Deuterons



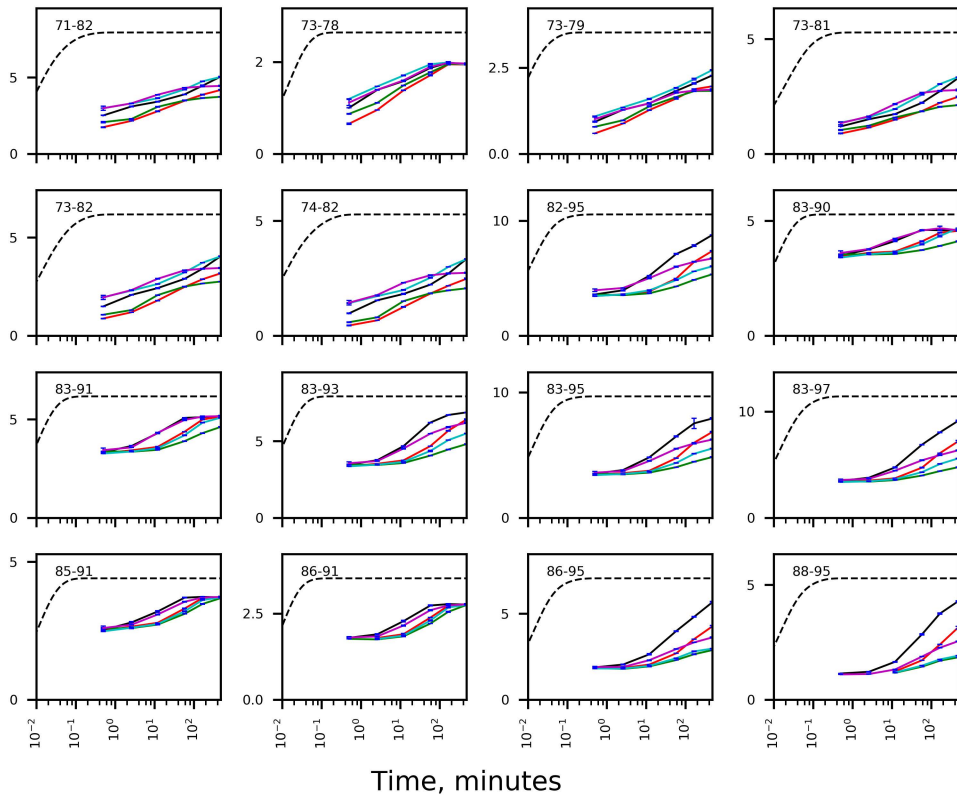
IRE1 Uptake Traces

Number of Deuterons



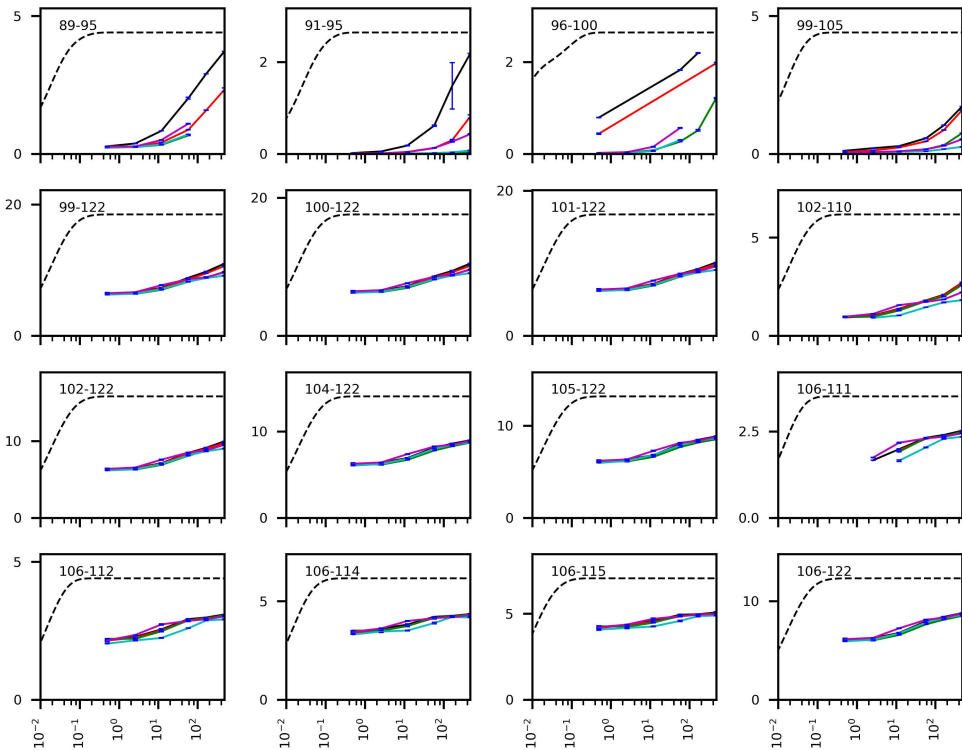
IRE1 Uptake Traces

Number of Deuterons



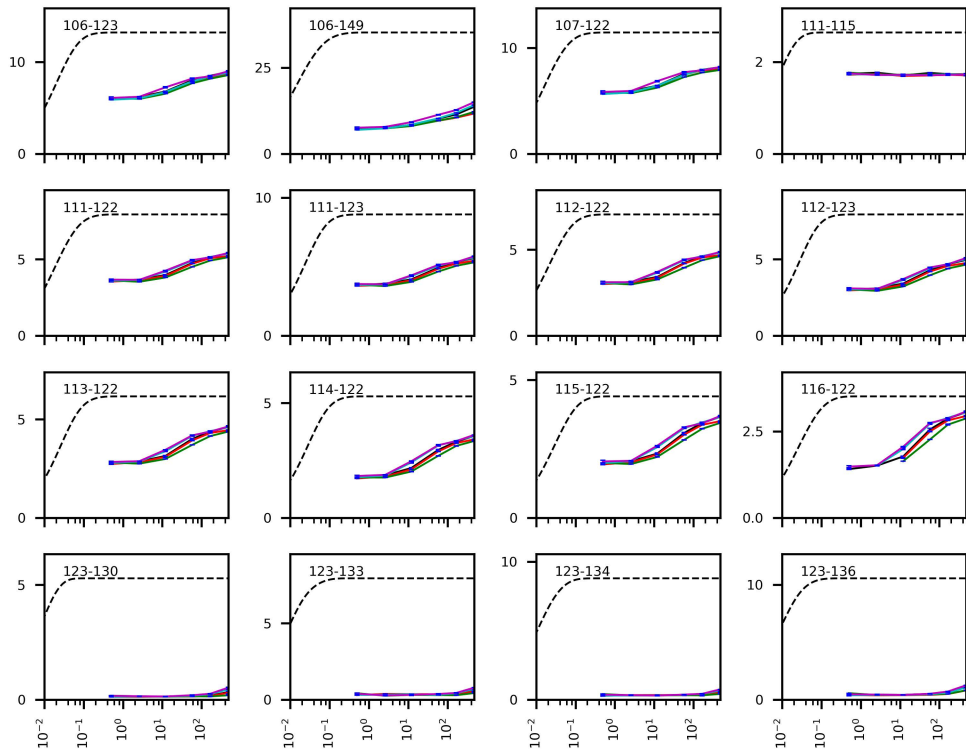
