Pushing the Boundaries:
From Detonations to Auto-Injectors

Joe Shepherd

Aerospace and Mechanical Engineering

California Institute of Technology

Pasadena CA 91011

Midwest Mechanics Tour – Spring 2018

Our journey

Physiology

Water Hammer

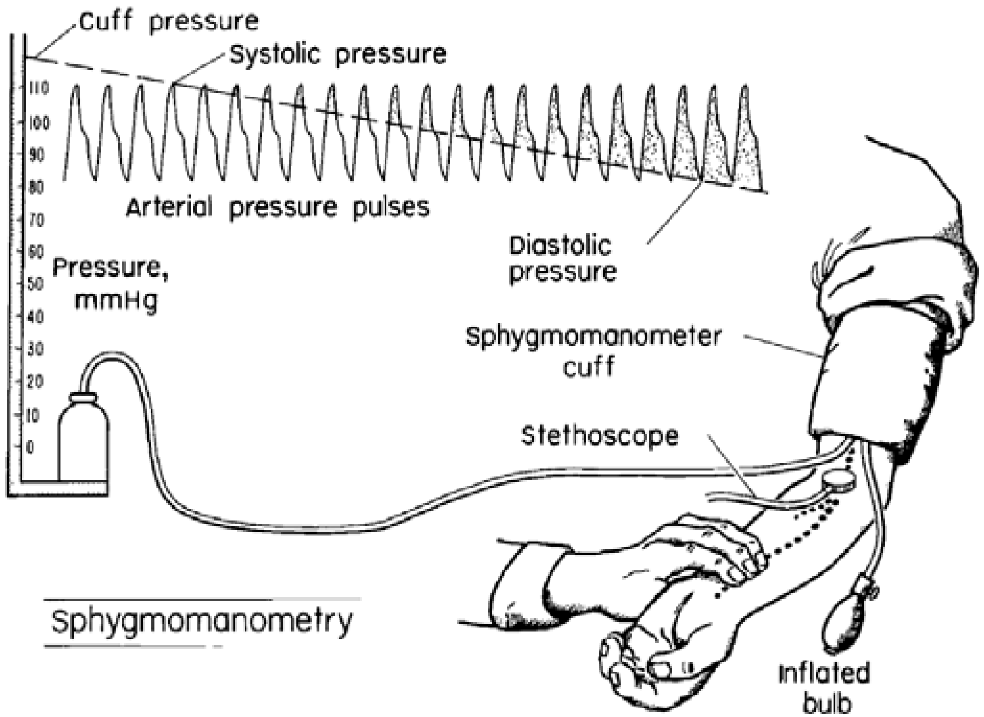
Traveling loads

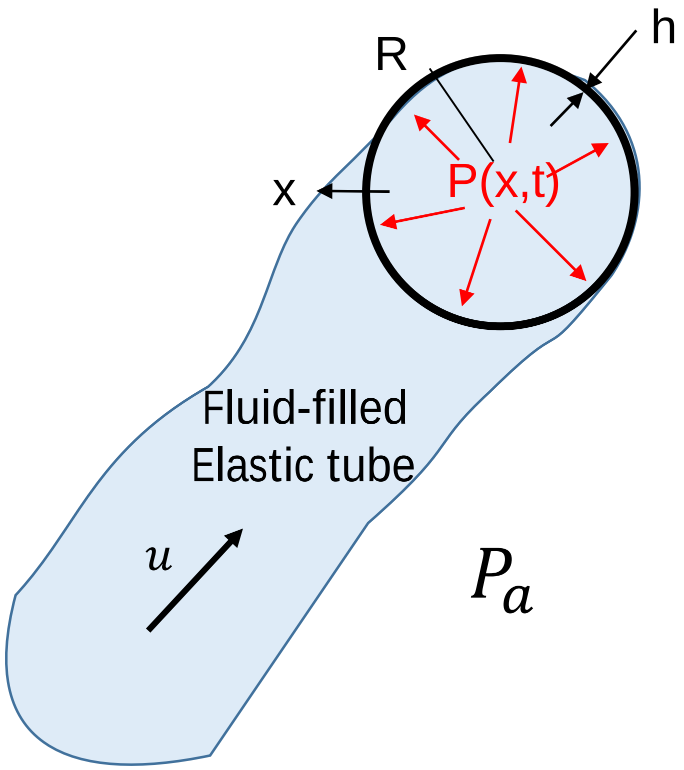
Shock and detonation waves

Physiology again – Auto-injectors

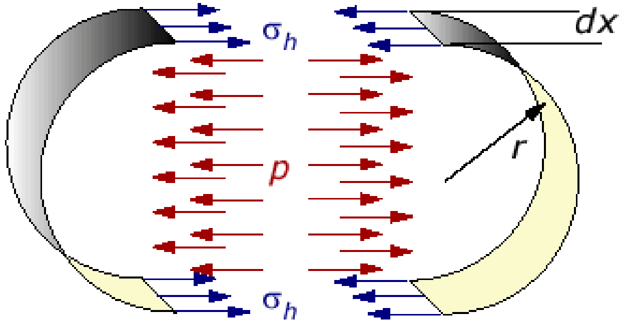
Physiology

Pressure waves in arteries, veins, airways, and intestines



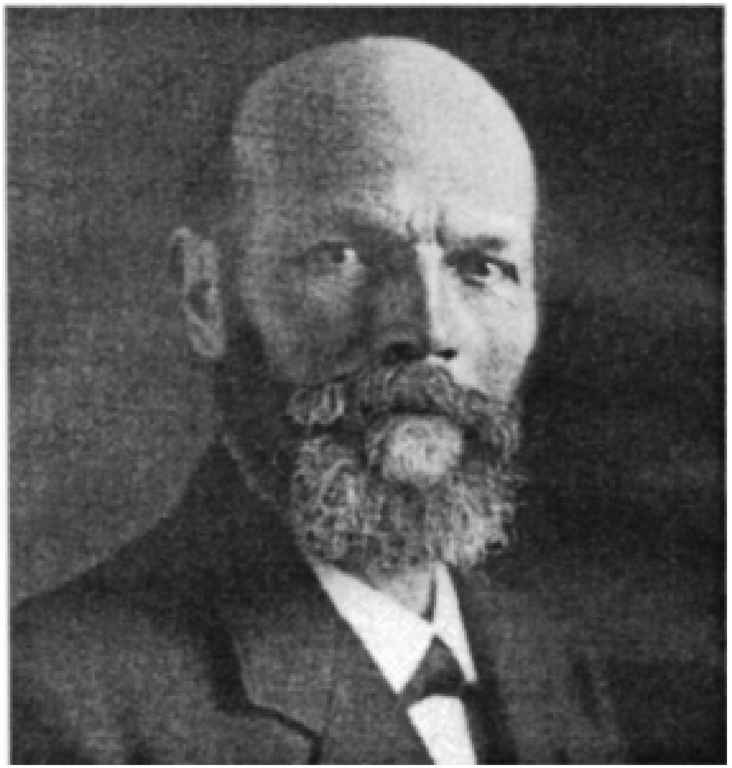


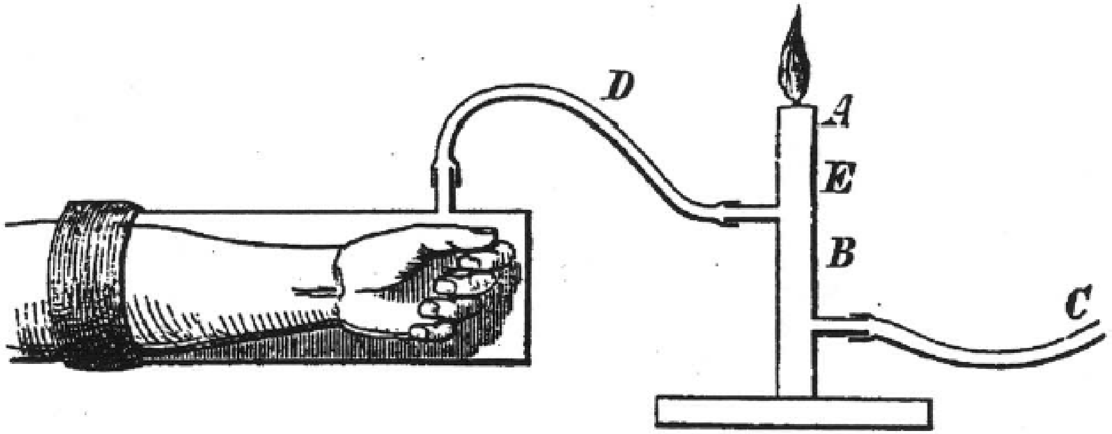
Statics



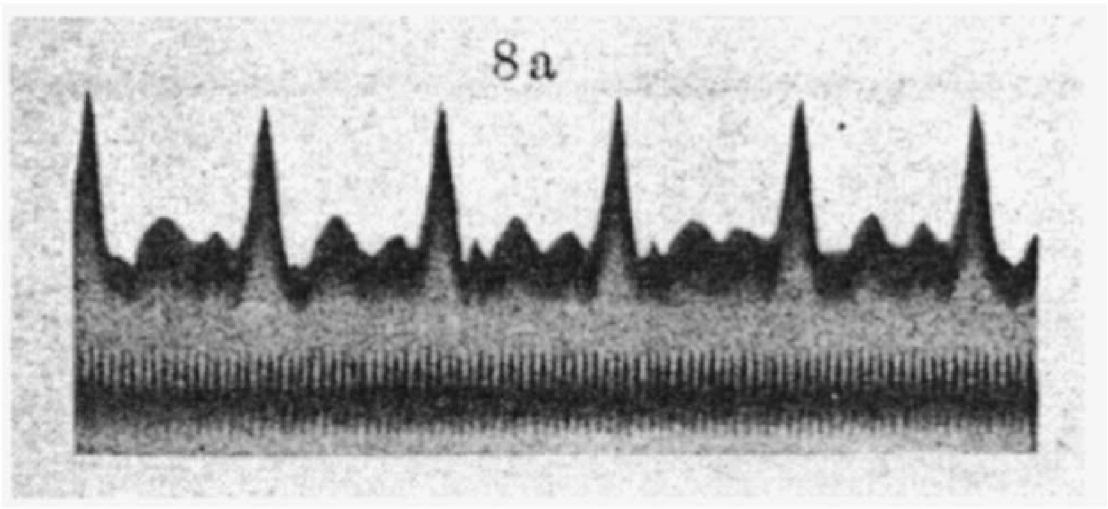
$$P - P_a = \Delta P \qquad \sigma_h = \frac{R}{h}\Delta P \qquad \varepsilon = \frac{\Delta R}{R} = \frac{\sigma}{E}$$

Johannes von Kries
1853–1928





(a)

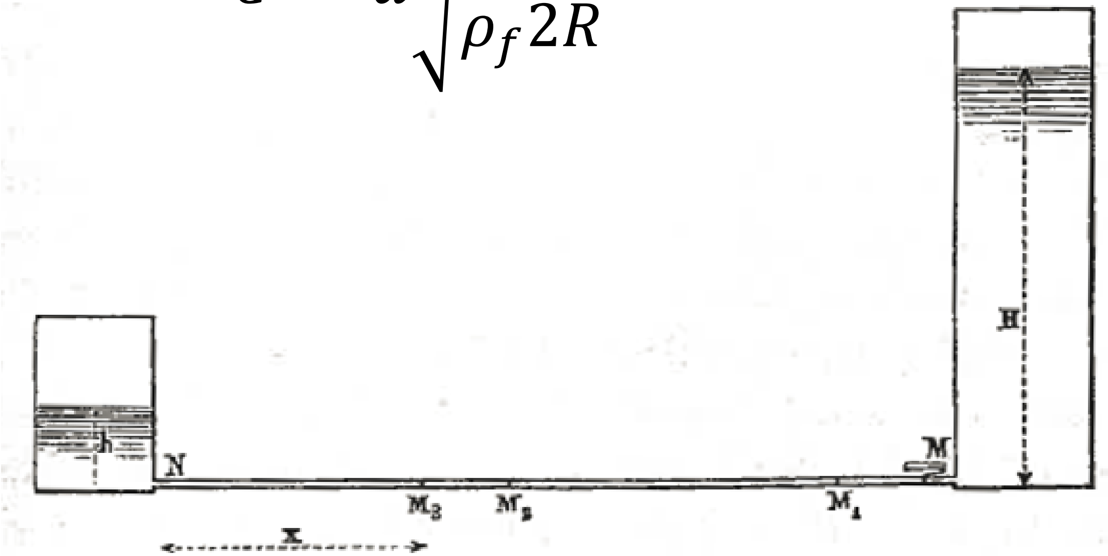


(b)

A. Isabree Moens
1846-1891

