Formal definition of Bounded Linear Multiscale Spatial Temporal Logic (BLMSTL)

Syntax

The syntax of BLMSTL will be defined by a context-free grammar using the Backus-Naur Form (BNF) notation. A definition of a non-terminal symbol (element) in such grammars has the following form:

\[
\langle \text{defined-element} \rangle ::= \langle \text{element1} \rangle \mid \langle \text{element2} \rangle \mid \ldots
\]

where ::= introduces a new definition and | represents an alternative. In natural language this reads \(<\text{defined-element}>\) is either an \(<\text{element1}>\) or \(<\text{element2}>\) or (...).

Definition. The syntax of BLMSTL is given by the following grammar expressed in BNF:

\[
\langle \text{logic-property} \rangle ::= \langle \text{temporal-numeric-measure} \rangle \langle \text{comparator} \rangle
\]

\[
\langle \text{temporal-numeric-measure} \rangle ::= \langle \text{real-number} \rangle \mid \langle \text{numeric-state-variable} \rangle \mid \langle \text{numeric-statistical-measure} \rangle \mid \langle \text{unary-numeric-measure} \rangle \langle \text{temporal-numeric-measure} \rangle \mid \langle \text{binary-numeric-measure} \rangle \langle \text{temporal-numeric-measure} \rangle, \langle \text{temporal-numeric-measure} \rangle
\]

\[
\langle \text{numeric-statistical-measure} \rangle ::= \langle \text{unary-statistical-measure} \rangle \langle \text{numeric-measure-collection} \rangle \mid \langle \text{binary-statistical-measure} \rangle \langle \text{numeric-measure-collection} \rangle, \langle \text{numeric-measure-collection} \rangle \mid \langle \text{binary-statistical-quantile-measure} \rangle \langle \text{numeric-measure-collection} \rangle, \langle \text{real-number} \rangle
\]
(numeric-measure-collection) ::= (spatial-measure-collection)
   | [unsigned-real-number,unsigned-real-number] (numeric-measure)

(numeric-measure) ::= (primary-numeric-measure)
   | (unary-numeric-measure)((numeric-measure))
   | (binary-numeric-measure)((numeric-measure),(numeric-measure))

(primary-numeric-measure) ::= (numeric-spatial-measure)
   | (real-number)
   | (numeric-state-variable)

(numeric-spatial-measure) ::= (unary-statistical-measure)(
   (spatial-measure-collection))
   | (binary-statistical-measure)((spatial-measure-collection),
   (spatial-measure-collection))
   | (binary-statistical-quantile-measure)((spatial-measure-collection),
   (real-number))

(unary-statistical-measure) ::= avg
   | count
   | geomean
   | harmean
   | kurt
   | max
   | median
   | min
   | mode
   | product
   | skew
   | stdev
   | sum
   | var

(binary-statistical-measure) ::= covar

(binary-statistical-quantile-measure) ::= percentile
   | quartile

(unary-numeric-measure) ::= abs
   | ceil
   | floor
   | round
   | sign
   | sqrt
   | trunc

(binary-numeric-measure) ::= add
   | div
   | log
   | mod
   | multiply
\[
\text{power} \quad \text{subtract}
\]

\[
\langle \text{spatial-measure-collection} \rangle ::= \langle \text{spatial-measure} \rangle (\langle \text{subset} \rangle)
\]

\[
\langle \text{spatial-measure} \rangle ::= \text{clusteredness}
\]

\[
\text{density} \quad \text{area} \quad \text{perimeter} \quad \text{distanceFromOrigin} \quad \text{angle} \quad \text{triangleMeasure} \quad \text{rectangleMeasure} \quad \text{circleMeasure} \quad \text{centroidX} \quad \text{centroidY}
\]

\[
\langle \text{subset} \rangle ::= \langle \text{subset-specific} \rangle
\]

\[
\text{filter}(\langle \text{subset-specific} \rangle, \langle \text{constraint} \rangle)
\]

\[
\langle \text{subset-operation} \rangle (\langle \text{subset} \rangle, \langle \text{subset} \rangle)
\]

\[
\langle \text{subset-specific} \rangle ::= \text{regions} \quad \text{clusters}
\]

\[
\langle \text{constraint} \rangle ::= \text{scaleAndSubsystem} (\text{comparator}) (\text{scale-and-subsystem})
\]

\[
\langle \text{spatial-measure} \rangle (\text{comparator}) (\langle \text{filter-numeric-measure} \rangle)
\]

\[
\sim (\langle \text{constraint} \rangle)
\]

\[
(\langle \text{constraint} \rangle) \land (\langle \text{constraint} \rangle)
\]

\[
(\langle \text{constraint} \rangle) \lor (\langle \text{constraint} \rangle)
\]

\[
(\langle \text{constraint} \rangle) \Rightarrow (\langle \text{constraint} \rangle)
\]

\[
(\langle \text{constraint} \rangle) \Leftrightarrow (\langle \text{constraint} \rangle)
\]

\[
(\langle \text{filter-numeric-measure} \rangle) ::= (\langle \text{primary-numeric-measure} \rangle)
\]

\[
\langle \text{spatial-measure} \rangle
\]

\[
\langle \text{unary-numeric-measure} \rangle (\langle \text{filter-numeric-measure} \rangle)
\]

\[
\langle \text{binary-numeric-measure} \rangle (\langle \text{filter-numeric-measure} \rangle, \langle \text{filter-numeric-measure} \rangle)
\]

\[
\langle \text{subset-operation} \rangle ::= \text{difference}
\]

\[
\text{intersection}
\]

\[
\text{union}
\]

\[
\langle \text{change-measure} \rangle ::= d
\]

\[
r
\]

\[
\langle \text{real-number} \rangle ::= (\langle \text{unsigned-real-number} \rangle)
\]

\[
(\langle \text{sign} \rangle) (\langle \text{unsigned-real-number} \rangle)
\]
\( \text{(unsigned-real-number)} ::= \text{(fractional-part)} \)
\[ \text{\mid \text{(fractional-part)} \text{(exponent-part)}} \]