IRE1 Uptake Traces

Number of Deuterons



IRE1 Uptake Traces

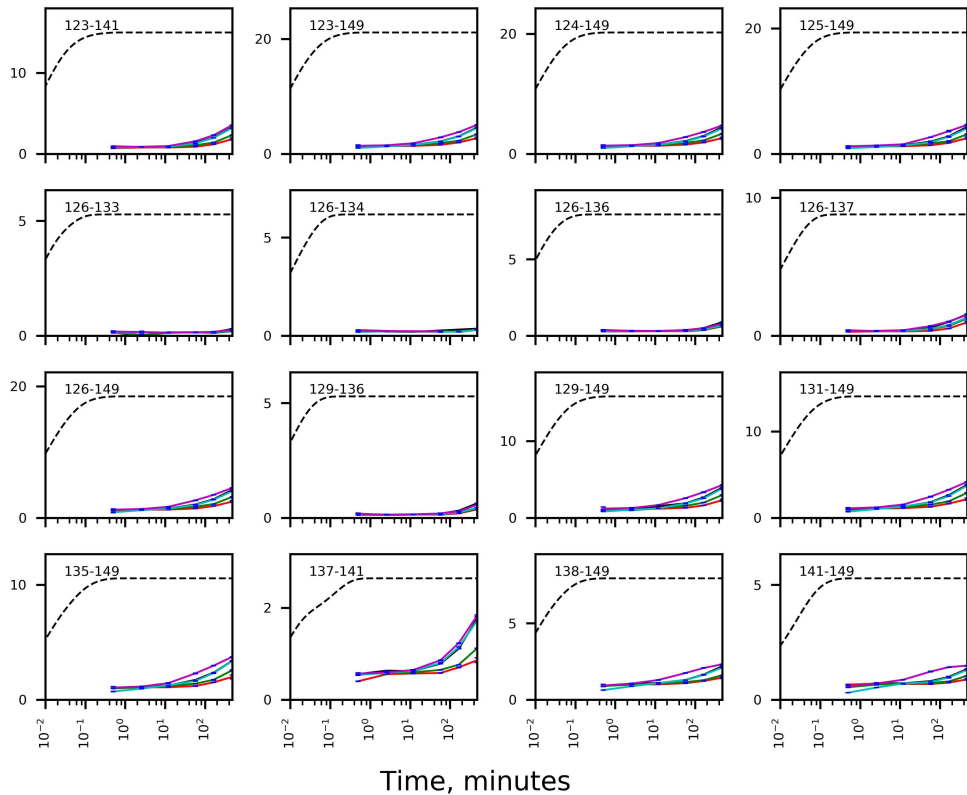
Number of Deuterons



Time, minutes

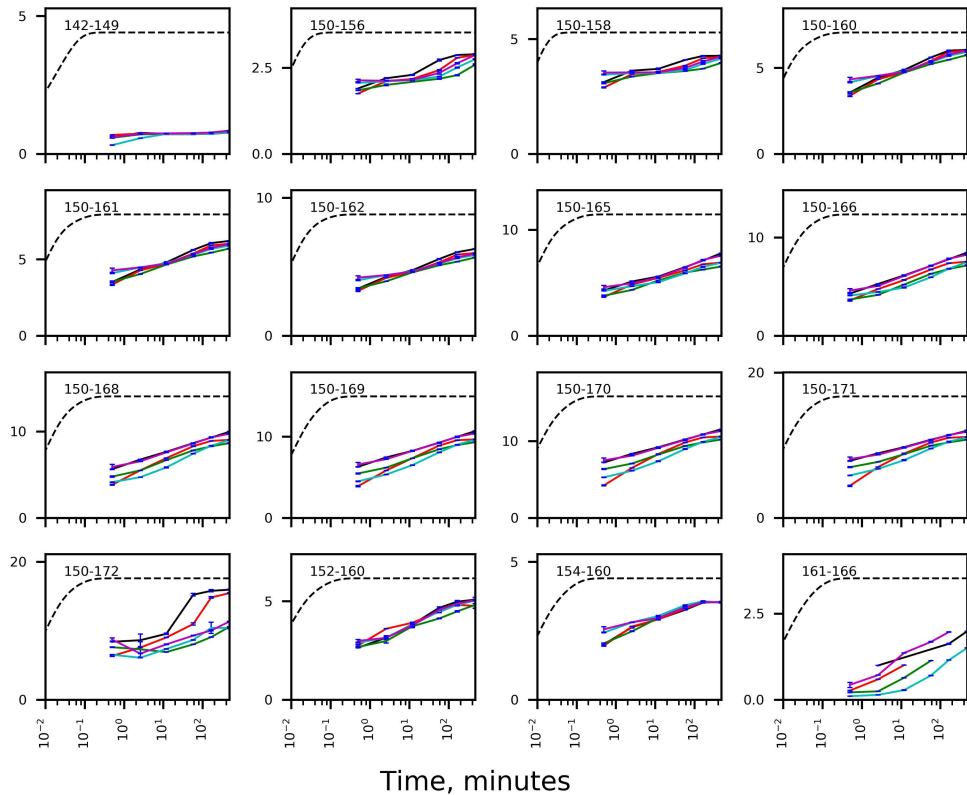
IRE1 Uptake Traces

Number of Deuterons