Measured wave speed in arteries, intestines, rubber tubes from oscillation period of water levels in his 1877 PhD thesis and deduced effective wave speed.

$$C = \alpha \sqrt{\frac{Eh}{\rho_f 2R}}$$



D. J. Korteweg
1848-1941

$$C_0 = \sqrt{\frac{K}{\rho_f}}$$

Compressible liquid
Rigid tube

$$C_1 = \sqrt{\frac{Eh}{\rho_f 2R}}$$

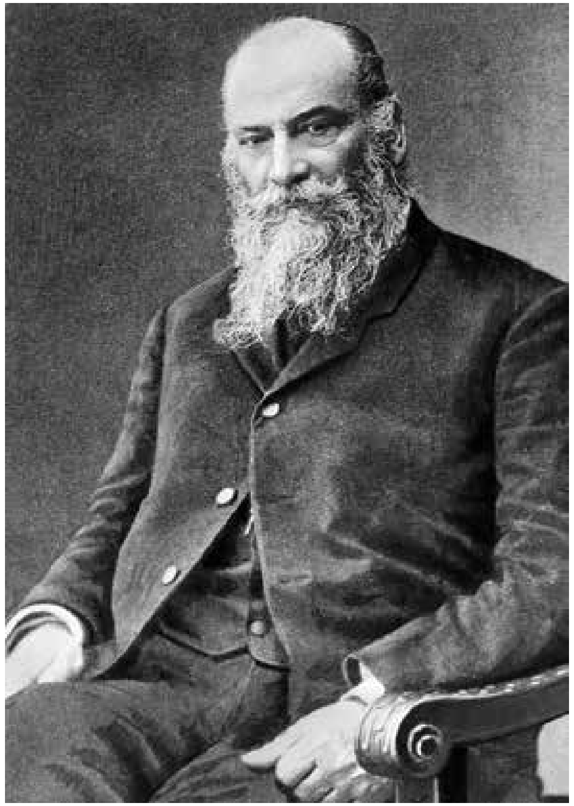
Incompressible liquid
Elastic tube

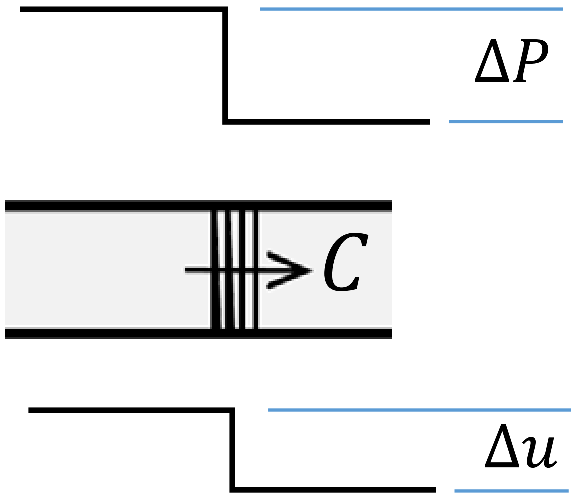
$$\frac{1}{C^2} = \frac{1}{C_1^2} + \frac{1}{C_0^2}$$

Elasticity of tube
and liquid combined

1878

Nikolai Zhukovsky (Jukowsky)
1847-1921





$$\Delta P = \rho c \Delta u$$

"Water hammer" equation

$$C = \frac{C_1}{\sqrt{1 + \frac{K}{E}\frac{2R}{h}}}$$

Korteweg speed

Joukowsky N. (1898). Über den hydraulischen Stoss in Wasserleitungsröhren. Mémoires de l'Académie Impériale des Sciences de St.-Pétersbourg (1900), Series 8, 9(5), 1-71.

