Competing remodeling mechanisms in the development of saccular aneurysms

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Simulated natural histories

In order to figure out what kind of control could prevent an aneurysm from rupture, we can conjecture different ways it would respond to some perturbation during hypothetical histories.

Let us assume that an aneurysm, subjected to a constant intramural pressure, has reached a spherical shape in a homeostatic state with hoop and radial stress:

$$\overset{\diamond}{\mathrm{T}}_{\mathsf{h}} \qquad \overset{\diamond}{\mathrm{T}}_{\mathsf{r}}$$

thanks to a full slipping recovery control force Q^c .

History A

1. Q^{c} is held fixed to the previous value for the rest of the time:

$$Q^{\mathsf{c}}(t) = -\left(1 + D^{\mathsf{c}}/D^{\mathsf{s}}\right)\left(\overset{\diamond}{\mathrm{T}}_{\mathsf{h}} - \overset{\diamond}{\mathrm{T}}_{\mathsf{r}}\right),$$

   simulating an inability of the slipping recovery mechanism to keep pace with a sudden perturbation;
2. the intramural pressure experiences a jump or an oscillation.

History B

1. Q^c experiences a jump or an oscillation around the previous homeostatic value:

$$Q^c(t) = -\left(1 + D^c/D^s\right)\left(\overset{\diamond}{\mathrm{T}}_h - \overset{\diamond}{\mathrm{T}}_r\right)h(t)\,,$$

   simulating a temporary damage or malfunction of the slipping recovery mechanism;
2. the intramural pressure is held constant.

History C

1. The intramural pressure experiences a jump or an oscillation;
2. Q^c is increased to a fraction of the value of a full slipping recovery control:

$$Q^c(t) = -(1+D^c/D^s)\left(\left(\overset{\diamond}{\mathrm{T}}_h - \overset{\diamond}{\mathrm{T}}_r\right) + g\left(\left(\mathrm{T}_h(t) - \overset{\diamond}{\mathrm{T}}_h\right) - \left(\mathrm{T}_r(t) - \overset{\diamond}{\mathrm{T}}_r\right)\right)\right),$$

which is meant to simulate an impaired recovery mechanism, not able to keep full pace with a sudden perturbation; if $g = 0$ then Q^c is held constant; if $g = 1$ then Q^c is a full slipping recovery control, synchronized with any perturbation.

History D

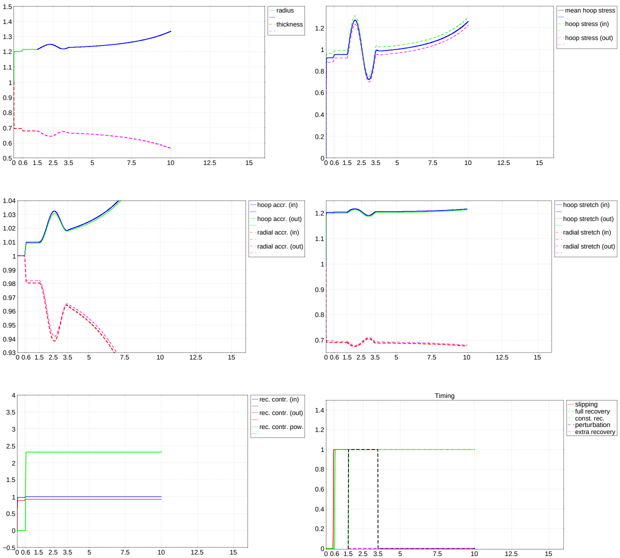
1. The intramural pressure experiences a jump or an oscillation;
2. Q^c is held fixed to the previous value for the rest of the time:

$$Q^c(t) = -\left(1 + D^c/D^s\right)\left(\overset{\diamond}{\mathrm{T}}_h - \overset{\diamond}{\mathrm{T}}_r\right);$$

3. a radial proliferation mechanisms comes into action through a stress driven control law:

$$Q^p = G^p\left(\mathrm{T}_h - \overset{\diamond}{\mathrm{T}}_h\right) - \left(\mathrm{T}_r - \overset{\diamond}{\mathrm{T}}_h\right).$$