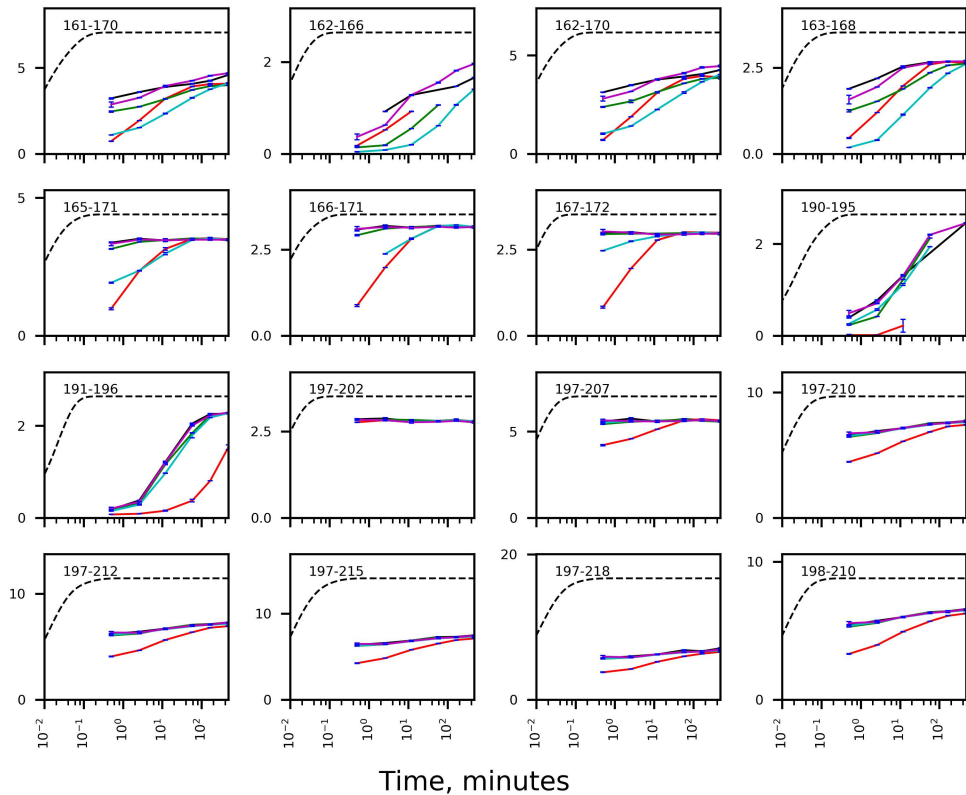
IRE1 Uptake Traces

Number of Deuterons



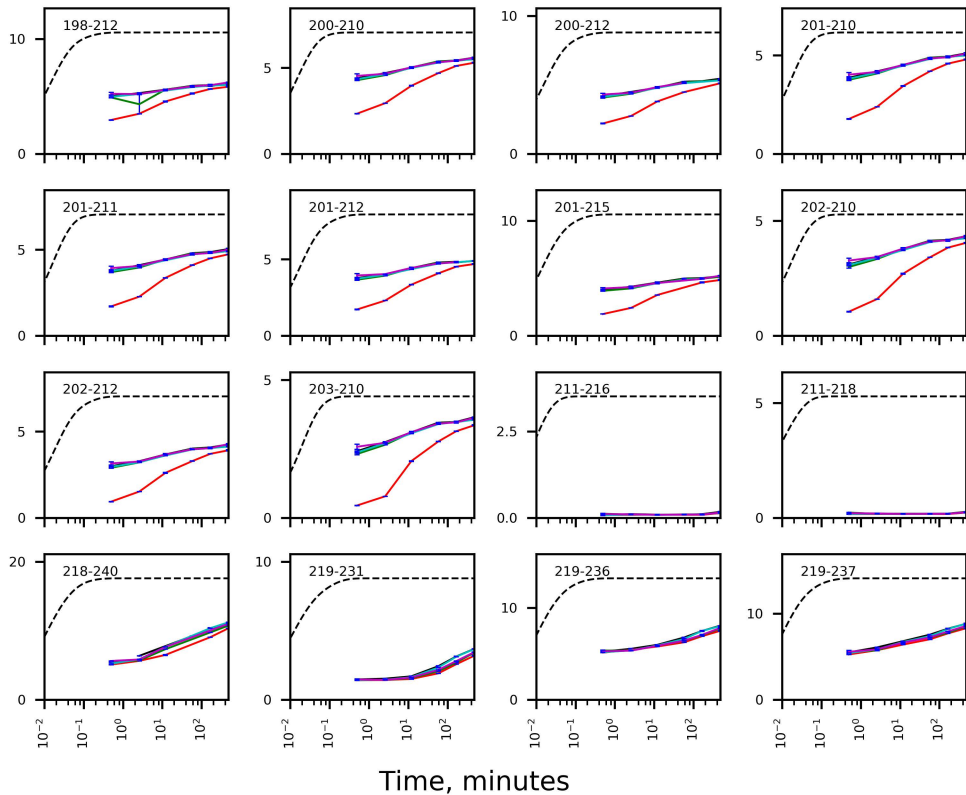
IRE1 Uptake Traces

Number of Deuterons



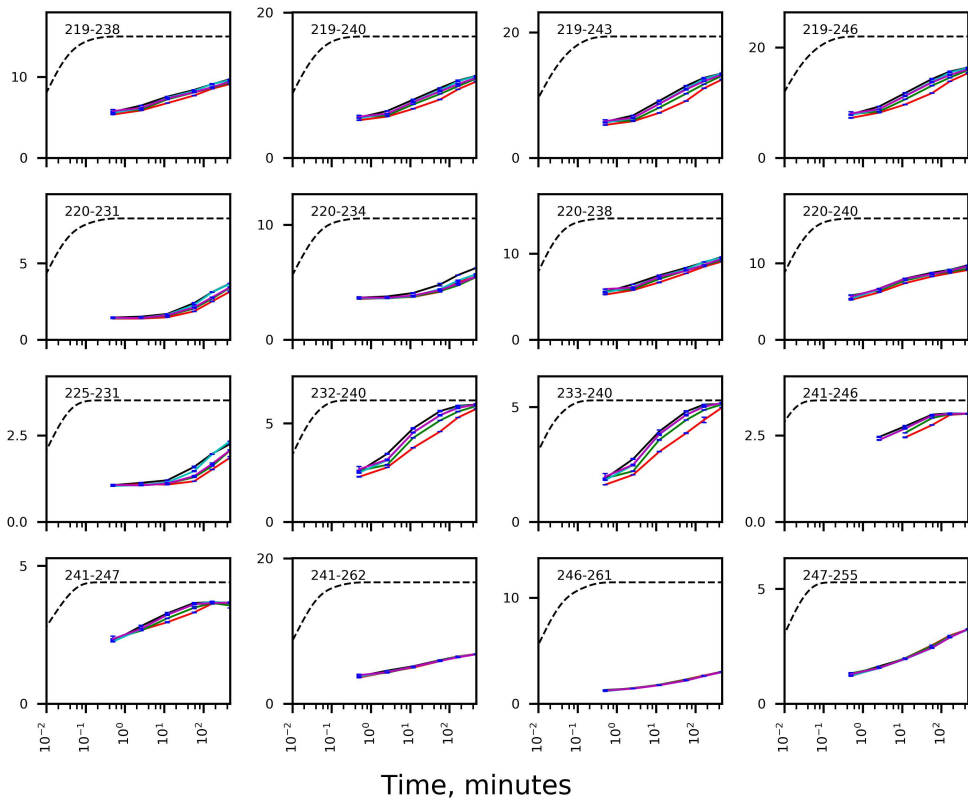
IRE1 Uptake Traces