\( \text{(fractional-part)} ::= \text{(digit-sequence)} \text{.} \text{(digit-sequence)} \)
\[ \text{\mid .} \text{(digit-sequence)} \]
\[ \text{\mid \text{(digit-sequence)} \text{.}} \]
\[ \text{\mid \text{(digit-sequence)}} \]

\( \text{(digit-sequence)} ::= \text{(digit)} \)
\[ \text{\mid \text{(digit)} \text{(digit-sequence)}} \]

\( \text{(digit)} ::= 0 \)
\[ \text{\mid 1} \]
\[ \text{\mid 2} \]
\[ \text{\mid 3} \]
\[ \text{\mid 4} \]
\[ \text{\mid 5} \]
\[ \text{\mid 6} \]
\[ \text{\mid 7} \]
\[ \text{\mid 8} \]
\[ \text{\mid 9} \]

\( \text{(natural-number)} ::= \text{(digit-sequence)} \)
\[ \text{\mid +} \text{(digit-sequence)} \]

\( \text{(exponent-part)} ::= e \text{(digit-sequence)} \)
\[ \text{\mid E} \text{(digit-sequence)} \]
\[ \text{\mid e} \text{\text{(sign)} \text{(digit-sequence)}} \]
\[ \text{\mid E} \text{\text{(sign)} \text{(digit-sequence)}} \]

\( \text{(sign)} ::= + \)
\[ \text{\mid -} \]

\( \text{(comparator)} ::= < \)
\[ \text{\mid <=} \]
\[ \text{\mid =} \]
\[ \text{\mid >=} \]
\[ \text{\mid >} \]

\( \text{(numeric-state-variable)} ::= \)
\[ \text{\text{(state-variable)} \text{(state-variable-scale-and-subsystem)}} \]

\( \text{(state-variable)} ::= \{ \text{(string)} \} \)

\( \text{(state-variable-scale-and-subsystem)} ::= e \)
\[ \text{\mid \text{(scaleAndSubsystem = (scale-and-subsystem)}} \)

\( \text{(string)} ::= \text{(character)} \mid \{ \text{(character)} \text{\text{(string)}} \}

\( \text{(character)} ::= \text{based on the Unicode character set except “{” and “}”} \)
\[
(scale-and-subsystem) ::= \langle \text{primary-scale-and-subsystem} \rangle.
\]
\[
\langle \text{primary-scale-and-subsystem} \rangle ::= \langle \text{scale-and-subsystem-character} \rangle
| \langle \text{scale-and-subsystem-character} \rangle \langle \text{primary-scale-and-subsystem} \rangle
\]
\[
\langle \text{scale-and-subsystem-character} \rangle ::= \langle \text{basic-latin-script-character} \rangle
| \langle \text{digit} \rangle
\]
\[
\langle \text{basic-latin-script-character} \rangle ::= a | b | c | d | e | f | g | h | i | j | k | l | m | n |
o | p | q | r | s | t | u | v | w | x | y | z | A | B | C | D | E | F | G | H | I
| J | K | L | M | N | O | P | Q | R | S | T | U | V | W | X | Y | Z
\]

The order of precedence of the operators is given by the definition of the BLMSTL syntax. In the absence of parentheses the logic expressions are evaluated from left to right.

**Semantics**

The semantics of BLMSTL is defined with respect to executions of an MSSpDES \( M \)

\[
\sigma = \{(s_0, t_0), (s_1, t_1), \ldots \}
\]

where \( s_0, s_1, \ldots \) represent the states of the execution and \( t_0, t_1, \ldots \in \mathbb{R}_+ \) the time durations spent in each corresponding state. Throughout it is assumed that execution traces are time-divergent which means that only a finite number of transitions can occur in a finite amount of time. Given an execution trace \( \sigma = \{(s_0, t_0), (s_1, t_1), \ldots \} \), a time value \( t \in \mathbb{R}_+ \) and a natural number \( i \), the length of (or the number of states in) the execution trace is denoted by \( |\sigma| \), the \( i \)-th state of the execution trace by \( \sigma[i] \), the execution trace suffix starting at the \( i \)-th state by \( \sigma^i \), the execution trace suffix starting after \( t \) time by \( \sigma(t) = \sigma^t \), where \( i \in \mathbb{N} \) is the minimum index such that \( t \leq \sum_{j=0}^{\infty} t_j \), and the fact that the execution \( \sigma \) satisfies a property \( \phi \) by \( \sigma \models \phi \). For an execution trace \( \sigma \) at state \( s \) the value of a numeric state variable \( nsv \) is given by \( NV(s, nsv) \) and its associated scale and subsystem by \( SVSS(nsv) \), respectively the value of a spatial state variable \( spsv \) is given by \( SpV(s, spsv) \) and its associated scale and subsystem by \( SVSS(spsv) \).

In order to have a compact and easy to follow semantics description the full symbol names specific to BLMSTL were replaced with shorter abbreviations as described in Table 1.

**Definition.** Let \( M = (S, T, \mu, NSV, SpSV, NV, CSvP, MA, SVSS) \) be an MSSpDES and \( \sigma \) an execution of \( M \). The semantics of BLMSTL for \( \sigma \) is defined as follows:

- \( \sigma \models tnm_1 \approx tnm_2 \text{ if and only if } tnm_1(\sigma) \approx tnm_2(\sigma), \text{ where } tnm_1(\sigma) \text{ and } tnm_2(\sigma) \in \mathbb{R}, \text{ and } \approx \in \{<, <=, =, >, >\}; \)

- \( \sigma \models cm(tnm_1) \approx tnm_2 \text{ if and only if } |\sigma| > 1 \text{ and } cm(tnm_1, \sigma) \approx tnm_2(\sigma), \text{ where } cm(tnm_1, \sigma), tnm_2(\sigma) \in \mathbb{R}, \text{ and } \approx \in \{<, <=, =, >, >\}; \)
Table 1: Translation of full BLMSTL symbol names to abbreviated forms. The left column contains the full BLMSTL symbol name. The right column contains the corresponding abbreviated form.