Constant slipping recovery control force

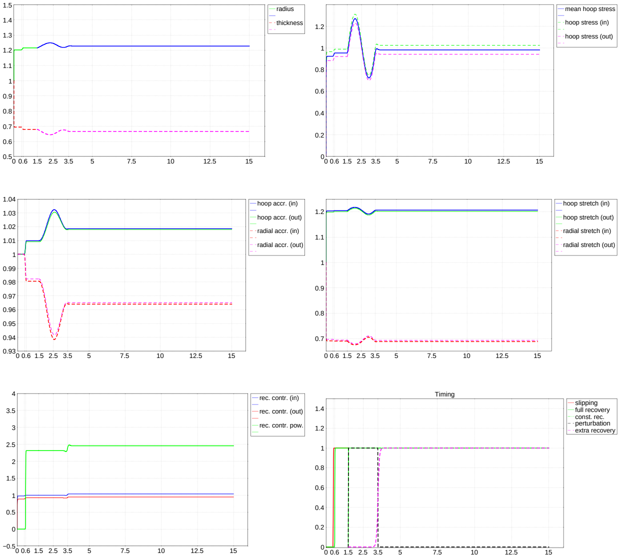


[case-42-001]

D^c/D^s D^c D^s	1000 0.01 1e-005
char time	10
δQ^c ampl δQ^c period	0 0
δp ampl δp period	0.25 2
Q^c factor g	0

A slipping recovery control force, held fixed to the previous homeostatic value, is unable to keep the aneurysm in a homeostatic state in response to a perturbation of the transmural pressure.

Full slipping recovery control force

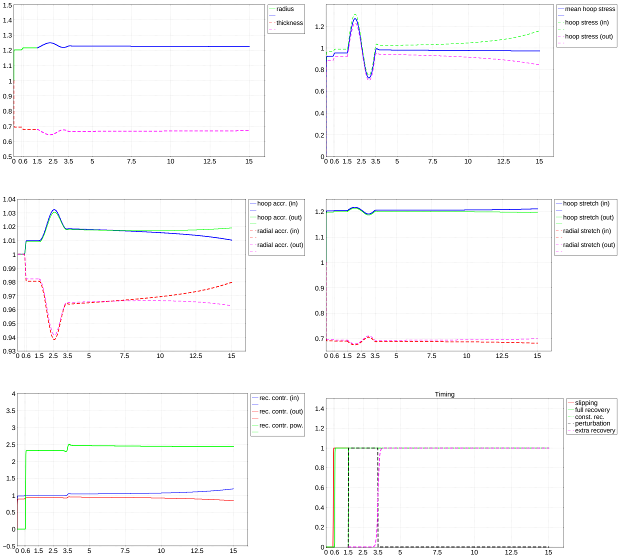


[case-41-001]

D^c / D^s D^c D^s	1000 0.01 1e-005
char time	10
δQ^c ampl δQ^c period	0 0
δp ampl δp period	0.25 2
Q^c factor g	1

After the end of a short perturbation of the transmural pressure, a full slipping recovery control force drives the aneurysm to a new homeostatic state, with a higher hoop stress.

Exceeding slipping recovery control force

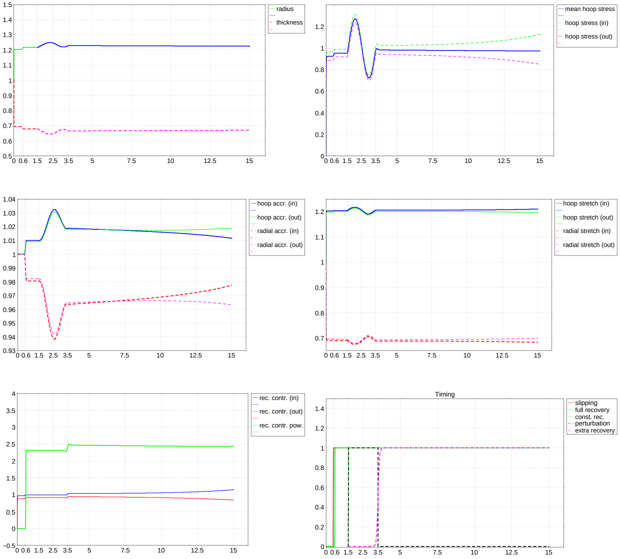


[case-41-002]

D^c / D^s D^c D^s	1000 0.01 1e-005
char time	10
δQ^c ampl δQ^c period	0 0
δp ampl δp period	0.25 2
Q^c factor g	1.1

After the end of a short perturbation of the transmural pressure, an exceeding slipping recovery control force keeps the aneurysm in a homeostatic state only on average, while the values of the stress on the boundary diverge.