Number of Deuterons



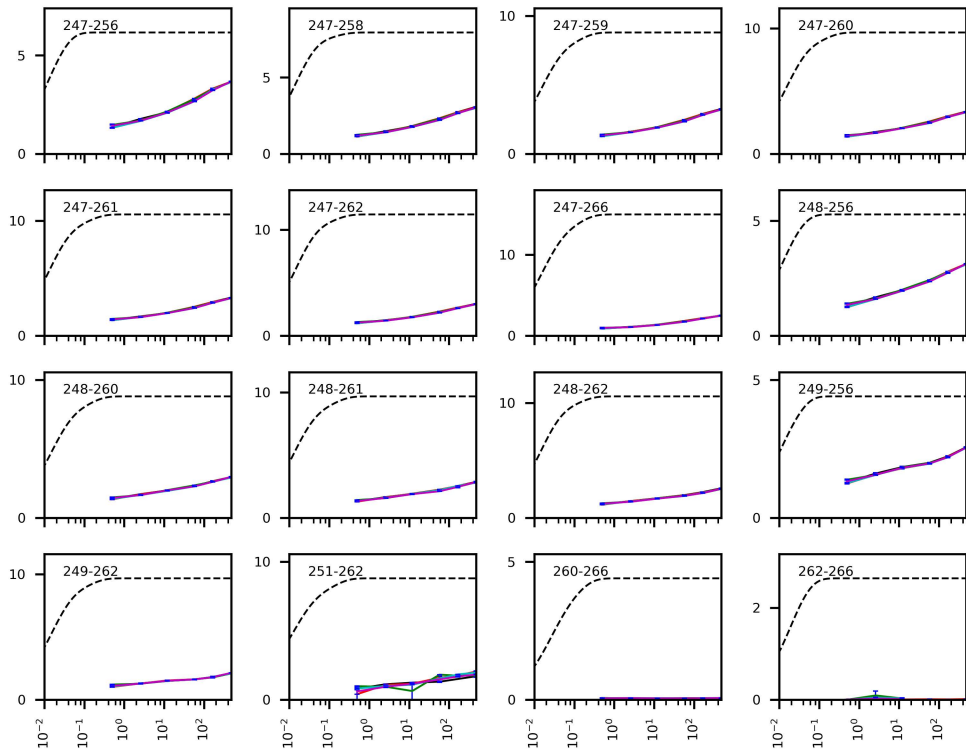
IRE1 Uptake Traces

Number of Deuterons



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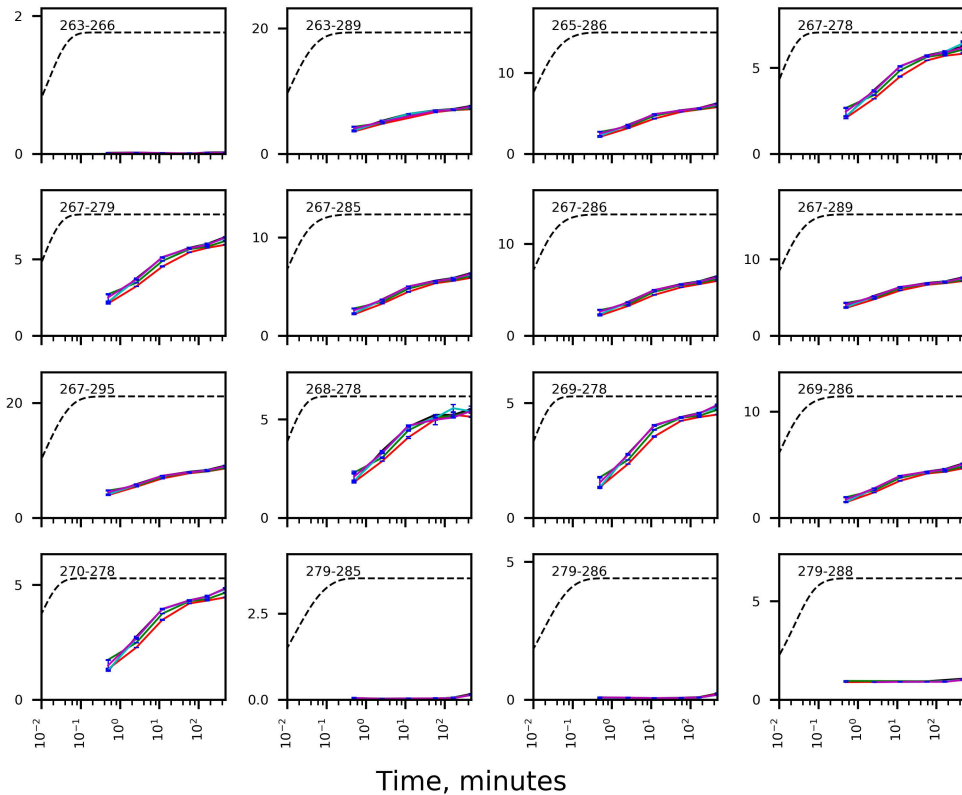
Number of Deuterons