The Korteweg Wave Equation

$$\frac{\partial}{\partial t}(\rho A) + \frac{\partial}{\partial x}(\rho \mathrm{u} A) = 0\,,$$

$$\rho \frac{\partial \mathrm{u}}{\partial t} + \rho \mathrm{u} \frac{\partial \mathrm{u}}{\partial x} = -\frac{\partial P}{\partial x}\,,$$

$$A' = A_o \frac{2R}{h} \frac{P'}{E}$$

Korteweg equation:

$$\frac{\partial^2 P'}{\partial x^2} = \frac{1}{c^2} \frac{\partial^2 P'}{\partial t^2}\,.$$

Wave speed:

$$c^{-2} = \frac{1}{A_o} \frac{\partial}{\partial P'}(\rho A)\,,$$

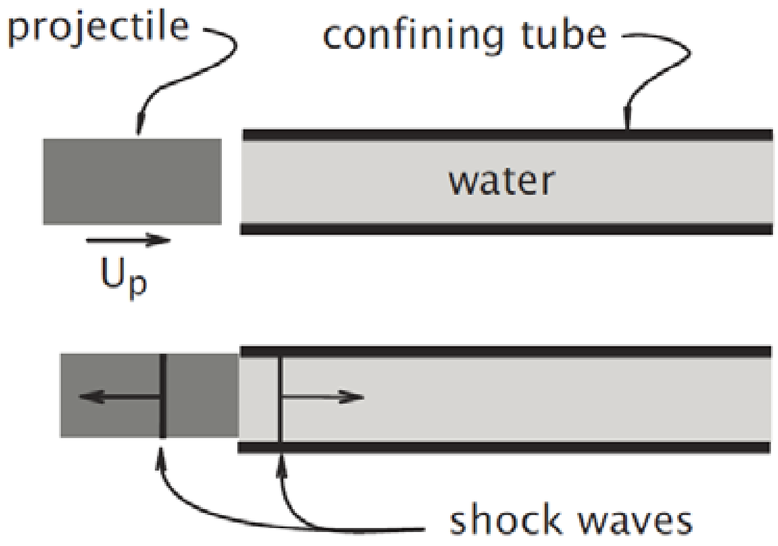
$$= \frac{\partial \rho}{\partial P'} + \frac{\rho}{A_o} \frac{\partial A}{\partial P'}\,.$$

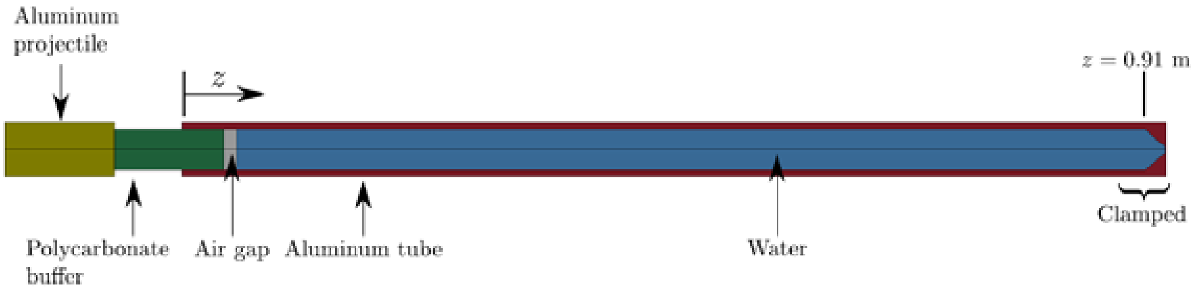
Fluid-Structure Coupling Parameter β

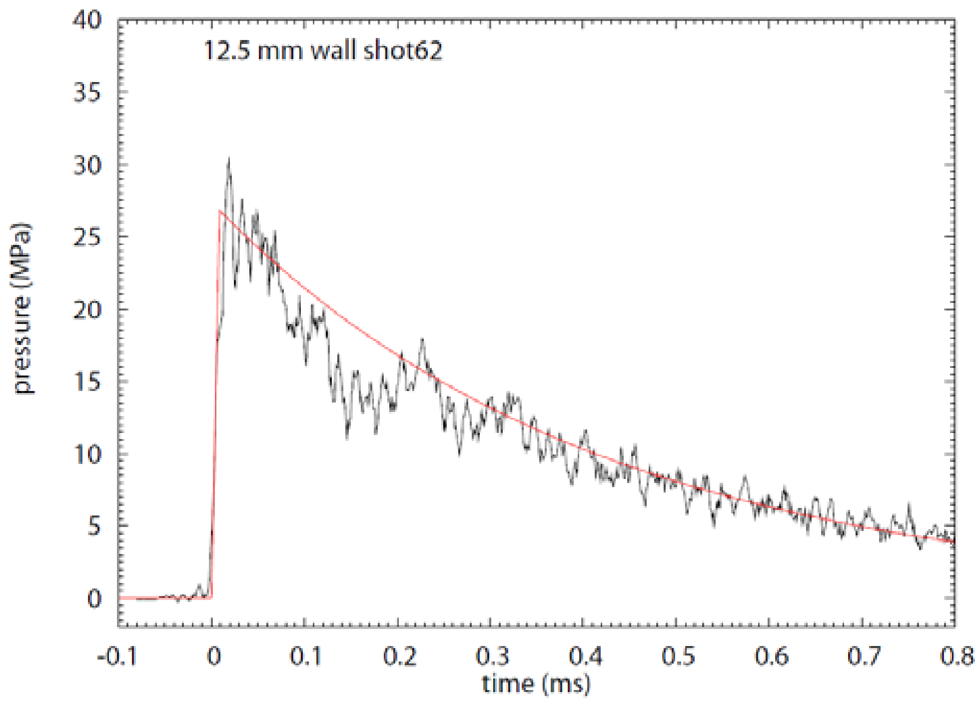
$$c = \frac{a_f}{\sqrt{1+\beta}}$$

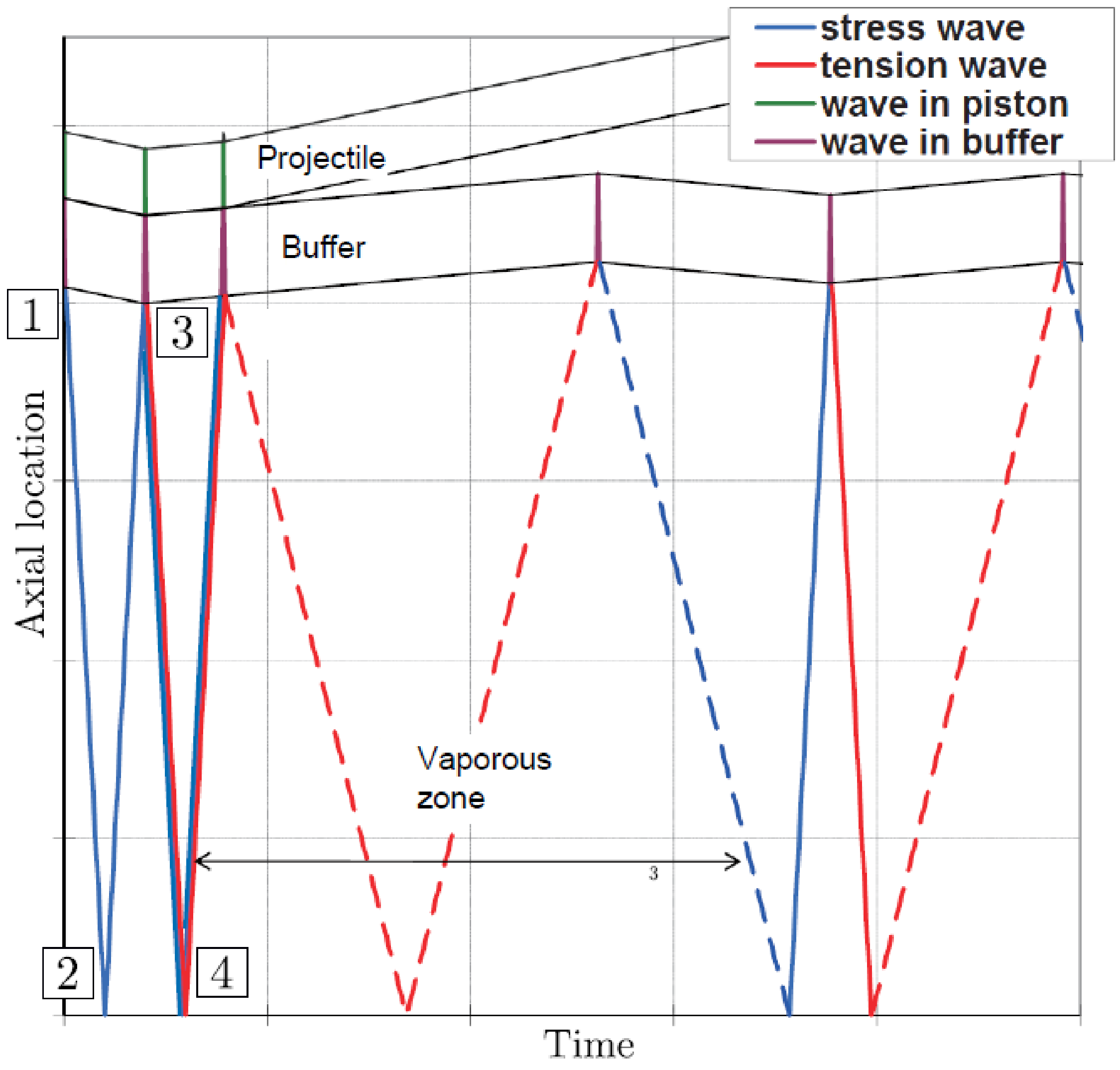
$$\beta = \underbrace{\left(\frac{a_f^2}{a_s^2}\right)}_{I} \underbrace{\left(\frac{\rho_f}{\rho_s}\right)}_{II} \underbrace{\left(\frac{2R}{h}\right)}_{III}$$

