S1 Differentiation rules

For approximating the tissue concentration rates of change we use the stand-alone fuzzy logic controller provided by MATLAB's Fuzzy Logic Toolbox (The MathWorks, Inc., Natick, MA), compiled as a shared C library with the following configuration:

Option	Value
Input variables	$c_\mathrm{w}, c_\mathrm{l}, c_\mathrm{c}, c_\mathrm{s}, c_\mathrm{v}, s_\mathrm{b}, s_\mathrm{v}, \gamma_\mathrm{peak}, \varepsilon_\mathrm{peak}, \gamma_\mathrm{eff}, \varepsilon_\mathrm{eff}$
Output variables	$\Delta c_\mathrm{w}, \Delta c_\mathrm{c}, \Delta c_\mathrm{v}$
Logical AND operator	$\min$
Logical OR operator	$\max$
Logical implication	$\min$ (Mamdani implication)
Logical aggregation	$\max$
Defuzzification	Center of area

Linguistic rules

The fuzzy logic controller evaluates the following 27 linguistic rules to determine the values of $\Delta c_\mathrm{w}, \Delta c_\mathrm{c}$ and Δc_v:

Rule no.	If …	then …
1	$\varepsilon_\mathrm{peak}$ is negative destructive	Δc_w is negative and Δc_c is negative and Δc_v is negative
2	$\varepsilon_\mathrm{peak}$ is positive destructive	Δc_w is negative and Δc_c is negative and Δc_v is negative
3	γ_peak is very high	Δc_w is negative and Δc_c is negative and Δc_v is negative
4	$\varepsilon_\mathrm{peak}$ is not negative destructive	Δc_w is about zero and Δc_c is about zero and Δc_v is about zero
5	$\varepsilon_\mathrm{peak}$ is not positive destructive	Δc_w is about zero and Δc_c is about zero and Δc_v is about zero
6	c_v is low and s_v is not low and $\varepsilon_\mathrm{peak}$ is not negative high and γ_peak is not high	Δc_v is positive

7	c_{v} is medium and s_{v} is not low and $\varepsilon_{\mathrm{peak}}$ is not negative high and γ_{peak} is not high	Δc_{v} is positive
8	c_{v} is high and $\varepsilon_{\mathrm{peak}}$ is not negative high and γ_{peak} is not high	Δc_{v} is positive
9	c_{c} is low and c_{v} is high and s_{v} is high and $\varepsilon_{\mathrm{eff}}$ is negative medium γ_{eff} is medium	Δc_{w} is positive
10	c_{c} is low and c_{v} is high and s_{v} is high and $\varepsilon_{\mathrm{eff}}$ is positive medium γ_{eff} is medium	Δc_{w} is positive
11	c_{b} is not high and c_{c} is low and $\varepsilon_{\mathrm{peak}}$ is negative high and γ_{peak} is not very high	Δc_{c} is positive
12	c_{b} is not high and c_{c} is low and $\varepsilon_{\mathrm{peak}}$ is negative medium and γ_{peak} is not very high	Δc_{c} is positive
13	c_{c} is not low and $\varepsilon_{\mathrm{peak}}$ is negative high and γ_{peak} is not very high	Δc_{c} is positive
14	c_{c} is not low and $\varepsilon_{\mathrm{peak}}$ is negative medium and γ_{peak} is not very high	Δc_{c} is positive
15	c_{c} is not low and c_{v} is not low and s_{b} is not low and $\varepsilon_{\mathrm{eff}}$ is negative medium and γ_{eff} is low	Δc_{w} is positive
16	c_{c} is not low and c_{v} is not low and s_{b} is not low and	Δc_{c} is negative

