



The ASI Interpreter

An innovative open source tool for calculating drug resistance.



Advantages

- Algorithm configuration files are easy to read, modify, and understand
- Tool provides consistent, reliable, and reproducible resistance results
- Easy to incorporate into an existing application
- Open source means it is easily extended and modified

The ASI Interpreter is designed, developed, and maintained by Frontier Science.

Learn more about Frontier Science at frontierscience.org

You can download and view the source code for the ASI Interpreter from GitHub. github.com/FrontierScience

The Algorithm Specification Interface (ASI) Interpreter is an open source Java library that makes antiretroviral drug resistance calculations using customizable algorithms.

The ASI Interpreter takes as its input an algorithm configuration file written in a human-readable XML grammar along with a list of mutations from genetic sequences. Using the rules described in the configuration file, the ASI Interpreter builds a complex abstract syntax tree. After evaluating the tree, the ASI Interpreter will provide a resistance level or a score (which is used to calculate a resistance level) and comments for each drug.

ASI Compliant Algorithms

ASI-compliant algorithms evaluate resistance for any drug based on mutations in the relevant gene, using rules stated in an XML file.

In the Stanford algorithm, each rule assigns points if a predicate condition is met. Conditions can be simple (true if a specific mutation is present) or complex (for example, true if three specified mutations are simultaneously present). The sum of all points across the set of rules for a drug produces a raw score. This score is then mapped to a resistance level using an equivalence table embedded in the XML file.

In other algorithms, such as ANRS and Rega, a predicate condition directly points to a resistance level, which is assigned when the condition is true. There are usually several rules, each pointing to a different level, for a given drug.

How It Works

The ASI Interpreter is a library, not a standalone application. It can be integrated with another program that needs to provide resistance results.

The ASI Interpreter requires three inputs: an algorithm file, a gene region, and a list of mutations to evaluate.

The algorithm file specifies the rules that are used to calculate resistance for each drug of interest. Each rule matches a condition (a set of mutation criteria) to an action. An action can be a score and resulting resistance level, a resistance level, or a comment.

The interpreter takes the algorithm file that it is given and converts the rules into a logical structure to evaluate the given list of mutations. The logical structure takes the form of a tree in which each step in the detailed logic evaluating a rule is a node. The ASI Interpreter then systematically walks through the tree.

Based on the type of actions specified in the rules, the interpreter can report a resistance level, a score (translated into a resistance level), and a set of comments.

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The ASI Interpreter

Example

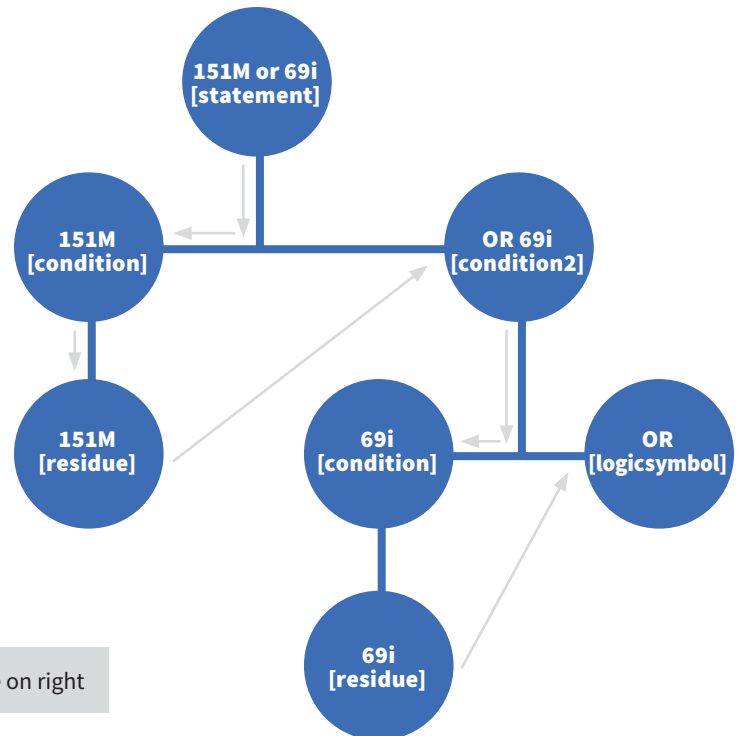
This example shows how the ASI Interpreter executes the rule (151M OR 69i) => 15 on a sequence with an RT mutation list of [10V, 151M].

```
<ALGORITHM>
<ALGNAME>HIVDB</ALGNAME>
<ALGVERSION>8.4</ALGVERSION>
<ALGDATE>2017-06-16</ALGDATE>
<GLOBALRANGE>
(-INF TO 9 => 1,
 10 TO 14 => 2,
 15 TO 29 => 3,
 30 TO 59 => 4,
 60 TO INF => 5)
</GLOBALRANGE>
<DRUG>
<NAME>3TC</NAME>
<FULLNAME>lamivudine</FULLNAME>
<RULE>
  <CONDITION>
    SCORE FROM(
      MAX (65N => 15, 65R => 30),
      67d => 15,
      MAX (69i => 30, 69d => 15),
      77L => 5,
      116Y => 5,
      MAX (151L => 10, 151M
        (151M OR 69i) => 15)
    )
  </CONDITION>
  <ACTIONS>
    <SCORERANGE>
      <USE_GLOBALRANGE/>
    </SCORERANGE>
  </ACTIONS>
</RULE>
</DRUG>
</ALGORITHM>
```

Translates score to resistance

Rule used in example on right

After processing this tree based on the rules defined in the XML file on the left, the resulting score will be 15, which translates to a resistance level of 3.



ASI Interpreter Output

At the level of a gene (such as protease or RT) in a sequence:

- › The mutations that were actively used in the scoring for the sequence
- › The comments that were generated at the gene level

At the level of each drug:

- › The point score (if the algorithm uses points)
- › The resistance level
- › Comments that were generated for the drug
- › (If the algorithm uses points) For each rule that was triggered in scoring the drug: the points conferred and mutation(s) that triggered the rule

About Frontier Science

Frontier Science is a not-for-profit research foundation dedicated to the advancement of data and statistical quality in medical research. Since 1975, Frontier Science has been providing data management and statistical services and expertise to clinical trials, university medical centers, and industry.

Get Involved

The ASI Interpreter is open source under the terms of the Apache 2.0 license. You can download and view the source code and get involved in development at github.com/FrontierScience