Time, minutes

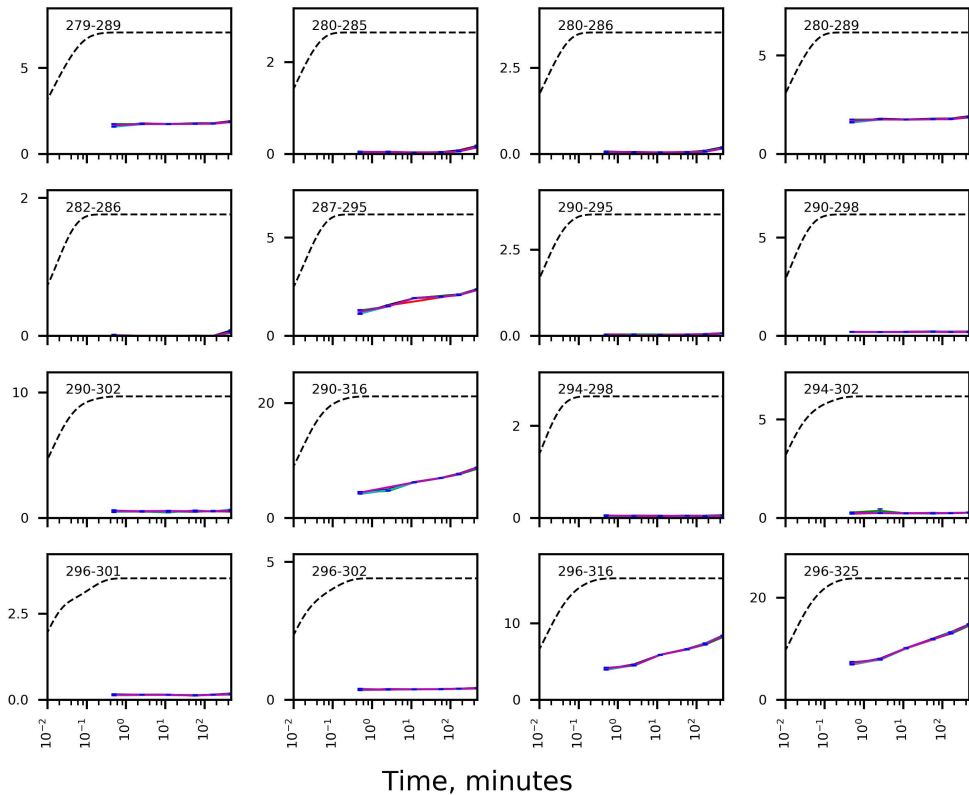
IRE1 Uptake Traces

Number of Deuterons



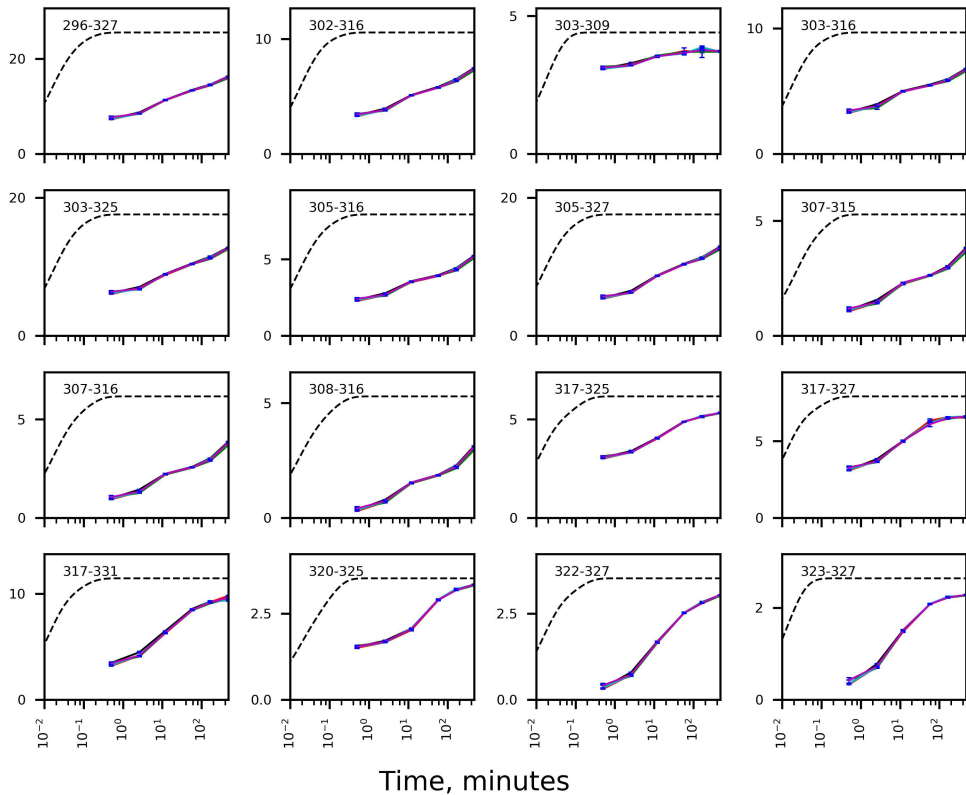
IRE1 Uptake Traces

Number of Deuterons



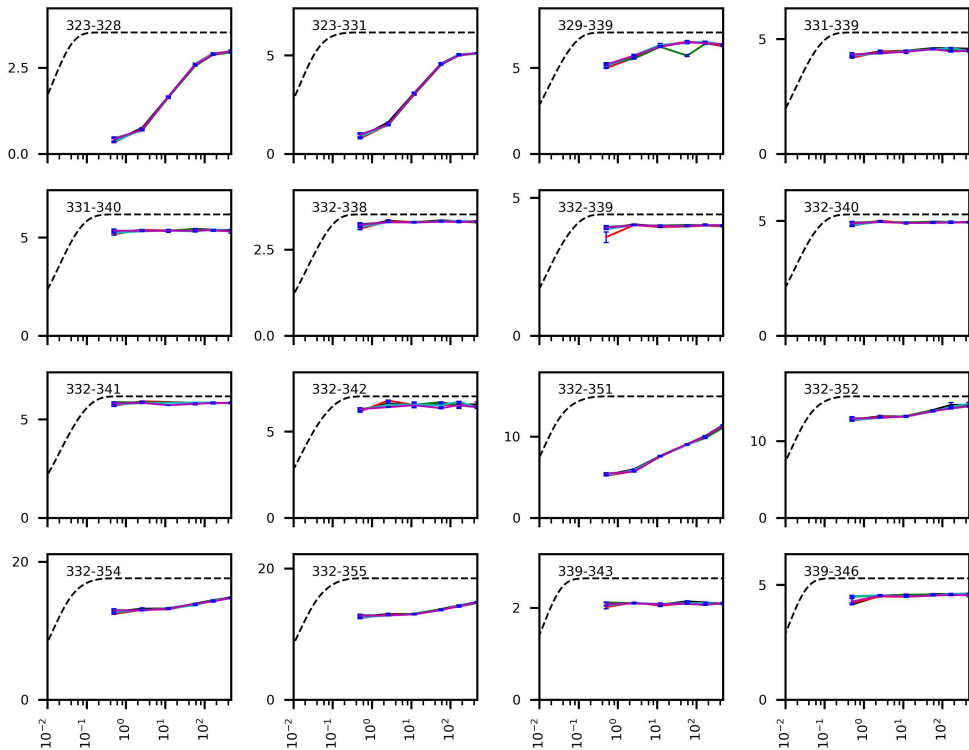