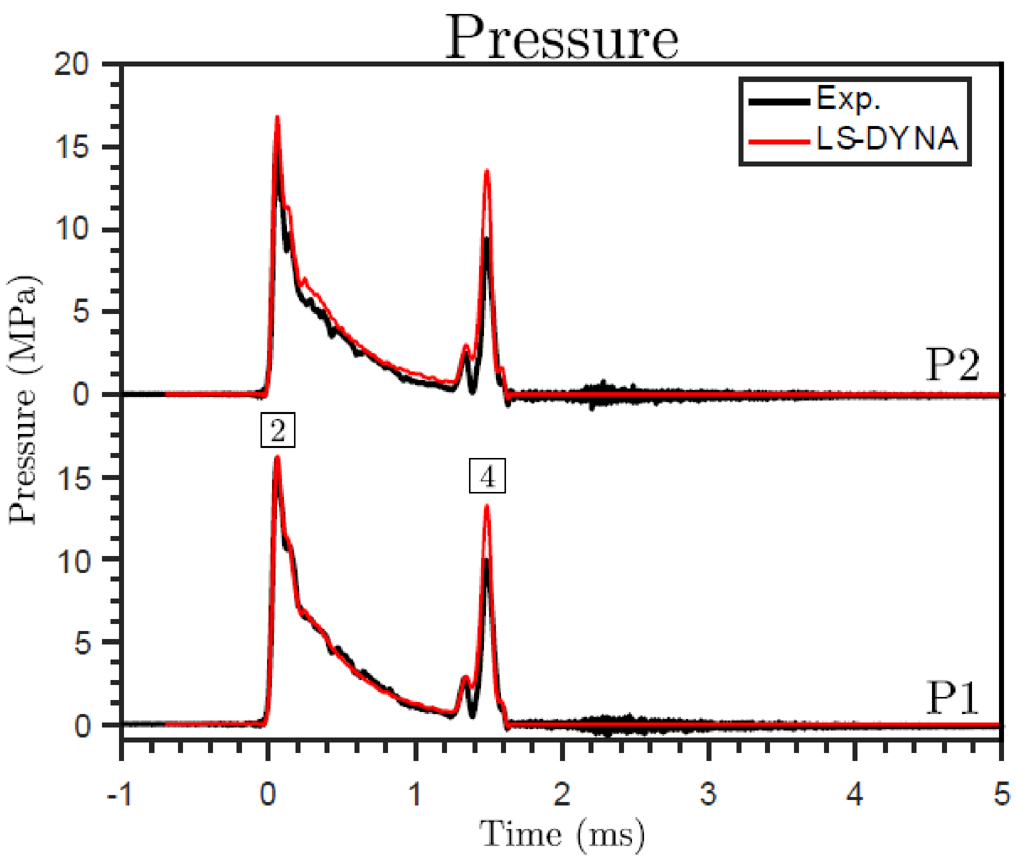
	Thin Tube		Thick Tube	
	h = 0.89 mm, *D = 38.5* mm		*h = 25* mm, *D = 100* mm	
	β	C (m/s)	β	C (m/s)
water-steel	0.48	1220	0.044	1450
water-glass	0.99	1050	0.092	1418
water-aluminum	1.4	961	0.13	1396
water-PMMA	29	271	2.7	1396
air-steel			2.8×10^{-6}	343