<table>
<thead>
<tr>
<th>Full BLMSTL symbol name</th>
<th>Abbreviated symbol name</th>
<th>BLMSTL symbol name</th>
</tr>
</thead>
<tbody>
<tr>
<td><code>&lt;logic-property&gt;</code></td>
<td><code>ψ</code></td>
<td></td>
</tr>
<tr>
<td><code>&lt;temporal-numeric-measure&gt;</code></td>
<td><code>tnm</code></td>
<td></td>
</tr>
<tr>
<td><code>&lt;numeric-statistical-measure&gt;</code></td>
<td><code>nstm</code></td>
<td></td>
</tr>
<tr>
<td><code>&lt;numeric-measure-collection&gt;</code></td>
<td><code>nmc</code></td>
<td></td>
</tr>
<tr>
<td><code>&lt;numeric-measure&gt;</code></td>
<td><code>nm</code></td>
<td></td>
</tr>
<tr>
<td><code>&lt;primary-numeric-measure&gt;</code></td>
<td><code>pnm</code></td>
<td></td>
</tr>
<tr>
<td><code>&lt;numeric-spatial-measure&gt;</code></td>
<td><code>nsm</code></td>
<td></td>
</tr>
<tr>
<td><code>&lt;unary-statistical-measure&gt;</code></td>
<td><code>usm</code></td>
<td></td>
</tr>
<tr>
<td><code>&lt;binary-statistical-measure&gt;</code></td>
<td><code>bsm</code></td>
<td></td>
</tr>
<tr>
<td><code>&lt;binary-statistical-quantile-measure&gt;</code></td>
<td><code>bsqm</code></td>
<td></td>
</tr>
<tr>
<td><code>&lt;binary-numeric-measure&gt;</code></td>
<td><code>bnm</code></td>
<td></td>
</tr>
<tr>
<td><code>&lt;spatial-measure-collection&gt;</code></td>
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<tr>
<td><code>&lt;spatial-measure&gt;</code></td>
<td><code>sm</code></td>
<td></td>
</tr>
<tr>
<td><code>&lt;subset&gt;</code></td>
<td><code>ss</code></td>
<td></td>
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<tr>
<td><code>&lt;filter-numeric-measure&gt;</code></td>
<td><code>fnm</code></td>
<td></td>
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<tr>
<td><code>&lt;comparator&gt;</code></td>
<td><code>≍</code></td>
<td></td>
</tr>
<tr>
<td><code>&lt;change-measure&gt;</code></td>
<td><code>cm</code></td>
<td></td>
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<tr>
<td><code>&lt;real-number&gt;</code></td>
<td><code>re</code></td>
<td></td>
</tr>
<tr>
<td><code>&lt;scale-and-subsystem&gt;</code></td>
<td><code>scsubsys</code></td>
<td></td>
</tr>
<tr>
<td><code>&lt;state-variable&gt;</code></td>
<td><code>sv</code></td>
<td></td>
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<tr>
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<td></td>
</tr>
<tr>
<td><code>&lt;spatial-state-variable&gt;</code></td>
<td><code>spsv</code></td>
<td></td>
</tr>
</tbody>
</table>

- \( \sigma \models ~ \psi \) if and only if \( \sigma \not\models \psi \);
- \( \sigma \models \psi_1 \land \psi_2 \) if and only if \( \sigma \models \psi_1 \) and \( \sigma \models \psi_2 \);
- \( \sigma \models \psi_1 \lor \psi_2 \) if and only if \( \sigma \models \psi_1 \) or \( \sigma \models \psi_2 \);
- \( \sigma \models \psi_1 \Rightarrow \psi_2 \) if and only if \( \sigma \models \Rightarrow \psi_1 \) or \( \sigma \models \psi_2 \);
- \( \sigma \models \psi_1 \Leftrightarrow \psi_2 \) if and only if \( \sigma \models \psi_1 \Rightarrow \psi_2 \) and \( \sigma \models \psi_2 \Rightarrow \psi_1 \);
- \( \sigma \models \psi_1 U [a, b] \psi_2 \) if and only if there exists \( i, i \in [a, b] \), such that \( \sigma(i) \models \psi_2 \), and for all \( j, j \in [a, i) \), it holds that \( \sigma(j) \models \psi_1 \) with \( a, b \in \mathbb{R}_+ \);
- \( \sigma \models F [a, b] \psi \) if and only if there exists \( i, i \in [a, b] \), such that \( \sigma(i) \models \psi \) with \( a, b \in \mathbb{R}_+ \);
- \( \sigma \models G [a, b] \psi \) if and only if for all \( i, i \in [a, b] \), it holds that \( \sigma(i) \models \psi \) with \( a, b \in \mathbb{R}_+ \);
- \( \sigma \models X \psi \) if and only if \( |\sigma| > 1 \) and \( \sigma^1 \models \psi \);
- \( \sigma \models X[k] \psi \) if and only if \( |\sigma| > k \) and \( \sigma^k \models \psi \) with \( k \in \mathbb{N} \);
• $\sigma \models (\psi)$ if and only if $\sigma \models \psi$.

An illustrative example of how to employ logic properties to encode the expected behaviour of a system is given below both in natural language and BLMSTL:

**Natural language:** Throughout the time interval $[0, 100]$ the concentration of protein $A$ is expected to always increase;

**BLMSTL:** $G[0, 100](d(\{A\}) > 0)$.

The $tnm$ symbol represents the category of temporal numeric measures. Considering a model execution $\sigma$, $tnm(\sigma)$ is evaluated to a real number based on one of the definitions below:

- **Real number:** if $tnm = re$, then $tnm(\sigma) = re \in \mathbb{R}$;
- **Numeric state variable:** if $tnm = nsv$, then $tnm(\sigma) = nsv(\sigma)$;
- **Unary numeric measure:** if $tnm = nstm$, then $tnm(\sigma) = nstm(\sigma)$;
- **Binary numeric measure:** if $tnm = bnm(tnm', tnm'')$, where $bnm$ is a binary numeric measure, and $tnm'$ and $tnm''$ are temporal numeric measures, then $tnm(\sigma) = bnm(tnm'(\sigma), tnm''(\sigma))$ such that $tnm'(\sigma), tnm''(\sigma) \in \mathbb{R}$.