Old style (naive) control force law

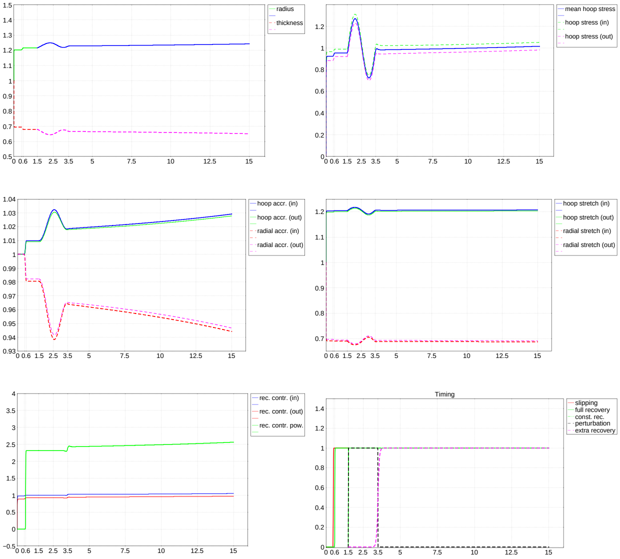


[case-41-002-alt]

D^c / D^s D^c D^s	1000 0.01 1e-005
char time	10
δQ^c ampl δQ^c period	0 0
δp ampl δp period	0.25 2
Q^c factor g	1.1

A simplified expression for the control law leads to the same evolution.

Insufficient extra slipping recovery control force

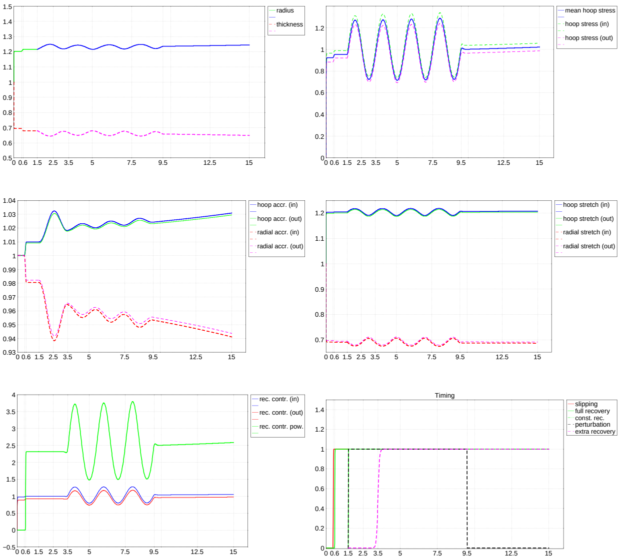


[case-41-003]

D^c / D^s D^c D^s	1000 0.01 1e-005
char time	10
δQ^c ampl δQ^c period	0 0
δp ampl δp period	0.25 2
Q^c factor g	0.8

After the end of a short perturbation of the transmural pressure, a slipping recovery control force, though higher than the previous homeostatic value but lower than the optimal value, can't prevent the unlimited increase of the radius.