IRE1 Uptake Traces

Number of Deuterons



IRE1 Uptake Traces

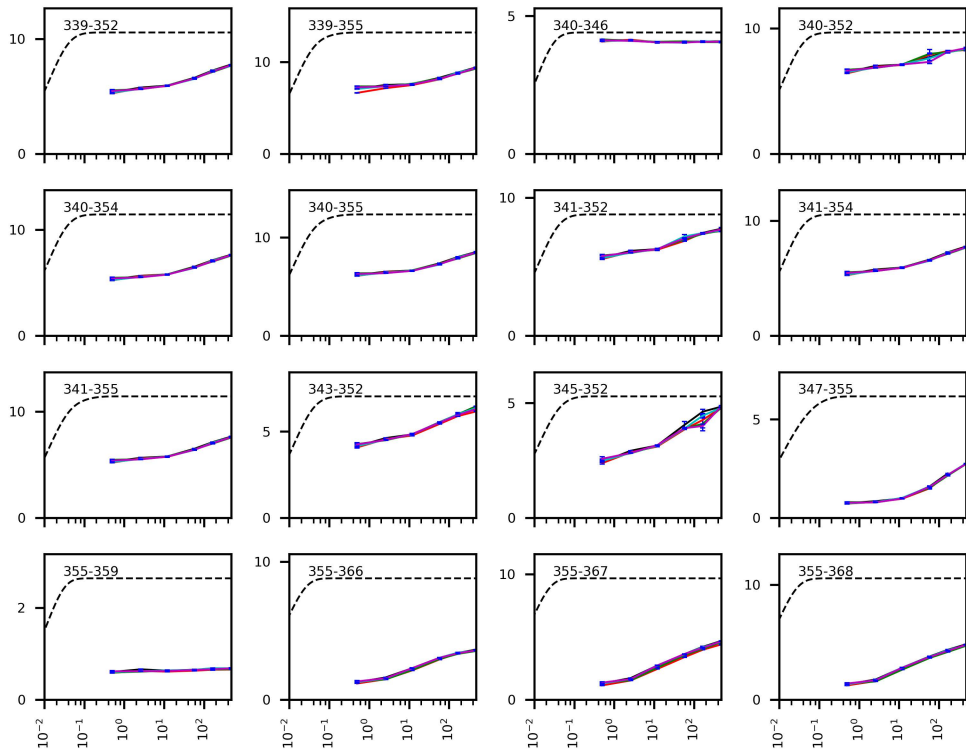
Number of Deuterons



Time, minutes

IRE1 Uptake Traces

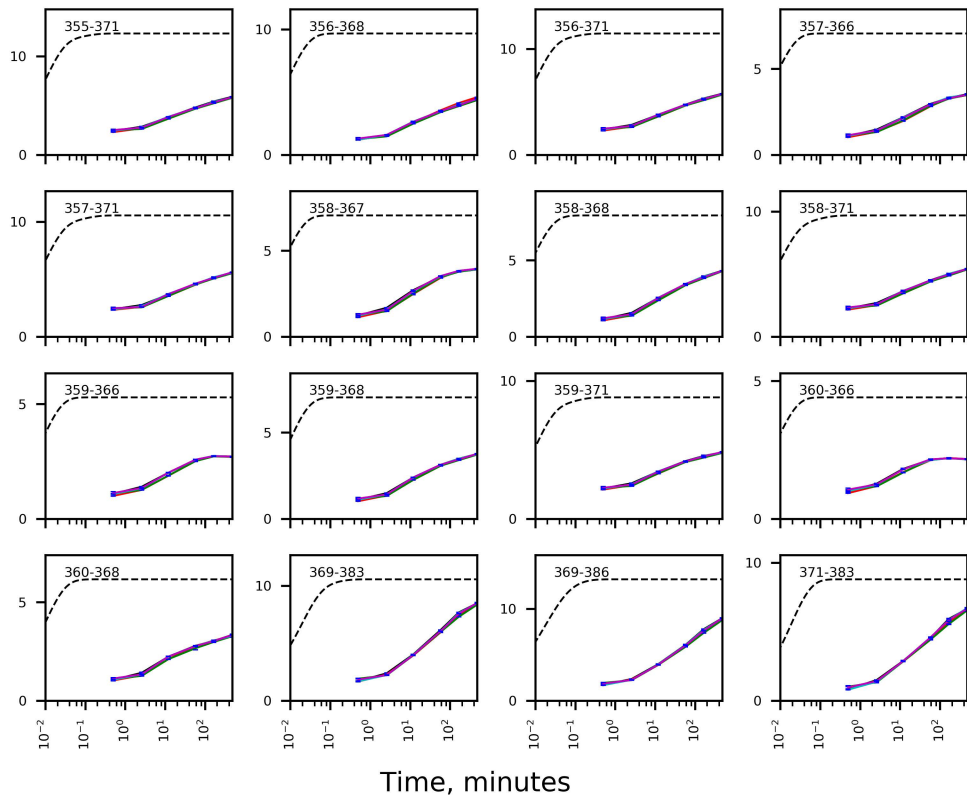