The values of the unary (i.e. $unm$) and binary (i.e. $bnm$) numeric measures considering one (i.e. $unm(re)$), respectively two real numbers (i.e. $bnm(re', re'')$) are computed as described in Appendix A (Tables 2, respectively 3).

An illustrative example of how to employ temporal numeric measures, unary numeric measures and binary numeric measures to encode the expected behaviour of a system is given below both in natural language and BLMSTL:

**Natural language:** At some point within the time interval $[0, 500]$ the (absolute value of the) difference between the concentration of chemical $X$ and chemical $Y$ is less than 20 M;

**BLMSTL:** $F[0, 500](abs(subtract(\{X\}, \{Y\})) < 20)$.

The category of numeric statistical measures is represented by the $nstm$ symbol. For a given model execution $\sigma$, $nstm(\sigma)$ is evaluated to a real number considering one of the definitions below:

- **Unary statistical numeric measure:** if $nstm = usm(nmc)$, where $usm$ is a unary statistical measure and $nmc$ is a numeric measure collection, then $nstm(\sigma) = usm(nmc(\sigma))$ such that $nmc(\sigma)$ represents a collection of real values;
- **Binary statistical numeric measure:** if $nstm = bsm(nmc', nmc'')$, where $bsm$ is a binary statistical measure, and $nmc'$ and $nmc''$ are numeric measure collections, then $nstm(\sigma) = bsm(nmc'(\sigma), nmc''(\sigma))$ such that $nmc'(\sigma)$ and $nmc''(\sigma)$ represent collections of real values;
• **Binary statistical quantile numeric measure**: if \( nstm = bsqm(nmc, re) \), where \( bsqm \) is a binary statistical quantile measure, \( nmc \) is a numeric measure collection and \( re \) is a real number, then \( nstm(\sigma) = bsqm(nmc(\sigma), re) \) such that \( nmc(\sigma) \) represents a collection of real values.

The value of *unary statistical* (i.e. \( usm \)), *binary statistical* (i.e. \( bsm \)) and *binary statistical quantile* (i.e. \( bsqm \)) measures considering a collection of real values (i.e. \( usm(nmc) \)), respectively two collections of real values (i.e. \( bsm(nmc', nmc'') \)) or a collection of real values and a real number (i.e. \( bsqm(nmc, re) \)) is computed as described in Appendix B (Tables 4, 5, respectively 6). In case the numeric measure collections considered contain insufficient elements the corresponding numeric statistical measures are evaluated to zero.

The \( nmc \) symbol represents numeric measure collections. Given a model simulation \( \sigma \), \( nmc(\sigma) \) is evaluated to a collection of real values according to one of the following definitions:

- **Spatial measure collection**: if \( nmc = smc \), then \( nmc(\sigma) = smc(\sigma) \);

- **Temporal numeric measure collection**: if \( nmc = [a,b] nm \), where \( nm \) is a numeric measure, and \( a \) and \( b \) are real numbers, then \( nmc(\sigma) = \{ nm(\sigma(i)) \mid nm(\sigma(i)) \in \mathbb{R} \text{ is the result of evaluating the numeric measure } nm \text{ against the subtrace } \sigma(i), \text{ for all } i \in [a,b] \text{ with } a,b \in \mathbb{R}_+ \} \).

An illustrative example of how to employ numeric measure collections and unary statistical measures to encode the expected behaviour of a system is given below both in natural language and BLMSTL:

**Natural language**: Considering the time interval \([100, 200]\) the maximum upper value of the blood pressure corresponding to scale organism and subsystem human is less than 150;

**BLMSTL**: \( \max([100, 200] \{ \text{bloodPressureUpperValue} \} \text{ (scaleAndSubsystem = Organism.Human)) < 150.} \)

The \( nm \) symbol represents the category of real-valued numeric measures.

Considering a given execution \( \sigma \), \( nm(\sigma) \) is evaluated to a real number according to one of the definitions described below:

- **Primary numeric measure**: if \( nm = pnm \), then \( nm(\sigma) = pnm(\sigma) \);

- **Unary numeric measure**: if \( nm = unm(nm') \), where \( unm \) is a unary numeric measure and \( nm' \) is a numeric measure, then \( nm(\sigma) = unm(nm'(\sigma)) \) such that \( nm'(\sigma) \in \mathbb{R} \);

- **Binary numeric measure**: if \( nm = bnm(nm', nm'') \), where \( bnm \) is a binary numeric measure, and \( nm' \) and \( nm'' \) are numeric measures, then \( nm(\sigma) = bnm(nm'(\sigma), nm''(\sigma)) \) such that \( nm'(\sigma), nm''(\sigma) \in \mathbb{R} \).

The \( pnm \) symbol corresponds to primary numeric (real-valued) measures.

Considering a given execution \( \sigma \), \( pnm(\sigma) \) is evaluated to a real number according to one of the following definitions:

- **Numeric spatial measure**: if \( nm = nsm \), then \( nm(\sigma) = nsm(\sigma) \);

- **Real number**: if \( nm = re \), then \( nm(\sigma) = re \in \mathbb{R} \);
• **Numeric state variable:** if \( nm = nsv \), then \( nm(\sigma) = nsv(\sigma) \).

The \( nsm \) symbol represents the category of numeric (real-valued) spatial measures. Considering a given execution \( \sigma \), \( nsm(\sigma) \) is evaluated to a real number according to one of the definitions described below:

- **Unary statistical spatial measure:** if \( nsm = usm(sm) \), where \( usm \) is a unary statistical measure and \( sm \) is a spatial measure collection, then \( nsm(\sigma) = usm(sm(\sigma)) \) such that \( sm(\sigma) \) represents a collection of real values;

- **Binary statistical spatial measure:** if \( nsm = bsm(sm', sm'') \), where \( bsm \) is a binary statistical measure, and \( sm' \) and \( sm'' \) are spatial measure collections, then \( nsm(\sigma) = bsm(sm'(\sigma), sm''(\sigma)) \) such that \( sm'(\sigma) \) and \( sm''(\sigma) \) represent collections of real values;

- **Binary statistical quantile spatial measure:** if \( nsm = bsqm(sm, re) \), where \( bsqm \) is a binary statistical quantile measure, \( sm \) is a spatial measure collection and \( re \) is a real number, then \( nsm(\sigma) = bsqm(sm(\sigma), re) \) such that \( sm(\sigma) \) represents a collection of real values.