Trying to face a longer pressure perturbation

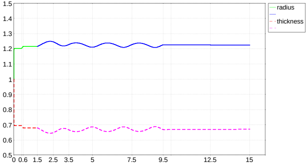


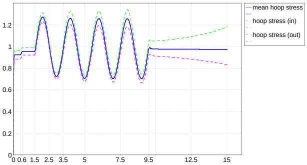
[case-41-004]

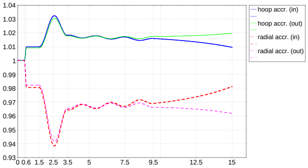
D^c / D^s	1000
D^c	0.01
D^s	1e-005
char time	10
δQ^c ampl	0
δQ^c period	0
δp ampl	0.25
δp period	2
Q^c factor g	0.8

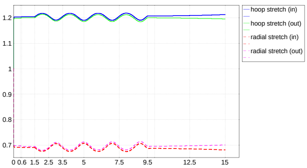
After the start of a longer perturbation of the transmural pressure, a slipping recovery control force, lower than the optimal value, succeedes in reducing the oscillation amplitude but can't prevent a slow but unlimited increase of the radius.

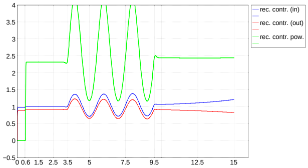
Trying to face a longer pressure perturbation

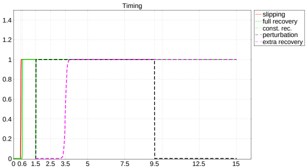










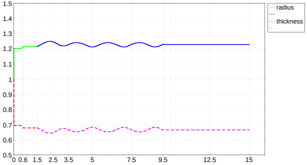


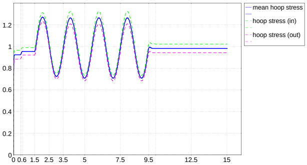
[case-41-005]

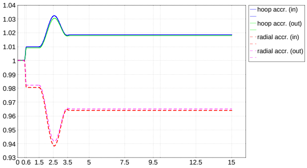
D^c/D^s	1000
D^c	0.01
D^s	1e-005
char time	10
δQ^c ampl	0
δQ^c period	0
δp ampl	0.25
δp period	2
Q^c factor g	1.1

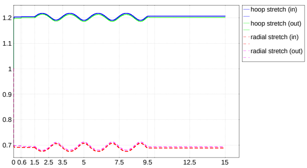
After the start of a longer perturbation of the transmural pressure, a slipping recovery control force, higher than the optimal value, succeedes in strongly reducing the radius increase but not in driving the aneurysm to a homeostatic state.

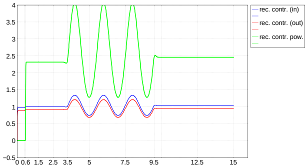
Full slipping recovery control force

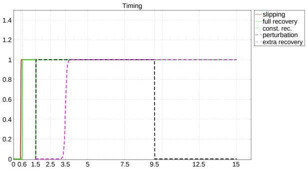










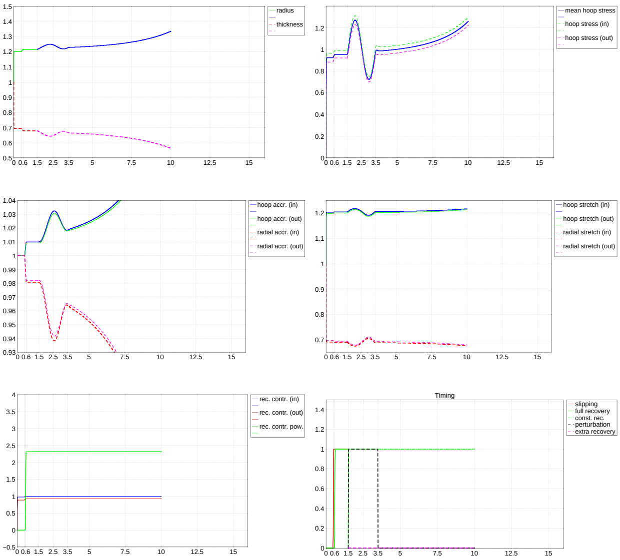


[case-41-006]

D^c / D^s D^c D^s	1000 0.01 1e-005
char time	10
δQ^c ampl δQ^c period	0 0
δp ampl δp period	0.25 2
Q^c factor g	1

Here is what happens with a full (synchronized) recovery control.