Number of Deuterons



Time, minutes

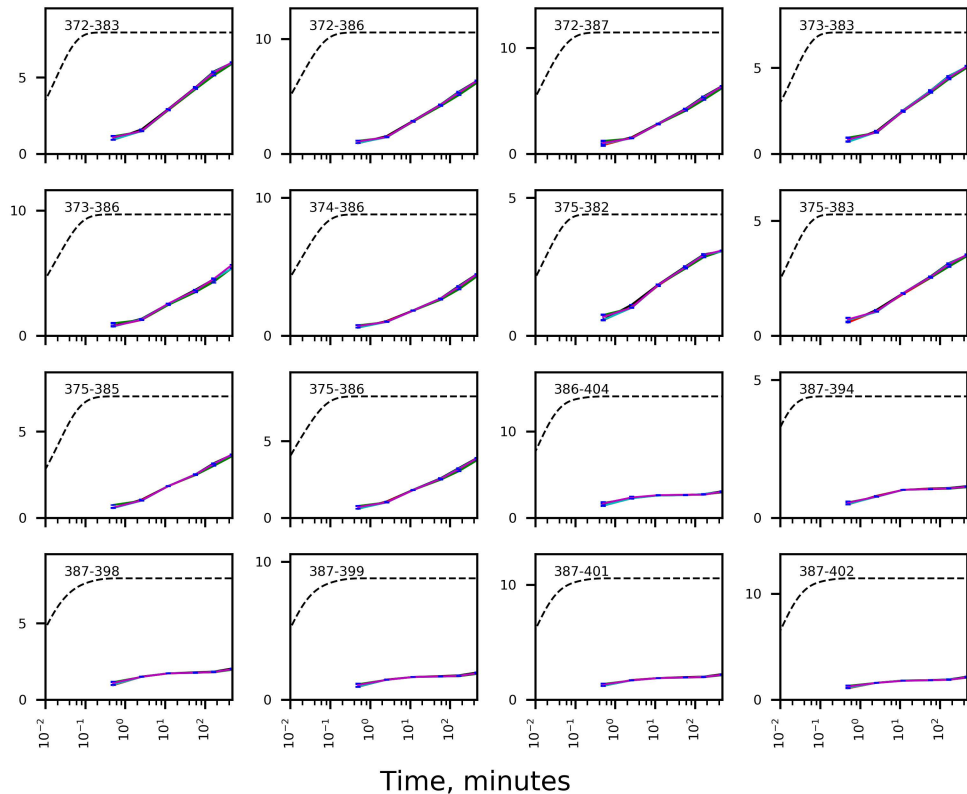
IRE1 Uptake Traces

Number of Deuterons



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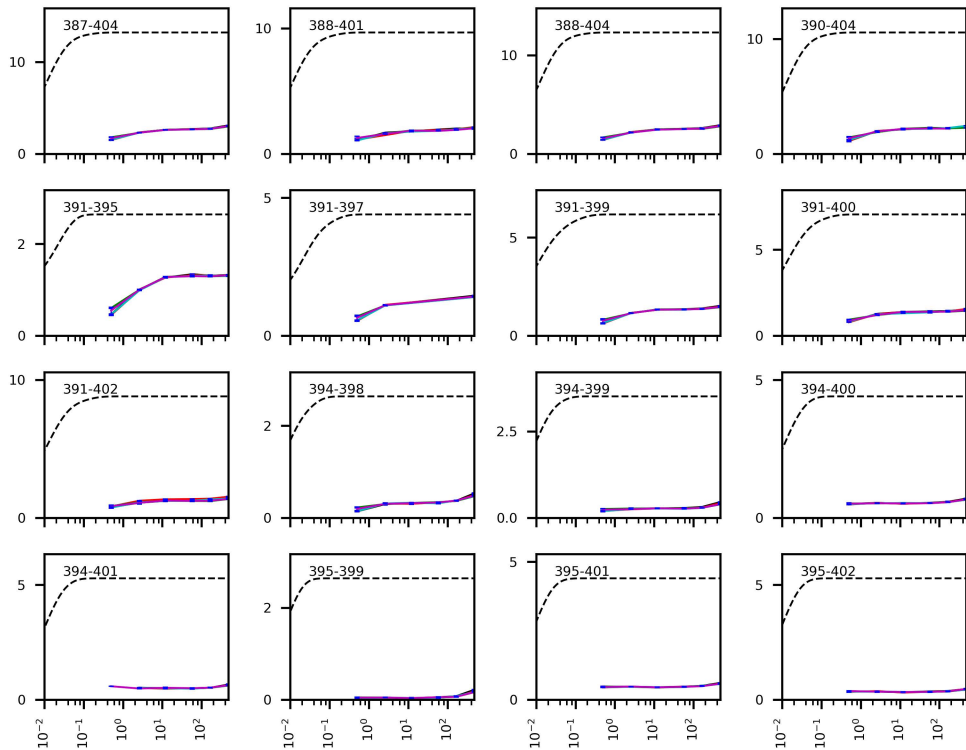