The \( nsc \) symbol represents spatial measure collections. Considering a model execution \( \sigma \), \( nsc(\sigma) \) is evaluated to a collection of real values using one of the definitions below:

- **Primary spatial measure collection:** if \( nsc = sm(ss) \), where \( sm \) is a spatial measure and \( ss \) is the subset of considered spatial entities, then \( nsc(\sigma) = \{ sm_value | sm_value \in \mathbb{R} \} \) is the result of evaluating the spatial measure \( sm \) for all spatial entities in \( ss(\sigma) \);

- **Unary numeric spatial measure collection:** if \( nsc = unm(sm') \), where \( unm \) is a unary numeric measure and \( sm' \) is a spatial measure collection, then \( nsc(\sigma) = unm(sm'(\sigma)) \), where \( unm(sm'(\sigma)) = \{ value | value = unm(sm'_{\text{value}}) \} \) for all \( sm'_{\text{value}} \in sm'(\sigma) \);

- **Binary numeric spatial measure collection:** if \( nsc = bnm(sm', sm'') \), where \( bnm \) is a binary numeric measure, and \( sm' \) and \( sm'' \) are spatial measure collections, then \( nsc(\sigma) = bnm(sm'(\sigma), sm''(\sigma)) \), where \( bnm(sm'(\sigma), sm''(\sigma)) = \{ value | value = bnm(sm'_{\text{value}}, sm''_{\text{value}}) \} \) where \( sm'_{\text{value}} \) and \( sm''_{\text{value}} \) are the \( i \)-th values in \( sm'(\sigma) \), respectively \( sm''(\sigma) \) for all \( i, 1 \leq i \leq \min(|sm'(\sigma)|, |sm''(\sigma)|) \).

Spatial measures \( sm \) are defined over the set \{clusteredness, density, area, perimeter, distanceFromOrigin, angle, triangleMeasure, rectangleMeasure, circleMeasure, centroidX, centroidY\} which is identical to the set of spatial measures computed for each detected region/cluster during the multiscale spatiotemporal analysis step of the model checking workflow.

Subsets of spatial entities are represented by the \( ss \) symbol. Considering a given execution \( \sigma \), \( ss(\sigma) \) is evaluated to a collection of spatial entities according to one of the definitions described below:

- **Specific subset:** if \( ss = \text{specificSubset} \), then \( ss(\sigma) = \text{specificSubset}(\sigma) \), where \( \text{specificSubset}(\sigma) \) represents the collection of all clusters/regions corresponding to \( \sigma[0] \);
• **Filtered specific subset**: if \( ss = \text{filter}(\text{specificSubset}, \text{constraint}) \), where \text{specificSubset} has the semantics defined above and \text{constraint} is a logic property for encoding constraints on spatial measure values (e.g. area > 10), then \( ss(\sigma) = \text{filter}(\text{specificSubset}(\sigma), \text{constraint}) \);

• **Subset operation result**: if \( ss = \text{subsetOperation}(ss', ss'') \), where \( ss' \) and \( ss'' \) are subsets of spatial entities, and \text{subsetOperation} is a subset operation, then \( ss(\sigma) = \text{subsetOperation}(ss'(\sigma), ss''(\sigma)) \) such that \( ss'(\sigma) \) and \( ss''(\sigma) \) represent collections of spatial entities.

Given an execution \( \sigma \) the value of \( \text{specificSubset}(\sigma) \) is computed using one of the definitions described below:

• **Regions**: if \( \text{specificSubset} = \text{regions} \), then \( \text{specificSubset}(\sigma) = \bigcup \{ \text{region} \mid \text{region} \in \text{regionsDetectionMechanism}(\text{SpV}(\sigma[0], \text{spsv})) \text{ such that } \text{SpV} \in \text{CSpV} \text{ is defined for state } \sigma[0] \text{ and spatial state variable } \text{spsv} \};

• **Clusters**: if \( \text{specificSubset} = \text{clusters} \), then \( \text{specificSubset}(\sigma) = \text{clustersDetectionMechanism}(\text{reg}) \), where \( \text{reg} = \bigcup \{ \text{region} \mid \text{region} \in \text{regionDetectionMechanism}(\text{SpV}(\sigma[0], \text{spsv})) \text{ such that } \text{SpV} \in \text{CSpV} \text{ is defined for state } \sigma[0] \text{ and spatial state variable } \text{spsv} \};

An illustrative example of how to employ specific subsets of spatial entities and unary statistical measures to encode the expected behaviour of a system is given below both in natural language and BLMSTL:

**Natural language**: During the time interval \([50.3, 112.7]\) the average area of the regions corresponding to scale tissue and subsystem cancerous liver tissue is increasing until it reaches a value greater than 2400;

**BLMSTL**: \((d(\text{avg}(\text{area}(\text{filter}(\text{regions}, \text{scaleAndSubsystem} = \text{Tissue}.\text{CancerousLiverTissue})))) > 0) \cup [50.3, 112.7]
\((\text{avg}(\text{area}(\text{filter}(\text{regions}, \text{scaleAndSubsystem} = \text{Tissue}.\text{CancerousLiverTissue})))) > 2400)\).