Constant slipping recovery control force

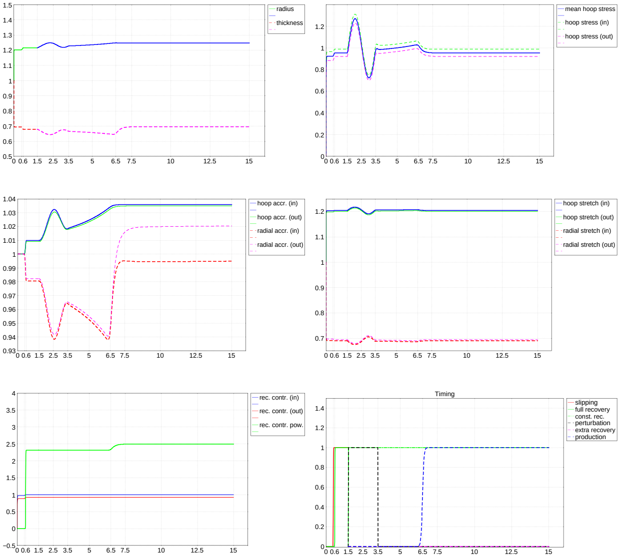


[case-42-001]

D^c/D^s D^c D^s	1000 0.01 1e-005
char time	10
δQ^c ampl δQ^c period	0 0
δp ampl δp period	0.25 2
Q^c factor g	0

A slipping recovery control force, held fixed to the previous homeostatic value, is unable to keep the aneurysm in a homeostatic state in response to a perturbation of the transmural pressure.

New mechanism of radial proliferation

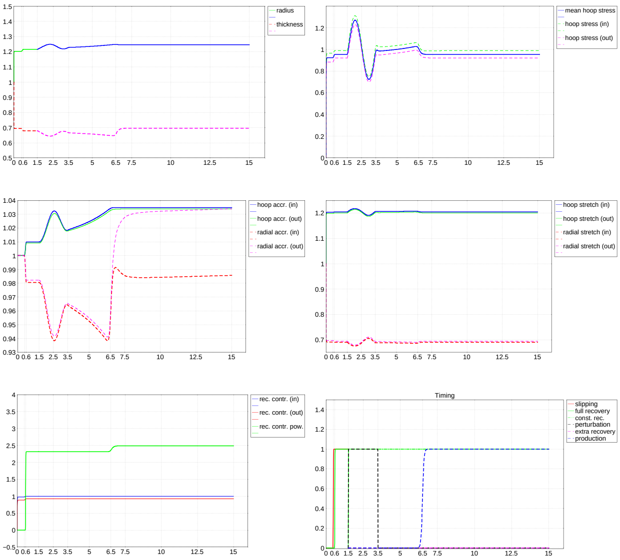


[case-42-002]

D^c/D^s D^c D^s	1000 0.01 1e-005
char time	10
δQ^c ampl δQ^c period	0 0
δp ampl δp period	0.25 2
Q^c factor g	0
G^p D^p	4000 0.001

After the end of a short perturbation of the transmural pressure, a new mechanism of radial proliferation makes the aneurysm thicken driving it to a new homeostatic state at the starting value of the hoop stress.

Radial proliferation (lower resistance)

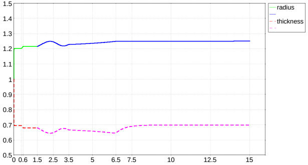


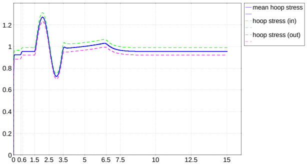
[case-42-003]

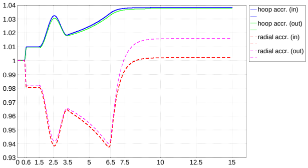
D^c / D^s D^c D^s	1000 0.01 1e-005
char time	10
δQ^c ampl δQ^c period	0 0
δp ampl δp period	0.25 2
Q^c factor g	0
G^p D^p	4000 0.0005

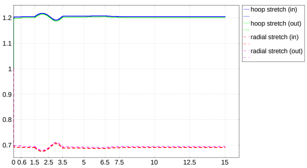
After the end of a short perturbation of the transmural pressure, a new mechanism of radial proliferation makes the aneurysm thicken driving it to a new homeostatic state at the starting value of the hoop stress. (Lower resistance to growth.)