Number of Deuterons



Time, minutes

IRE1 Uptake Traces

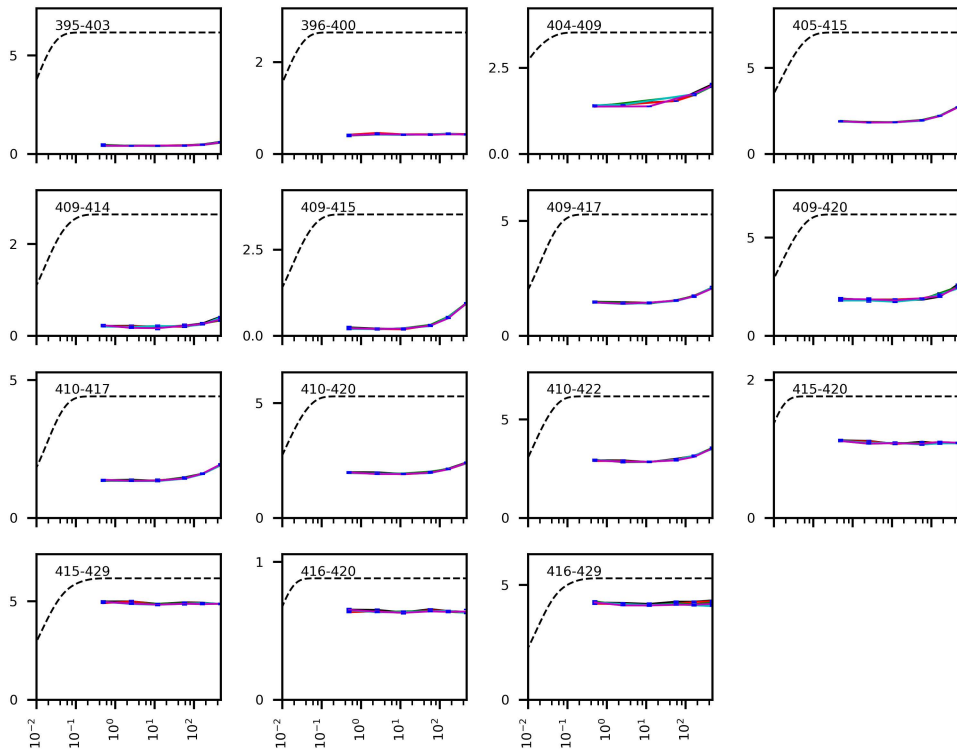
Number of Deuterons



Time, minutes

IRE1 Uptake Traces

Number of Deuterons



Time, minutes