Subsets of spatial entities collections recorded by \text{specificSubset} can be computed using the \text{filter} predicate. Considering an execution \( \sigma \), a collection of spatial entities \text{specificSubset} and a constraint on spatial measure values \text{constraint}, \text{filter}(\text{specificSubset}(\sigma), \text{constraint}) \) is evaluated to a collection of spatial entities using the definition described below:

\[
\text{filter}(\text{specificSubset}(\sigma), \text{constraint}) = \{ \text{se} \mid \text{se} \text{ is a spatial entity in } \text{specificSubset}(\sigma) \text{ which satisfies } \text{constraint} \text{ i.e. } \text{se} \models \text{constraint} \}.
\]

The semantics of the constraint satisfaction problem considering an execution \( \sigma \), a spatial entity \( \text{se} \) and a constraint \text{constraint} is defined as follows:

• if \( \text{constraint} = \text{scaleAndSubsystem} \models \text{scsubsys} \), then \( \text{se} \models \text{scaleAndSubsystem} \models \text{scsubsys} \text{ if and only if } \) there exists a vertex \( v_{\text{scsubsys}} \in V_{\text{MA}} \) encoding the scale and subsystem \text{scsubsys}, \( \text{se} \) was annotated with a scale and subsystem \( \text{se}\text{scaleAndSubsystem} \text{ which has a corresponding vertex } v_{\text{se}\text{scaleAndSubsystem}} \in V_{\text{MA}} \), and \( v_{\text{se}\text{scaleAndSubsystem}} \models
$v_{\text{scsubsys}}$, where $V_{MA}$ is the set of vertices in the multiscale architecture graph $MA$, and $\varepsilon \in \{<, \leq, =, \geq, >\}$. To determine the truth value of expressions of the form $v_{\text{scaleAndSubsystem}} \varepsilon v_{\text{scsubsys}}$ the partial orders $<$ and $\leq$ defined over the set of vertices $V_{MA}$ are considered. Therefore $v_{\text{scaleAndSubsystem}} < v_{\text{scsubsys}}$ holds if the path from the root of $MA$ to $v_{\text{scaleAndSubsystem}}$ passes through $v_{\text{scsubsys}}$. Conversely $v_{\text{scaleAndSubsystem}} > v_{\text{scsubsys}}$ holds if the path from the root of $MA$ to $v_{\text{scaleAndSubsystem}}$ passes through $v_{\text{scsubsys}}$.

Expressions $v_{\text{scaleAndSubsystem}} \leq v_{\text{scsubsys}}$ and $v_{\text{scaleAndSubsystem}} \geq v_{\text{scsubsys}}$ hold if $v_{\text{scaleAndSubsystem}} < v_{\text{scsubsys}}$ or $v_{\text{scaleAndSubsystem}} > v_{\text{scsubsys}}$, respectively if $v_{\text{scaleAndSubsystem}} \geq v_{\text{scsubsys}}$ or $v_{\text{scaleAndSubsystem}} \leq v_{\text{scsubsys}}$.

- If $\text{constraint} = \text{sm} \succ \text{fnm}$, then $se \models \text{sm} \succ \text{fnm}$ if and only if $\text{sm}(se) \succ \text{fnm}(se, \sigma)$, where $\text{sm}(se)$ evaluates the spatial measure $\text{sm}$ for the given spatial entity $se$, $\text{sm} \in \{\text{clusteredness, density, area, perimeter, distanceFromOrigin, angle, triangleMeasure, rectangleMeasure, circleMeasure, centroidX, centroidY}\}$, $\text{fnm}(se, \sigma) \in \mathbb{R}$ represents a real number obtained by evaluating the filter numeric measure $\text{fnm}$ against $se$ and $\sigma$, and $\varepsilon \in \{<, \leq, =, \geq, >\}$.

- If $\text{constraint} = \sim \text{constraint}_1$, then $se \models \sim \text{constraint}_1$ if and only if $se \not\models \text{constraint}_1$.

- If $\text{constraint} = \text{constraint}_1 \land \text{constraint}_2$, then $se \models \text{constraint}_1 \land \text{constraint}_2$ if and only if $se \models \text{constraint}_1$ and $se \models \text{constraint}_2$.

- If $\text{constraint} = \text{constraint}_1 \lor \text{constraint}_2$, then $se \models \text{constraint}_1 \lor \text{constraint}_2$ if and only if $se \models \text{constraint}_1$ or $se \models \text{constraint}_2$.

- If $\text{constraint} = \text{constraint}_1 \Rightarrow \text{constraint}_2$, then $se \models \text{constraint}_1 \Rightarrow \text{constraint}_2$ if and only if $se \models \sim \text{constraint}_1$ or $se \models \text{constraint}_2$.

- If $\text{constraint} = \text{constraint}_1 \Leftrightarrow \text{constraint}_2$, then $se \models \text{constraint}_1 \Leftrightarrow \text{constraint}_2$ if and only if $se \models \sim \text{constraint}_1$ or $se \models \text{constraint}_2$.

- If $\text{constraint} = (\text{constraint})$, then $se \models (\text{constraint})$ if and only if $se \models \text{constraint}$.

The $\text{fnm}$ symbol represents the (real-valued) numeric measure computed for the filter predicate. Given a spatial entity $se$ and an execution $\sigma$, $\text{fnm}(se, \sigma)$ is evaluated to a real number using one of the definitions given below:

- **Primary numeric measure**: if $\text{fnm} = \text{pnm}$, then $\text{fnm}(se, \sigma) = \text{pnm}(\sigma)$;

- **Spatial measure**: if $\text{fnm} = \text{sm}$, where $\text{sm} \in \{\text{clusteredness, density, area, perimeter, distanceFromOrigin, angle, triangleMeasure, rectangleMeasure, circleMeasure, centroidX, centroidY}\}$, then $\text{fnm}(se, \sigma) = \text{sm}(se)$;

- **Unary filter numeric measure**: if $\text{fnm} = \text{unm}(\text{fnm}')$, where $\text{unm}$ is a unary numeric measure and $\text{fnm}'$ is a filter numeric measure, then $\text{fnm}(se, \sigma) = \text{unm}(\text{fnm}'(se, \sigma))$ such that $\text{fnm}'(se, \sigma) \in \mathbb{R}$. 

11
• Binary filter numeric measure: if $fnm = bnm(fnm', fnm'')$, where $bnm$ is a binary numeric measure, and $fnm'$ and $fnm''$ are filter numeric measures, then $fnm(se, \sigma) = bnm(fnm'(se, \sigma), fnm''(se, \sigma))$ such that $fnm'(se, \sigma), fnm''(se, \sigma) \in \mathbb{R}$.