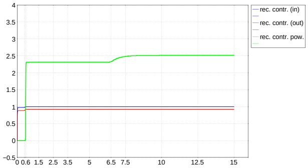
Radial proliferation

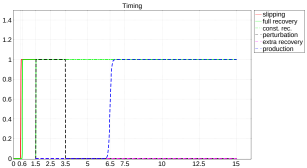










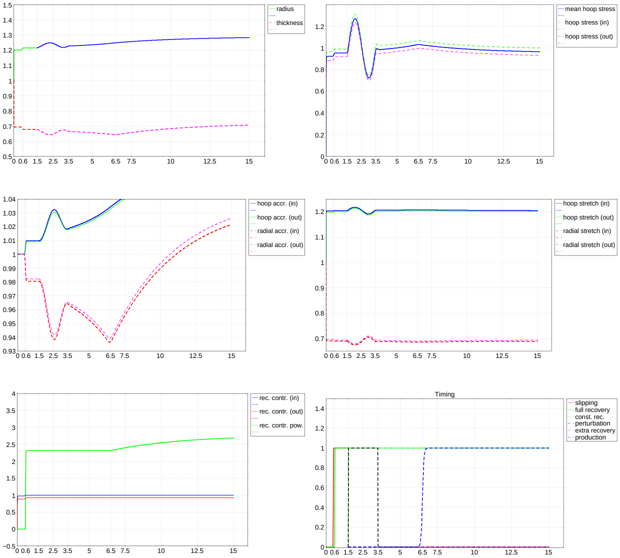


[case-42-004]

D^c/D^s	1000
D^c	0.01
D^s	1e-005
char time	10
δQ^c ampl	0
δQ^c period	0
δp ampl	0.25
δp period	2
Q^c factor g	0
G^p	4000
D^p	0.002

After the end of a short perturbation of the transmural pressure, a new mechanism of radial proliferation makes the aneurysm thicken driving it to a new homeostatic state at the starting value of the hoop stress. (Higher resistance to growth.)

Radial proliferation (lower gain)

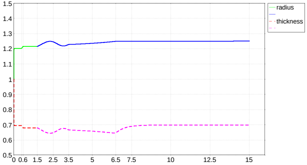


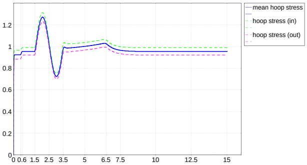
[case-42-005]

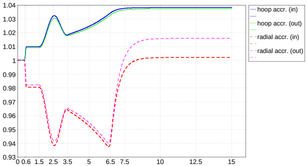
D^c / D^s D^c D^s	1000 0.01 1e-005
char time	10
δQ^c ampl δQ^c period	0 0
δp ampl δp period	0.25 2
Q^c factor g	0
G^p D^p	1000 0.002

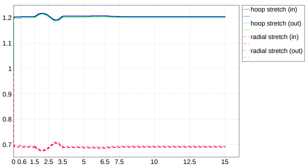
After the end of a short perturbation of the transmural pressure, a mechanism of radial proliferation makes the aneurysm thicken but fails to drive it quickly to a new homeostatic state. (The gain coefficient is too low.)