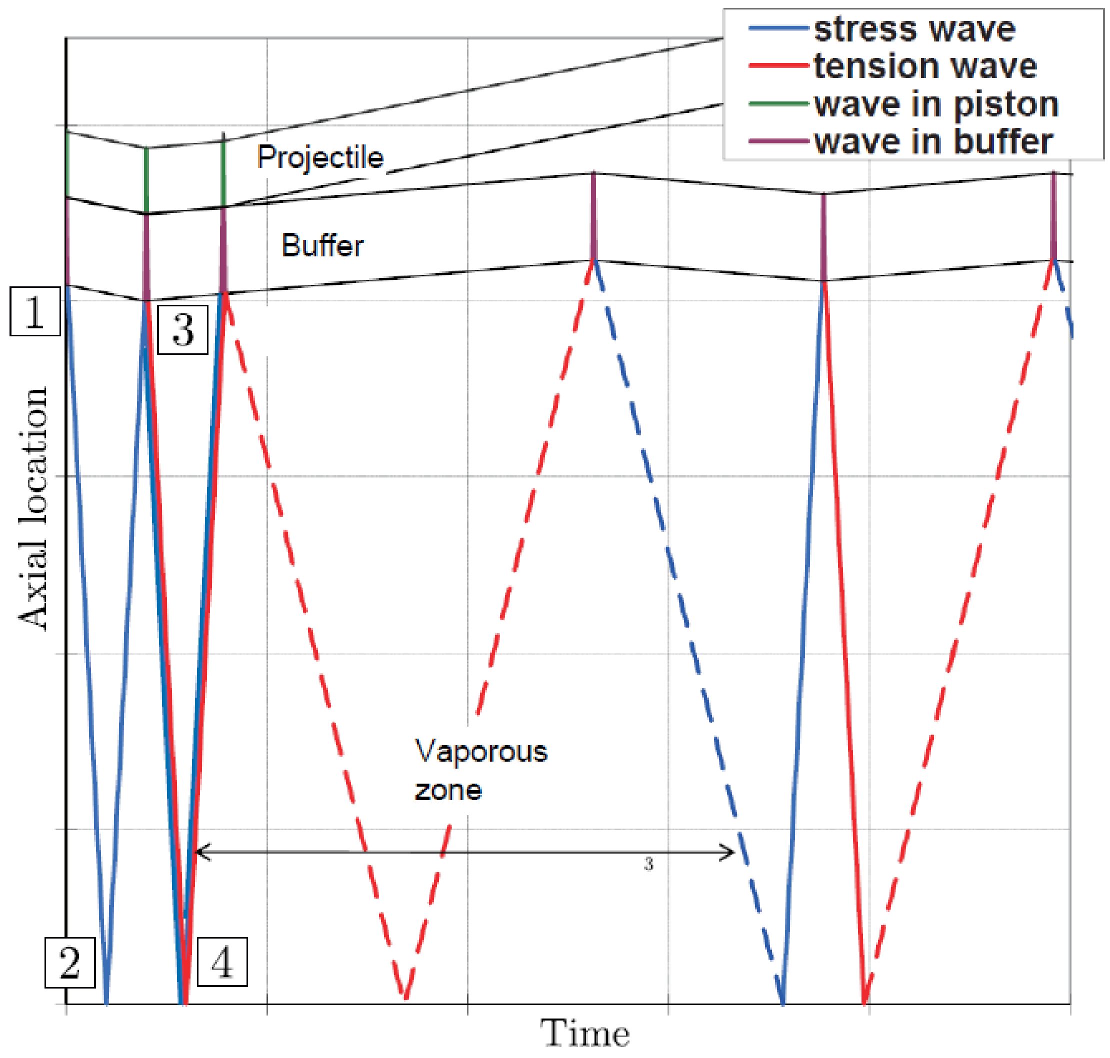

projectile
confining tube
water
Up
shock waves

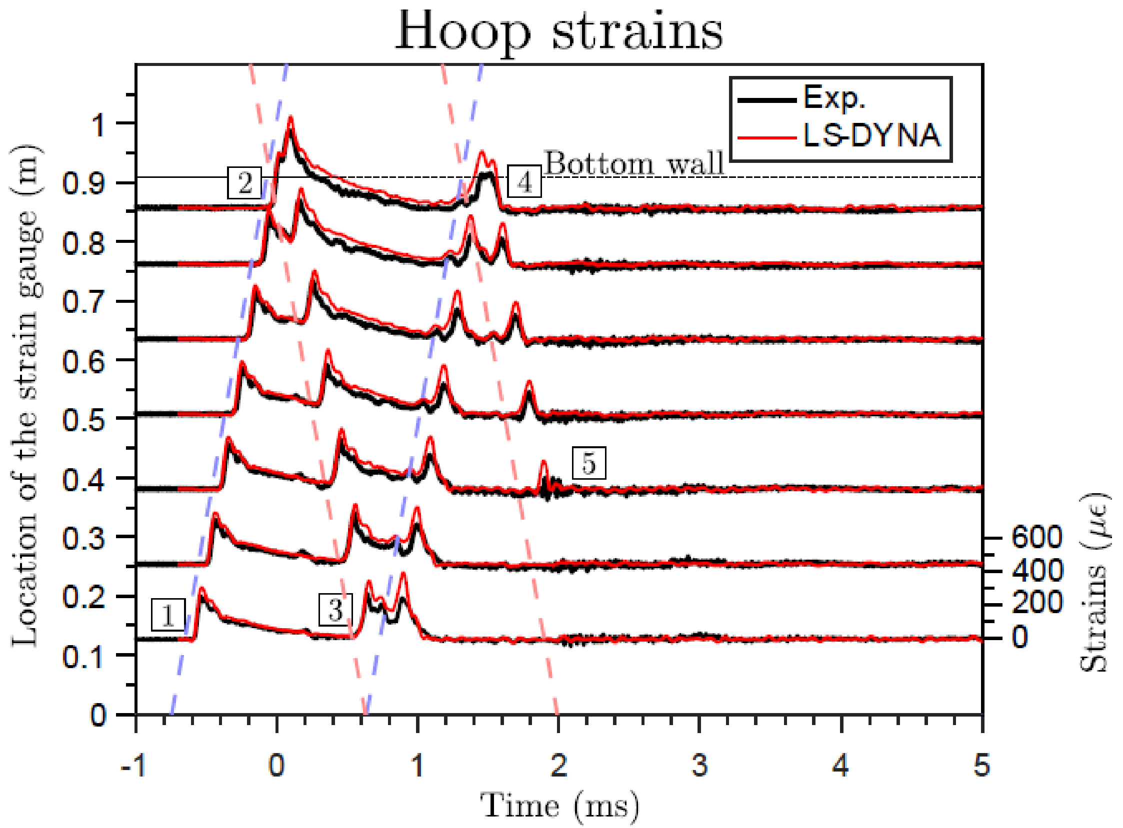

Aluminum projectile
z
z = 0.91 m
Polycarbonate buffer
Air gap
Aluminum tube
Water
Clamped


12.5 mm wall shot62
pressure (MPa)
time (ms)
40
35
30
25
20
15
10
5
0
-0.1
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8


stress wave
tension wave
wave in piston
wave in buffer
Projectile
Buffer
1
3
2
4
Vaporous zone
Axial location
Time


Pressure
Exp.
LS-DYNA
P2
P1
2
4
Pressure (MPa)
Time (ms)

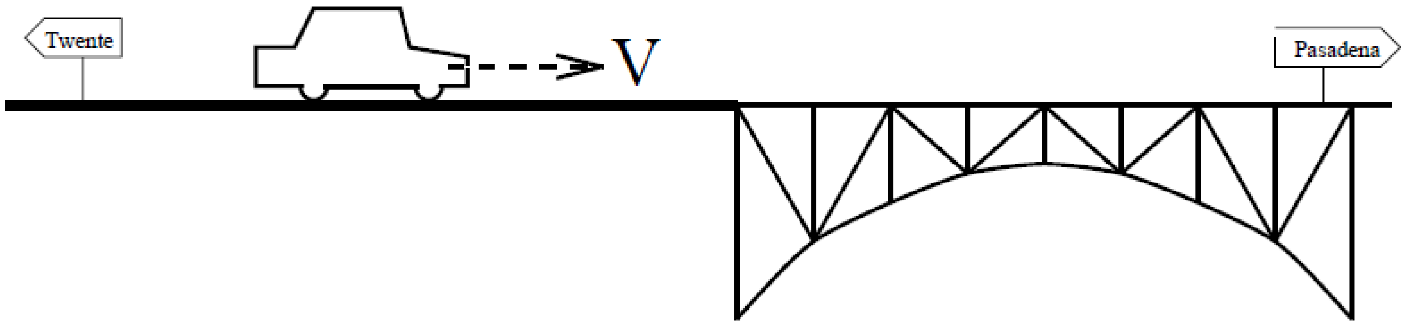


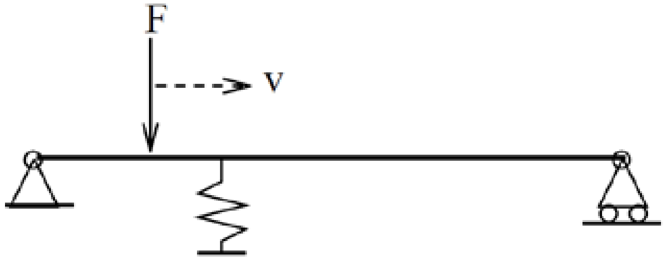


- Oblique lines → Korteweg speed c;
- $c = \dfrac{a}{\sqrt{1+\beta}} \approx 1350$ m/s;
- $\beta = KD/(Eh)$

Traveling Loads

Guns, trains, bridges detonation and shock waves in tubes or pipes





Stephen Timoshenko
1878-1972

CV. *On the Forced Vibrations of Bridges.*
By Professor S. P. Timoshenko *.

It is now generally agreed that imperfect balance of the locomotive driving-wheels is the principal source of impact effect in bridges of long span. The laws governing this effect have not yet been definitely formulated, and much more information is needed on the experimental side †.

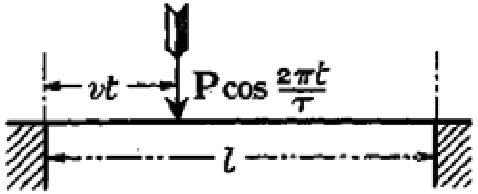
Some idea of the forced vibrations which are thus induced may be obtained by considering the bridge as a beam of constant cross-section with supported ends (fig. 1). The deflexion of the vibrating beam may be represented as follows :—

$$y=\phi_1\sin\frac{\pi x}{l}+\phi_2\sin\frac{2\pi x}{l}+\phi_3\sin\frac{3\pi x}{l}+\dots \quad (1)$$

where ϕ_1, ϕ_2, ..., etc. are functions of t only. Then if EI denotes the flexural rigidity of the beam, and w its weight per unit length, the expressions for the potential and kinetic energies will be

$$\left.\begin{aligned} V&=\frac{1}{2}EI\int_0^l\left(\frac{\partial^2 y}{\partial x^2}\right)^2dx=\frac{1}{4}\cdot\frac{EI\pi^4}{l^3}\sum_{n=1}^{\infty}[n^4\phi_n^2],\\ T&=\frac{1}{2}\frac{w}{g}\int_0^l\dot{y}^2dx=\frac{1}{4}\frac{wl}{g}\sum_{n=1}^{\infty}[\dot{\phi}_n^2]. \end{aligned}\right\} \quad (2)$$

Fig. 1.



We suppose that a single variable force $P\cos 2\pi t/\tau$ moves along the beam with a constant velocity v (fig. 1). The corresponding differential equations may be written in the form

$$\frac{wl}{2g}\ddot{\phi}_n+\frac{EI\pi^4}{2l^3}n^4\phi_n=P\cos\frac{2\pi t}{\tau}\sin\frac{n\pi vt}{l}. \quad (3)$$

Then taking $\phi_n=\dot{\phi}_n=0$ at the instant $t=0$, and writing

$$a^2=\frac{gEI}{w},$$

* Communicated by Mr. R. V. Southwell.
† *Cf.* 'Engineering,' vol. cxii. p. 80 (1921).

The London, Edinburgh, and Dublin Philosophical Magazine and Journal of Science Series 6, Volume 43, 1922 - Issue 257

Exact analogues:

Train moving on rails supported by ground – Euler-Bernoulli beam model on Winkler foundation.

Traveling load inside elastic cylinder modeled as a simple shell.

$$\frac{Eh^2}{12\rho(1-\nu^2)}\frac{\partial^4 w}{\partial x^4}+\frac{\partial^2 w}{\partial t^2}+\omega_o^2 w=\frac{\Delta P(x,t)}{\rho h}$$

$$\omega_o=\frac{1}{R}\sqrt{\frac{E}{\rho}}$$

Shell model:

$$\frac{\partial N_{xx}}{\partial x} = \rho h \frac{\partial^2 u}{\partial t^2}, \qquad \frac{\partial M_{xx}}{\partial x} - Q_x = \rho h^3 \frac{\partial^2 \psi}{\partial t^2},$$

$$\frac{\partial Q_x}{\partial x} - \frac{N_{\theta\theta}}{R} + \Delta P = \rho h \frac{\partial^2 w}{\partial t^2}. \qquad (27)$$

For elastic motions, the stress resultants N_{xx}, $N_{\theta\theta}$, M_{xx} and Q_x are defined as:

$$N_{xx} = \frac{Eh}{1-\nu^2}\left[\frac{\partial u}{\partial x} + \nu\frac{w}{R}\right], \qquad M_{xx} = \frac{Eh^3}{12(1-\nu^2)}\frac{\partial \psi}{\partial x},$$

$$N_{\theta\theta} = \frac{Eh}{1-\nu^2}\left[\nu\frac{\partial u}{\partial x} + \frac{w}{R},\right], \qquad Q_x = \kappa G h\left[\psi + \frac{\partial w}{\partial x}\right], \qquad (28)$$