The $\text{subsetOperation} \in \{\text{difference}, \text{intersection}, \text{union}\}$ symbol represents the collection of operations defined over spatial entities subsets. Given two spatial entities subsets $ss'$ and $ss''$, $\text{subsetOperation}(ss', ss'')$ is evaluated to a collection of spatial entities using one of the following definitions:

- **Difference**: if $\text{subsetOperation} = \text{difference}$, then $\text{subsetOperation}(ss', ss'') = \{se | se \in ss' \text{ and } se \not\in ss''\}$;
- **Intersection**: if $\text{subsetOperation} = \text{intersection}$, then $\text{subsetOperation}(ss', ss'') = \{se | se \in ss' \text{ and } se \in ss''\}$;
- **Union**: if $\text{subsetOperation} = \text{union}$, then $\text{subsetOperation}(ss', ss'') = \{se | se \in ss' \text{ or } se \in ss''\}$.

An illustrative example of how to employ subset operations and multiple filtered subsets of spatial entities to encode the expected behaviour of a system is given below both in natural language and BLMSTL:

**Natural language**: The number of clusters of cells having the area greater than 20 or cellular regions having the area smaller than 50 is greater than 0;

**BLMSTL**: $\text{count(area(union(filter(clusters, area > 20), filter(regions, area < 50))))} > 0$.

The $cm \in \{d, r\}$ symbol represents the collection of measures which compute the rate at which the value of a temporal numeric measure $tnm$ changes from the current state to the next. Considering a temporal numeric measure $tnm$ and a given execution $\sigma$, such that $|\sigma| > 1$, $cm(tnm, \sigma)$ is evaluated to a real number according to one of the definitions below:

- **Derivative**: if $cm = d$, then $cm(tnm, \sigma) = d(tnm, \sigma)$, where
  
  $$d(tnm, \sigma) = \frac{tnm(\sigma^1) - tnm(\sigma^0)}{t_0};$$

- **Ratio**: if $cm = r$, then $cm(tnm, \sigma) = r(tnm, \sigma)$, where
  
  $$r(tnm, \sigma) = \frac{tnm(\sigma^1)}{tnm(\sigma^0)};$$

where $t_0$ represents the time duration spent in state $\sigma[0]$.

Finally the symbol $nsv$ represents real-valued numeric state variables. Given an execution $\sigma$, $nsv(\sigma)$ is evaluated to a real number according to one of the following definitions:

- **Numeric state variable without an associated scale and subsystem**: if $nsv = sv$, where $sv$ is the identifier of a numeric state variable having no associated scale and subsystem (i.e. $\text{SVSS}(sv)$ is not defined), then $nsv(\sigma) = NV(\sigma[0], sv)$:
• **Numeric state variable with an associated scale and subsystem:**
  if $nsv = sv(scaleAndSubsystem = scsubsys)$, where $sv$ is the identifier of a numeric state variable having the associated scale and subsystem $scsubsys$, then $nsv(\sigma) = NV(\sigma[0], sv)$ and $SVSS(sv) = v_{scsubsys}$ such that $v_{scsubsys} \in V_{MA}$ corresponds to the scale and subsystem $scsubsys$.

An illustrative example of how to employ change measures and numeric state variables to encode the expected behaviour of a system is given below both in natural language and BLMSTL:

**Natural language:** Throughout the time interval $[20.1, 20.5]$ the concentration of calcium doubles from one time point to the next relative to the duration spent in each state;

**BLMSTL:** $G [20.1, 20.5] (r(\{Calcium\}) = 2)$. 
## Appendices

### A Numeric measures

Table 2: Name, description and semantics of unary numeric measures

<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
<th>Semantics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>abs</strong></td>
<td>Returns the absolute value of a number ( n )</td>
<td>( \text{abs}(n) =</td>
</tr>
<tr>
<td><strong>ceil</strong></td>
<td>Rounds the number ( n ) upward, returning the smallest integral value that is not less than ( n )</td>
<td>( \text{ceil}(n) = \lceil n \rceil )</td>
</tr>
<tr>
<td><strong>floor</strong></td>
<td>Rounds the number ( n ) downward, returning the largest integral value that is not greater than ( n )</td>
<td>( \text{floor}(n) = \lfloor n \rfloor )</td>
</tr>
<tr>
<td><strong>round</strong></td>
<td>Returns the integral value that is nearest to number ( n ), with halfway cases rounded away from zero</td>
<td>( \text{round}(n) = \begin{cases} \lfloor n + 0.5 \rfloor, &amp; \text{if } n \geq 0 \ \lceil n - 0.5 \rceil, &amp; \text{otherwise} \end{cases} )</td>
</tr>
<tr>
<td><strong>sign</strong></td>
<td>Returns the sign of a number ( n )</td>
<td>( \text{sign}(n) = \begin{cases} 1, &amp; \text{if } n &gt; 0 \ 0, &amp; \text{if } n = 0 \ -1, &amp; \text{otherwise} \end{cases} )</td>
</tr>
<tr>
<td><strong>sqrt</strong></td>
<td>Returns the square root of a number ( n )</td>
<td>( \sqrt[n]{n} )</td>
</tr>
<tr>
<td><strong>trunc</strong></td>
<td>Rounds number ( n ) toward zero</td>
<td>( \text{trunc}(n) = \text{sign}(n) \lfloor</td>
</tr>
</tbody>
</table>

Table 3: Name, description and semantics of binary numeric measures

<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
<th>Semantics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>add</strong></td>
<td>Returns the sum of two numbers ( n_1 ) and ( n_2 )</td>
<td>( \text{add}(n_1, n_2) = n_1 + n_2 )</td>
</tr>
<tr>
<td><strong>div</strong></td>
<td>Returns the integer part of the division ( n_1/n_2 )</td>
<td>( \text{div}(n_1, n_2) = \lfloor n_1/n_2 \rfloor )</td>
</tr>
<tr>
<td><strong>log</strong></td>
<td>Returns the logarithm of a number ( n ) in the given base ( b )</td>
<td>( \text{log}(n, b) = \log_b (</td>
</tr>
<tr>
<td>Function</td>
<td>Description</td>
<td>Semantics</td>
</tr>
<tr>
<td>----------</td>
<td>-------------</td>
<td>-----------</td>
</tr>
<tr>
<td><code>mod</code></td>
<td>Returns the remainder of the division ( n_1/n_2 )</td>
<td>( \text{mod}(n_1, n_2) = n_1 - (n_2 \times \text{div}(n_1, n_2)) )</td>
</tr>
<tr>
<td><code>multiply</code></td>
<td>Returns the multiplication of two numbers ( n_1 ) and ( n_2 )</td>
<td>( \text{multiply}(n_1, n_2) = n_1 \times n_2 )</td>
</tr>
<tr>
<td><code>power</code></td>
<td>Returns the base ( b ) raised at the power ( e )</td>
<td>( \text{pow}(b, e) = b^e )</td>
</tr>
<tr>
<td><code>subtract</code></td>
<td>Returns the difference between two numbers ( n_1 ) and ( n_2 )</td>
<td>( \text{subtract}(n_1, n_2) = n_1 - n_2 )</td>
</tr>
</tbody>
</table>