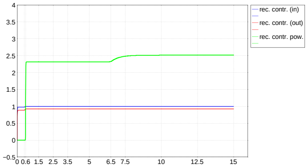
Radial proliferation

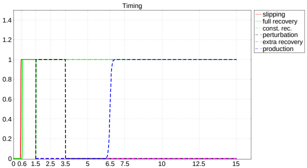










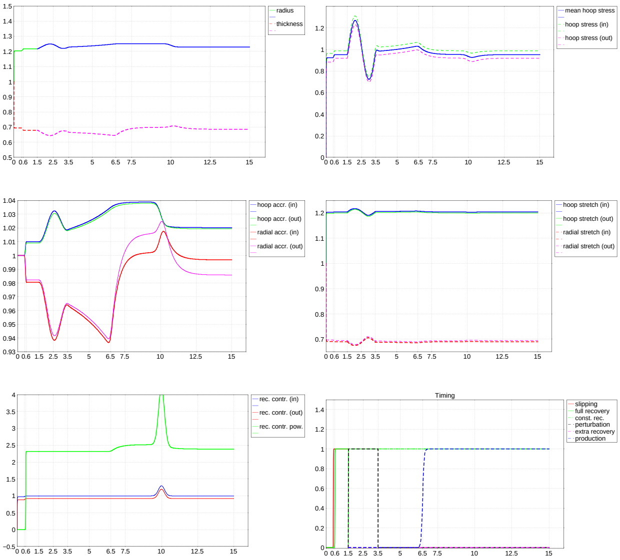


[case-42-004]

D^c / D^s	1000
D^c	0.01
D^s	1e-005
char time	10
δQ^c ampl	0
δQ^c period	0
δp ampl	0.25
δp period	2
Q^c factor g	0
G^p	4000
D^p	0.002

After the end of a short perturbation of the transmural pressure, a new mechanism of radial proliferation makes the aneurysm thicken driving it to a new homeostatic state at the starting value of the hoop stress. (Higher resistance to growth.)

Radial proliferation & slipping recovery impulse

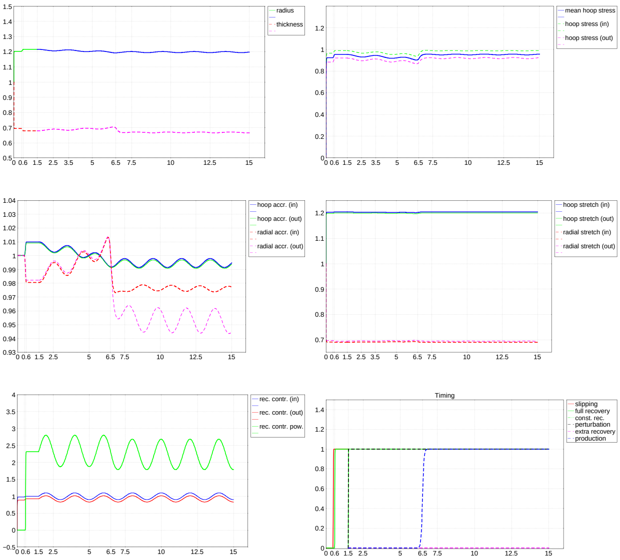


[case-42-006]

D^c / D^s D^c D^s	1000 0.01 1e-005
char time	10
δQ^c ampl δQ^c period	0.3 10
δp ampl δp period	0.25 2
Q^c factor g	0
G^p D^p	4000 0.002

After the end of a short perturbation of the transmural pressure, the new mechanism of radial proliferation cooperates with a strong impulse of the recovery mechanism driving the aneurysm to a new homeostatic state while decreasing the radius.

Slipping recovery control force perturbation

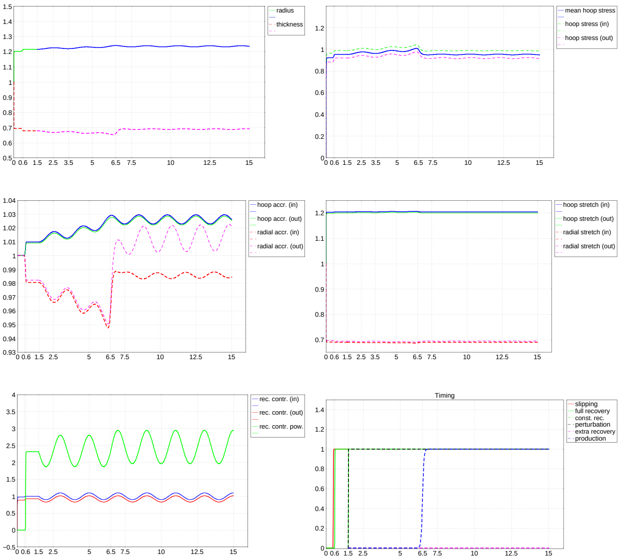


[case-43-001]

D^c / D^s	1000
D^c	0.01
D^s	1e-005
char time	10
δQ^c ampl	0.1
δQ^c period	2
δp ampl	0
δp period	0
Q^c factor g	0
G^p	4000
D^p	0.0005

The homeostatic state is lost because of a strong perturbation of the recovery control force. After a while the radial proliferation synchronizes itself with the perturbation keeping the stress oscillating near the starting value of the hoop stress.