Fluid acoustics:

$$P' = P - P_o = -\rho_o \frac{\partial \phi}{\partial t},$$

$$\rho' = \rho - \rho_o = P'/a_o^2,$$

$$\mathbf{u} = (\mathrm{u}, \mathrm{v}),$$

$$= \nabla \phi,$$

$$\nabla^2 \phi - \frac{1}{a_o^2}\frac{\partial^2 \phi}{\partial t^2} = 0.$$

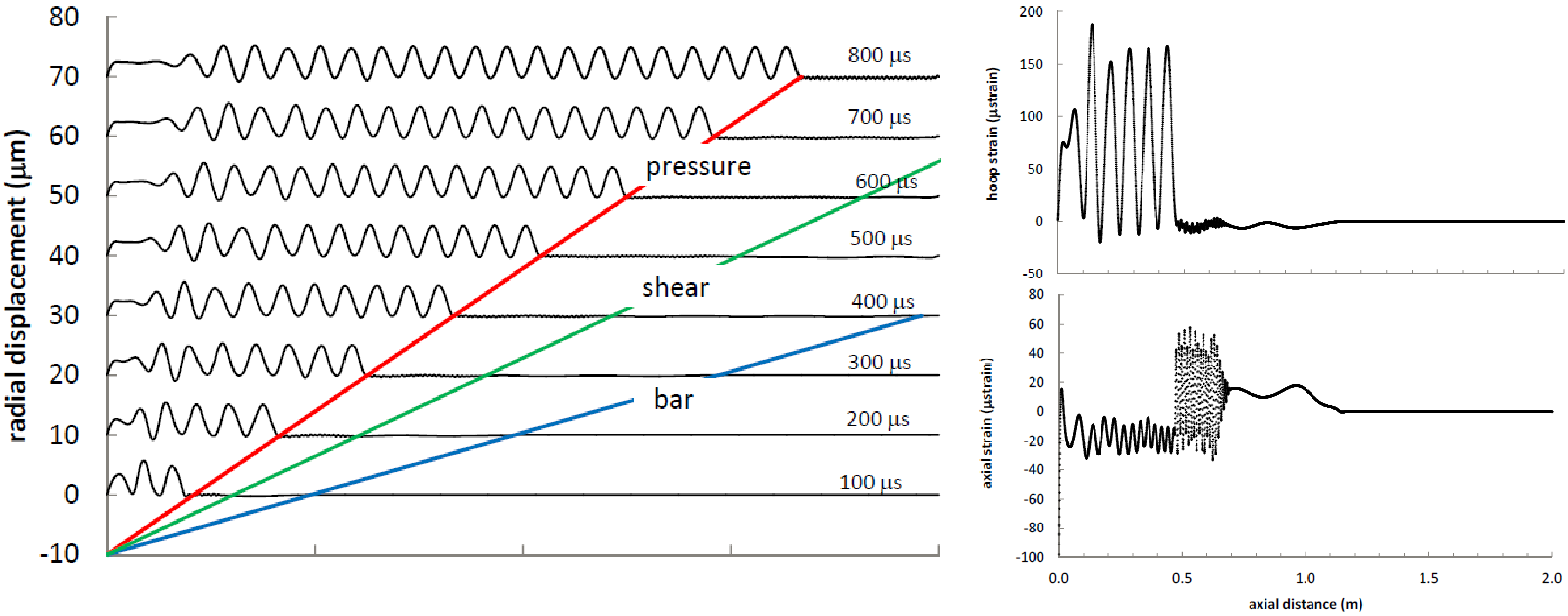
Fluid-Solid Coupling:

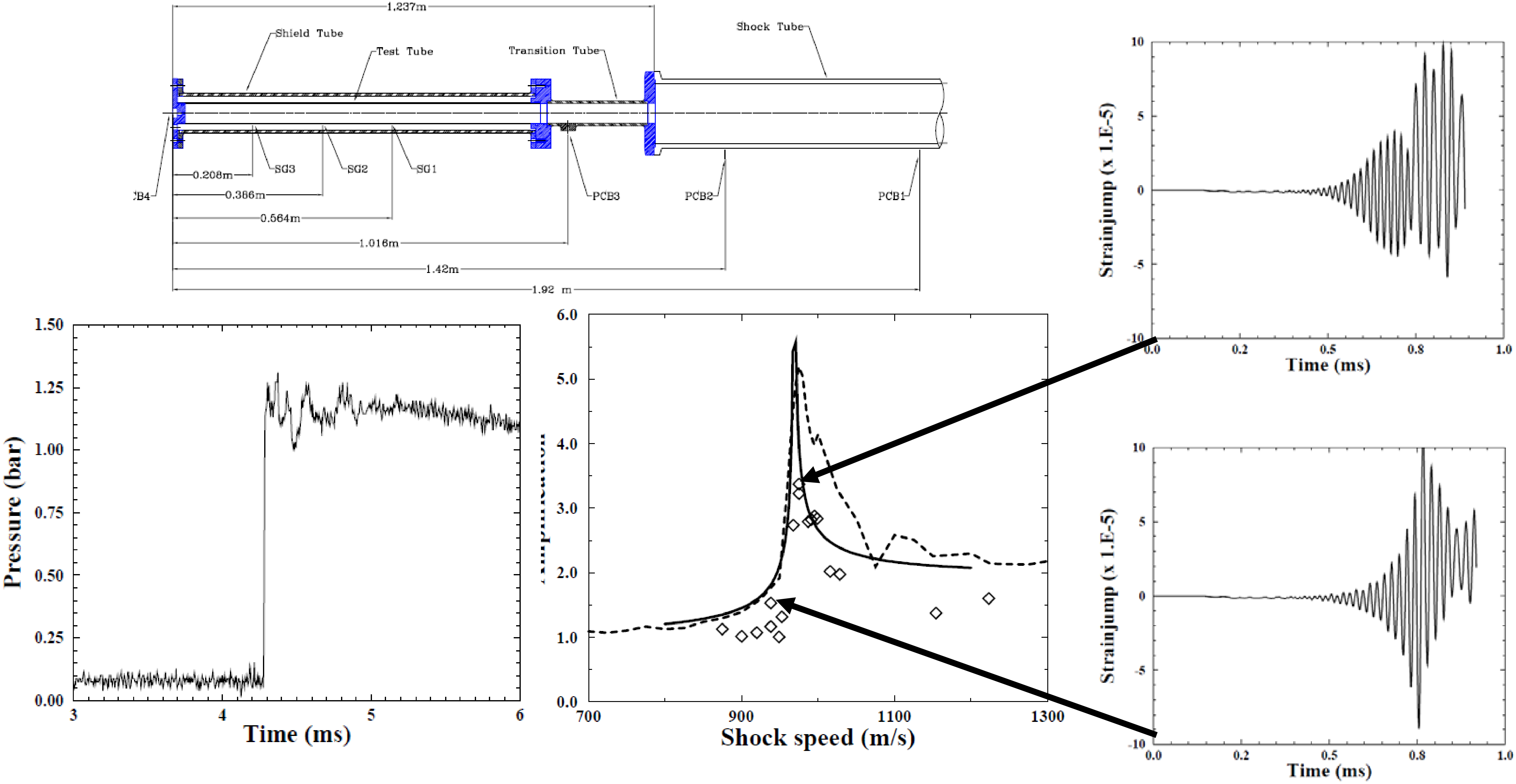
$$\frac{\partial w}{\partial t} = \mathrm{v}(x, r = R_o, t),$$