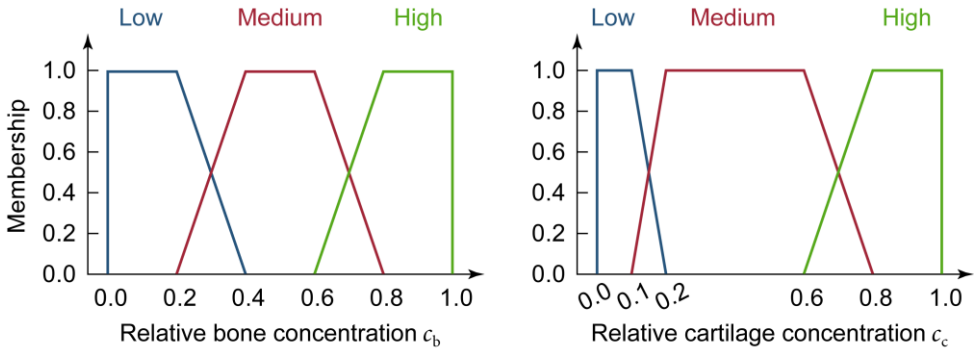
	$\varepsilon_{\mathrm{peak}}$ is negative medium and γ_{peak} is low	
17	c_{c} is not low and c_{v} is not low and s_{b} is not low and $\varepsilon_{\mathrm{eff}}$ is negative high and γ_{eff} is low	Δc_{w} is positive
18	c_{c} is not low and c_{v} is not low and s_{b} is not low and $\varepsilon_{\mathrm{peak}}$ is negative high and γ_{peak} is low	Δc_{c} is negative
19	c_{c} is not low and c_{v} is not low and s_{b} is not low and $\varepsilon_{\mathrm{eff}}$ is negative high and γ_{eff} is medium	Δc_{w} is positive
20	c_{c} is not low and c_{v} is not low and s_{b} is not low and $\varepsilon_{\mathrm{peak}}$ is negative high and γ_{peak} is medium	Δc_{c} is negative
21	c_{c} is not low and c_{v} is not low and s_{b} is not low and $\varepsilon_{\mathrm{eff}}$ is negative medium and γ_{eff} is medium	Δc_{w} is positive
22	c_{c} is not low and c_{v} is not low and s_{b} is not low and $\varepsilon_{\mathrm{peak}}$ is negative medium and γ_{peak} is medium	Δc_{c} is negative
23	c_{c} is low and c_{v} is not low and c_{b} is high and s_{b} is high and $\varepsilon_{\mathrm{eff}}$ is negative medium and γ_{eff} is medium	Δc_{w} is positive
24	c_{c} is low and	Δc_{c} is negative

	c_v is not low and c_b is high and s_b is high and ε_{peak} is negative medium and γ_{peak} is medium	
25	c_c is low and c_v is not low and c_b is high and s_b is high and ε_{eff} is negative medium and γ_{eff} is low	Δc_w is positive
26	c_c is low and c_v is not low and c_b is high and s_b is high and ε_{peak} is negative medium and γ_{peak} is low	Δc_c is negative
27	ε_{eff} is about zero and γ_{eff} is very low	Δc_w is negative

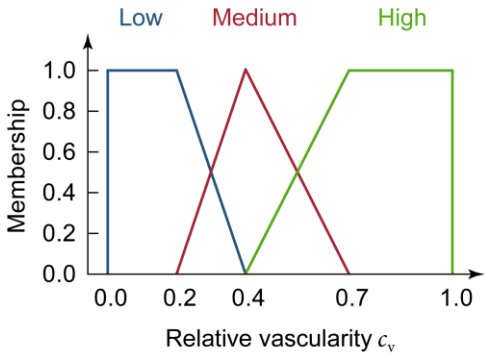
Note that Rule 27 (bone resorption due to understimulation) is evaluated separately from the other rules as a post-processing step in order to determine resorption rates for both woven and lamellar bone (for implementation details, please refer to the main text as well as Frank Niemeyer's PhD thesis [pages 329 and 330; DOI: 10.18725/OPARU-2961]).