Slipping recovery control force perturbation

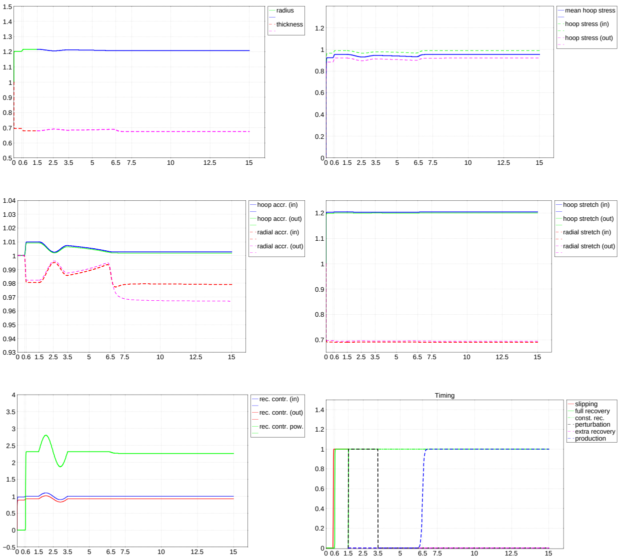


[case-43-001m]

D^c / D^s D^c D^s	1000 0.01 1e-005
char time	10
δQ^c ampl δQ^c period	-0.1 2
δp ampl δp period	0 0
Q^c factor g	0
G^p D^p	4000 0.0005

The homeostatic state is lost because of a strong perturbation of the recovery control force. After a while the radial proliferation synchronizes itself with the perturbation keeping the stress oscillating near the starting value of the hoop stress.

Slipping recovery control force perturbation

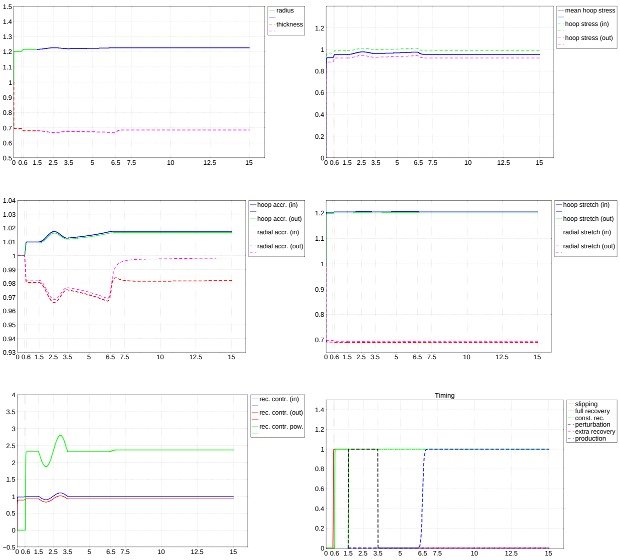


[case-43-002]

D^c/D^s D^c D^s	1000 0.01 1e-005
char time	10
δQ^c ampl δQ^c period	0.1 2
δp ampl δp period	0 0
Q^c factor g	0
G^p D^p	4000 0.0005

After the end of a short perturbation of the recovery control force, the radial proliferation drives the aneurysm to a new homeostatic state at the starting value of the hoop stress.

Slipping recovery control force perturbation



[case-43-002m]

D^c/D^s D^c D^s	1000 0.01 1e-005
char time	10
δQ^c ampl δQ^c period	-0.1 2
δp ampl δp period	0 0
Q^c factor g	0
G^p D^p	4000 0.0005

After the end of a short perturbation of the recovery control force, the radial proliferation drives the aneurysm to a new homeostatic state at the starting value of the hoop stress.