$$= \left.\frac{\partial \phi}{\partial r}\right|_{r=R_o}.$$

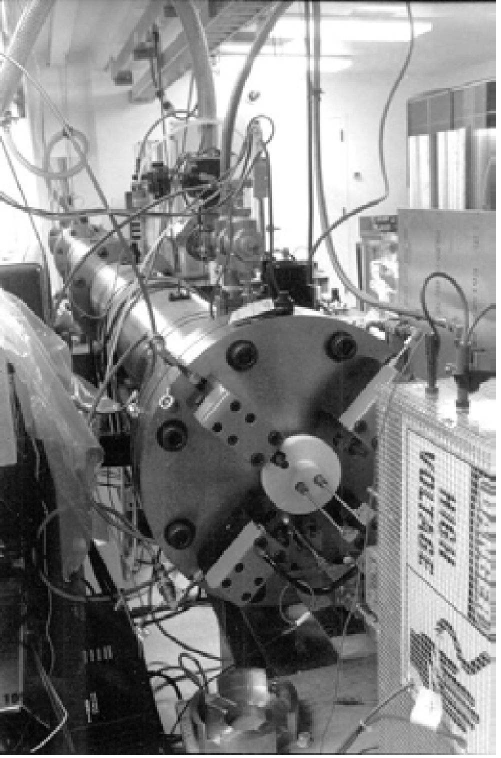
$$\Delta P = P'(x, r = R_o, t),$$

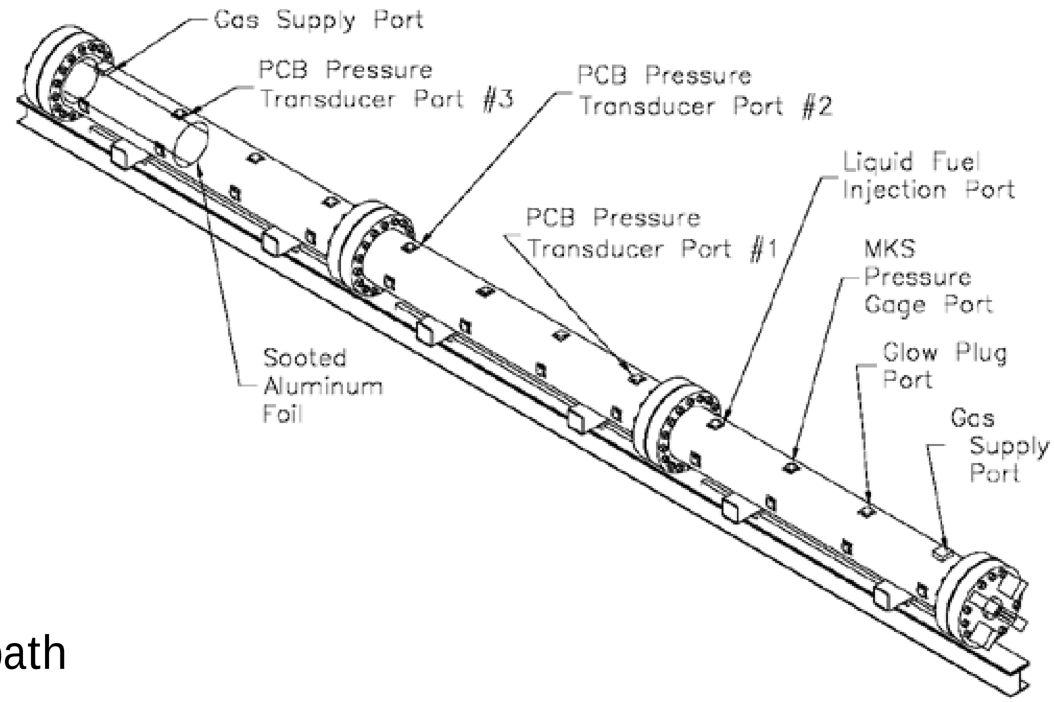
$$= -\rho_o \left.\frac{\partial \phi}{\partial t}\right|_{r=R_o}.$$

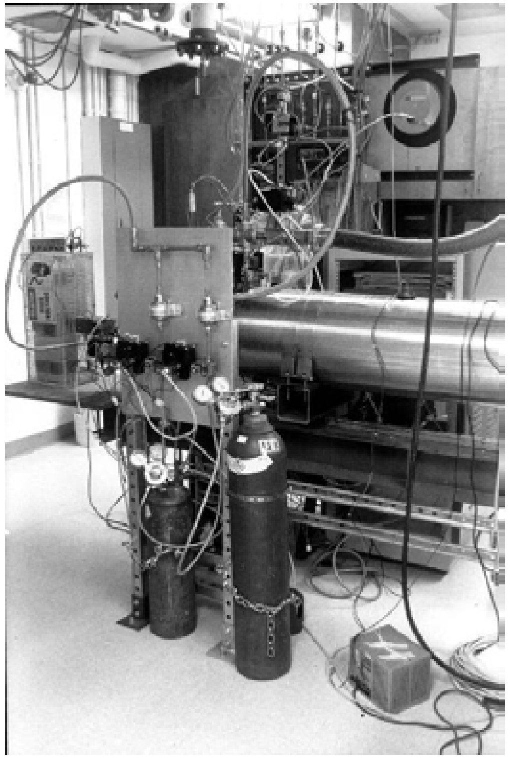

radial displacement (μm)
80
70
60
50
40
30
20
10
0
-10
800 μs
700 μs
600 μs
500 μs
400 μs
300 μs
200 μs
100 μs
pressure
shear
bar
hoop strain (μstrain)
200
150
100
50
0
-50
axial strain (μstrain)
80
60
40
20
0
-20
-40
-60
-80
-100
0.0
0.5
1.0
1.5
2.0
axial distance (m)

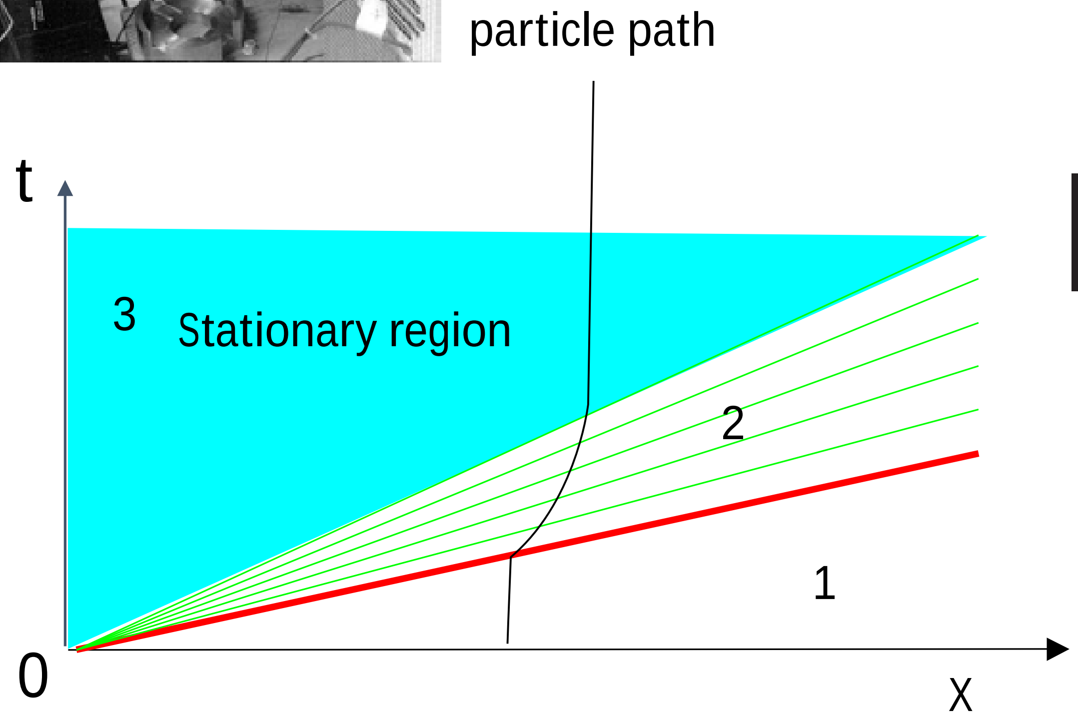


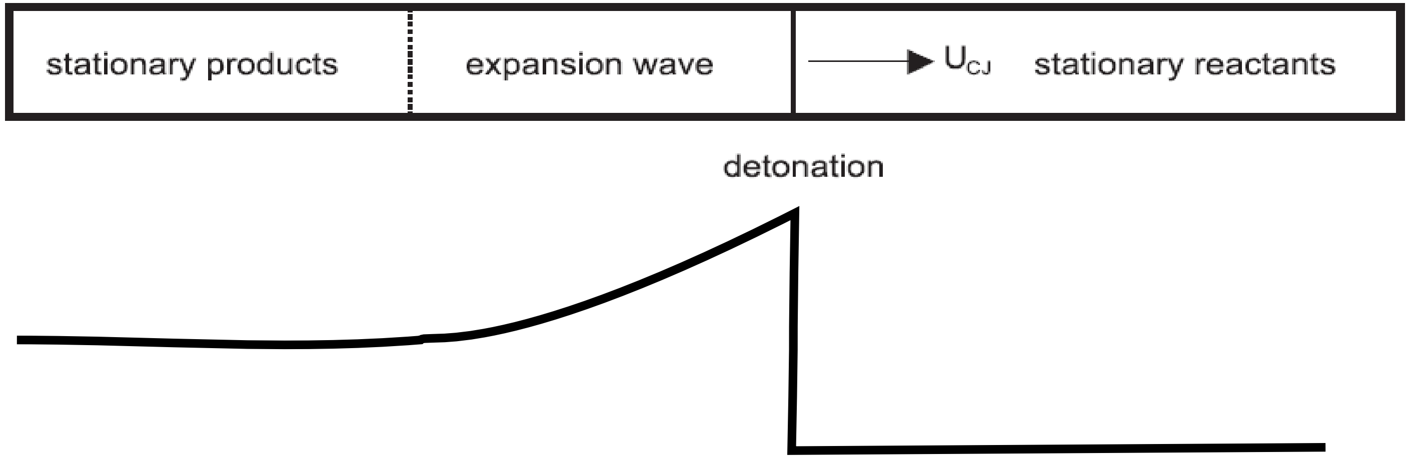
1.237m
Shield Tube
Test Tube
Transition Tube
Shock Tube
0.208m
SG3
SG2
SG1
PCB3
PCB2
PCB1
0.386m
0.564m
1.016m
1.42m
1.92 m
Pressure (bar)
Time (ms)
Shock speed (m/s)
Strainjump (x 1.E-5)
Time (ms)
Strainjump (x 1.E-5)
Time (ms)