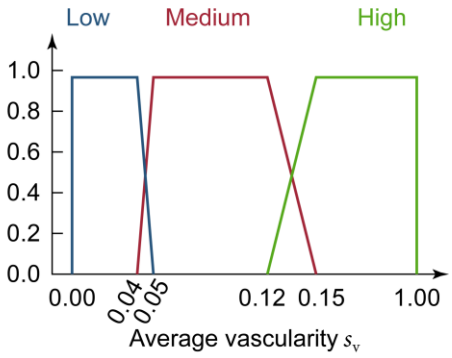
Membership functions

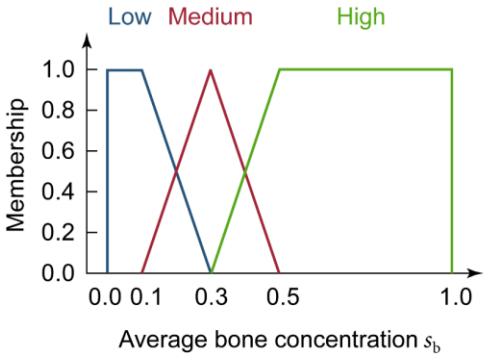
The fuzzy sets the linguistic rules refer to are defined as the following trapezoidal membership functions:

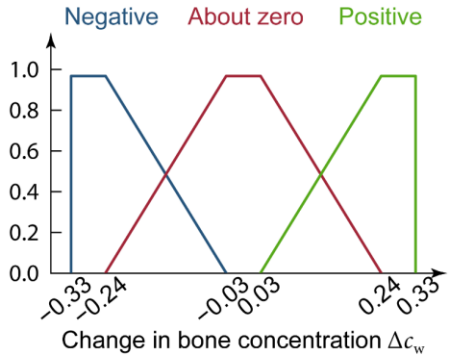

Low
Medium
High
Membership
1.0
0.8
0.6
0.4
0.2
0.0
0.0 0.2 0.4 0.6 0.8 1.0
Relative bone concentration c_b

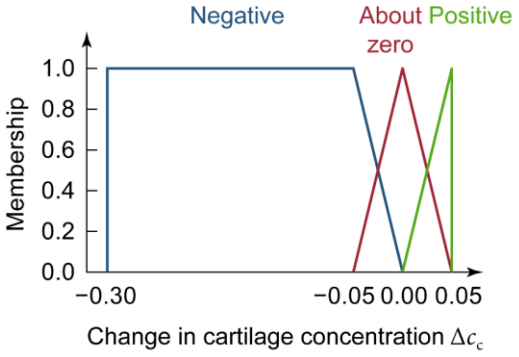
Low
Medium
High
1.0
0.8
0.6
0.4
0.2
0.0
0.0 0.1 0.2 0.6 0.8 1.0
Relative cartilage concentration c_c

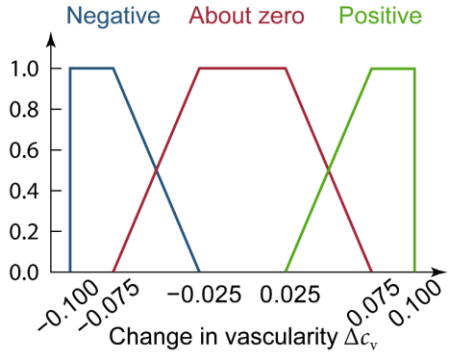

Low
Medium
High
Membership
1.0
0.8
0.6
0.4
0.2
0.0
0.0 0.2 0.4 0.7 1.0
Relative vascularity c_v