### B Statistical measures

Table 4: Name, description and semantics of unary statistical measures

<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
<th>Semantics</th>
</tr>
</thead>
<tbody>
<tr>
<td><code>avg</code></td>
<td>Returns the arithmetic mean for the considered collection of values</td>
<td>( \text{avg}(\text{values}) = \frac{1}{n} \sum_{i=1}^{n} (\text{values}_i) ), where ( n =</td>
</tr>
<tr>
<td><code>count</code></td>
<td>Returns the number of elements in the considered collection of values</td>
<td>( \text{count}(\text{values}) =</td>
</tr>
<tr>
<td><code>geomean</code></td>
<td>Returns the geometric mean for the considered collection of values</td>
<td>( \text{geomean}(\text{values}) = \left( \prod_{i=1}^{n} (\text{values}_i) \right)^{\frac{1}{n}} ), where ( n =</td>
</tr>
<tr>
<td><code>harmean</code></td>
<td>Returns the harmonic mean for the considered collection of values</td>
<td>( \text{harmean}(\text{values}) = \frac{n}{\sum_{i=1}^{n} (\text{values}_i)} ), where ( n =</td>
</tr>
<tr>
<td><code>kurt</code></td>
<td>Returns the kurtosis for the considered collection of values</td>
<td>( \text{kurt}(\text{values}) = \frac{n(n+1)}{(n-1)(n-2)(n-3)} \sum_{i=1}^{n} \left( \frac{(\text{values}_i) - \text{avg}(\text{values})}{\text{std}(\text{values})} \right)^4 - \frac{3(n-1)^2}{(n-2)(n-3)} ), where ( n =</td>
</tr>
<tr>
<td><code>max</code></td>
<td>Returns the maximum for the considered collection of values</td>
<td>( \text{max}(\text{values}) = \max_{i=1}^{n} (\text{values}_i) ), where ( n =</td>
</tr>
</tbody>
</table>
**median** Returns the median for the considered collection of values

\[
\text{median}(\text{values}) = \text{middle element from position } \left\lfloor \frac{|\text{values}|}{2} \right\rfloor \text{ (0-based indexing)} \text{ in the ordered list of values}
\]

**min** Returns the minimum for the considered collection of values

\[
\text{min}(\text{values}) = \min_{i=1}^{n}(\text{values}_i), \quad \text{where } n = |\text{values}|
\]

**mode** Returns the mode for the considered collection of values

\[
\text{mode}(\text{values}) = \text{element which appears most often in the list of values}
\]

**product** Returns the product for the considered collection of values

\[
\text{product}(\text{values}) = \prod_{i=1}^{n}(\text{values}_i), \quad \text{where } n = |\text{values}|
\]

**skew** Returns the skewness for the considered collection of values

\[
\text{skew}(\text{values}) = \frac{n}{(n-1)(n-2)} \sum_{i=1}^{n} \left( \frac{\text{values}_i - \text{avg}(\text{values})}{\text{stddev}(\text{values})} \right)^3,
\]

where \( n = |\text{values}| \)

**stdev** Returns the standard deviation for the considered collection of values

\[
\text{stdev}(\text{values}) = \sqrt{\frac{\sum_{i=1}^{n} (\text{values}_i - \text{avg}(\text{values}))^2}{(n-1)}},
\]

where \( n = |\text{values}| \)

**sum** Returns the sum for the considered collection of values

\[
\text{sum}(\text{values}) = \sum_{i=1}^{n}(\text{values}_i), \quad \text{where } n = |\text{values}|
\]

**var** Returns the variance for the considered collection of values

\[
\text{var}(\text{values}) = \frac{\sum_{i=1}^{n} (\text{values}_i - \text{avg}(\text{values}))^2}{(n-1)},
\]

where \( n = |\text{values}| \)
Table 5: Name, description and semantics of binary statistical measures

<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
<th>Semantics</th>
</tr>
</thead>
<tbody>
<tr>
<td>covar</td>
<td>Returns the covariance for the considered collections of values $values_1$ and $values_2$</td>
<td>$covar(values_1, values_2) = \frac{1}{n-1} \sum_{i=1}^{n} ((values_1)_i - \text{avg}(values_1))((values_2)_i - \text{avg}(values_2))$, where $n = \min(</td>
</tr>
</tbody>
</table>

Table 6: Name, description and semantics of binary statistical quantile measures

<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
<th>Semantics</th>
</tr>
</thead>
<tbody>
<tr>
<td>percentile</td>
<td>Returns the $pc$-th ($0 \leq pc \leq 100$) percentile for the considered collection of values</td>
<td>$percentile(values, pc) = i$-th value in the ordered list of values, where $i = \left\lfloor \frac{pc}{100} \times n + \frac{1}{2} \right\rfloor$, and $n =</td>
</tr>
<tr>
<td>quartile</td>
<td>Returns the $i$-th ($i \in {25, 50, 75}$) quartile for the considered collection of values</td>
<td>Let $v$ be the ordered list of values, $m = \text{median}(values)$, $L$ the sublist of values in $v$ smaller than $m$, and $U$ the sublist of values in $v$ greater than $m$. $quartile(values) = \text{median}(L)$ if $i = 25$, $m$ if $i = 50$, and $\text{median}(U)$ if $i = 75$.</td>
</tr>
</tbody>
</table>