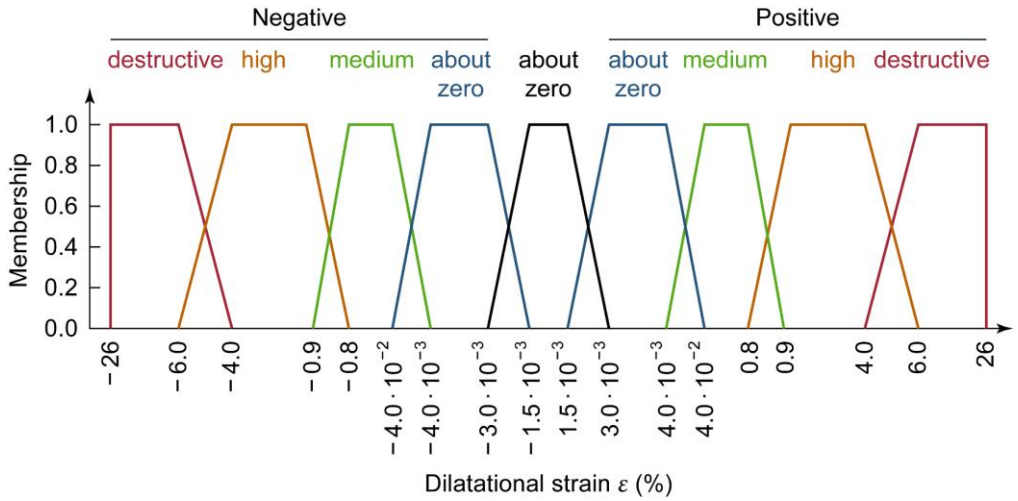

Low
Medium
High
1.0
0.8
0.6
0.4
0.2
0.0
0.00 0.04 0.05 0.12 0.15 1.00
Average vascularity s_v

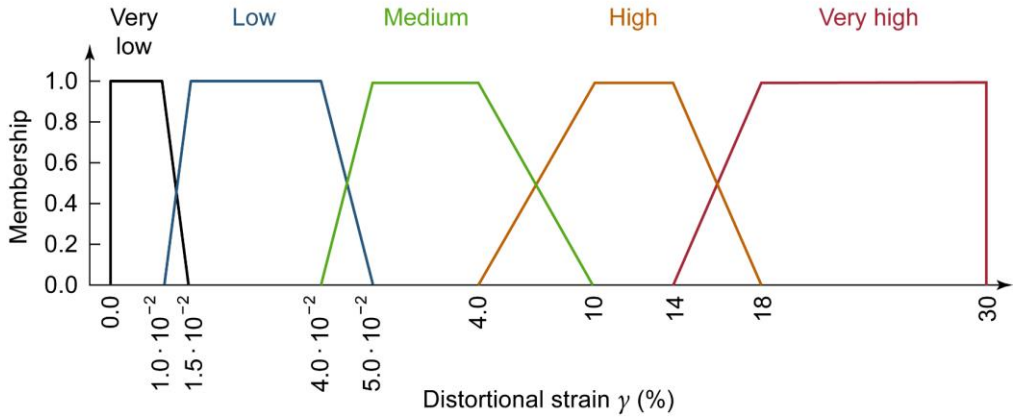

Low
Medium
High
Membership
1.0
0.8
0.6
0.4
0.2
0.0
0.0 0.1 0.3 0.5 1.0
Average bone concentration s_b


Negative
About zero
Positive
1.0
0.8
0.6
0.4
0.2
0.0
−0.33 −0.24 −0.03 0.03 0.24 0.33
Change in bone concentration Δc_w


Negative
About zero
Positive
Membership
1.0
0.8
0.6
0.4
0.2
0.0
−0.30 −0.05 0.00 0.05
Change in cartilage concentration Δc_c


Negative
About zero
Positive
1.0
0.8
0.6
0.4
0.2
0.0
−0.100 −0.075 −0.025 0.025 0.075 0.100
Change in vascularity Δc_v


Negative
Positive
destructive
high
medium
about zero
about zero
about zero
medium
high
destructive
Membership
1.0
0.8
0.6
0.4
0.2
0.0
– 26
– 6.0
– 4.0
– 0.9
– 0.8
– 4.0 · 10–2
– 4.0 · 10–3
– 3.0 · 10–3
– 1.5 · 10–3
1.5 · 10–3
3.0 · 10–3
4.0 · 10–3
4.0 · 10–2
0.8
0.9
4.0
6.0
26
Dilatational strain ε (%)


Very low
Low
Medium
High
Very high
Membership
1.0
0.8
0.6
0.4
0.2
0.0
0.0
1.0 · 10–2
1.5 · 10–2
4.0 · 10–2
5.0 · 10–2
4.0
10
14
18
30
Distortional strain γ (%)