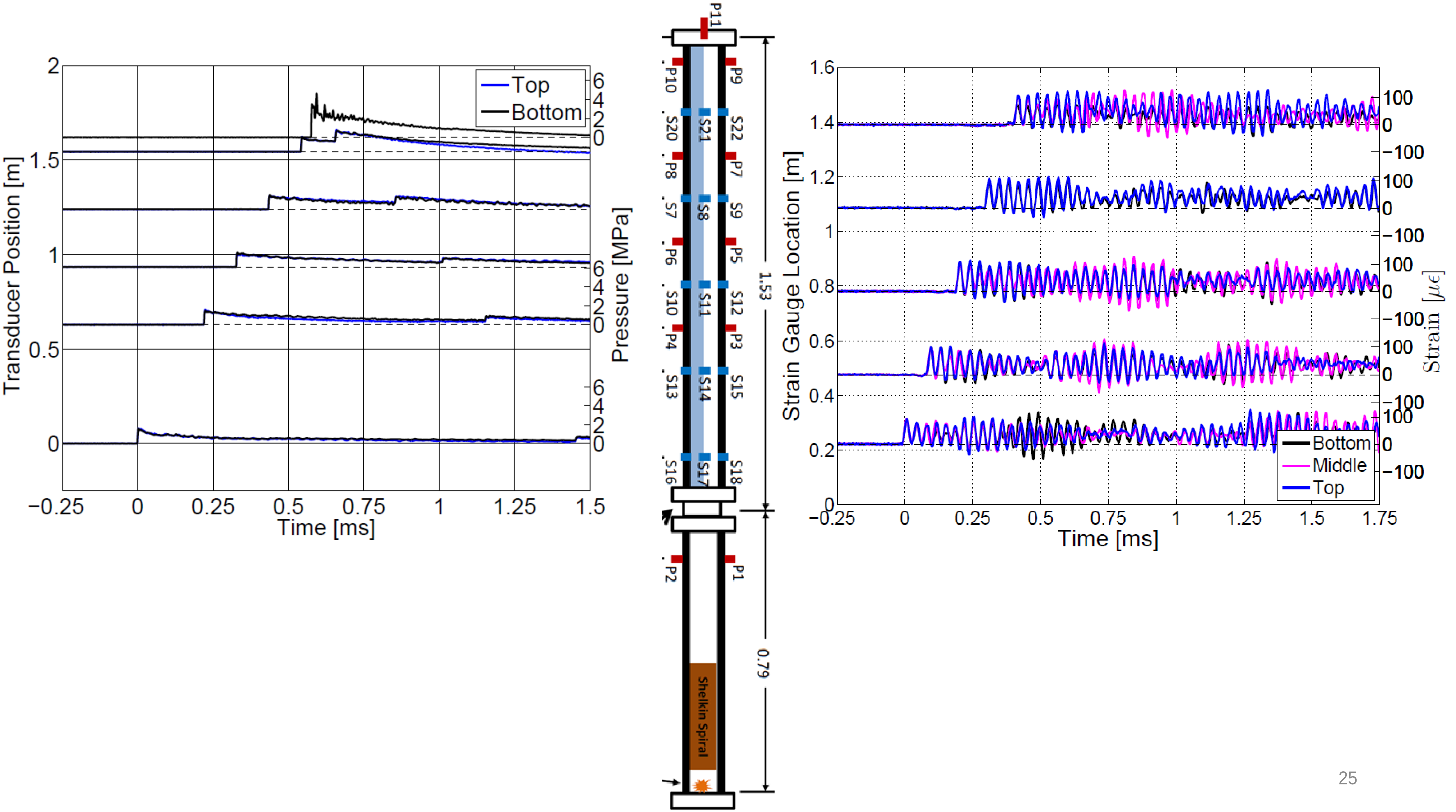


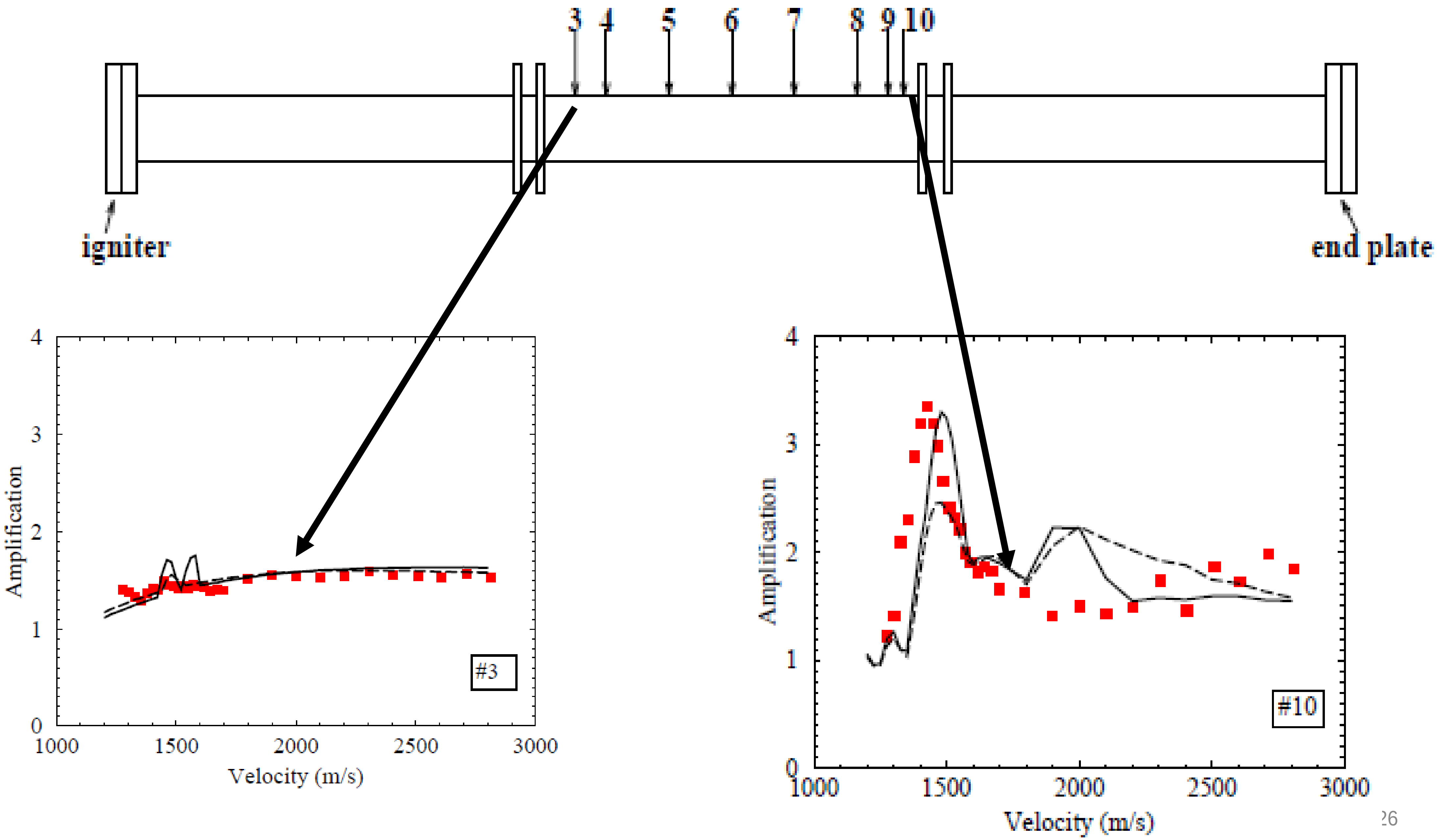

Gas Supply Port
PCB Pressure Transducer Port #3
PCB Pressure Transducer Port #2
Liquid Fuel Injection Port
PCB Pressure Transducer Port #1
MKS Pressure Gage Port
Glow Plug Port
Gas Supply Port
Sooted Aluminum Foil




particle path
t
3
Stationary region
2
1
0
X


stationary products
expansion wave
U_{CJ}
stationary reactants
detonation


Transducer Position [m]
Time [ms]
Pressure [MPa]
Top
Bottom
P11
P9
P10
S20
S21
S22
P8
P7
S7
S8
S9
P6
P5
S10
S11
S12
P4
P3
S13
S14
S15
S16
S17
S18
P2
P1
1.53
0.79
Shelkin Spiral
Strain Gauge Location [m]
Strain [$\mu\epsilon$]
Bottom
Middle
Top
Time [ms]


3
4
5
6
7
8
9
10
igniter
end plate
Amplification
Velocity (m/s)
#3
Amplification
Velocity (m/s)
#10

Physiology - Again

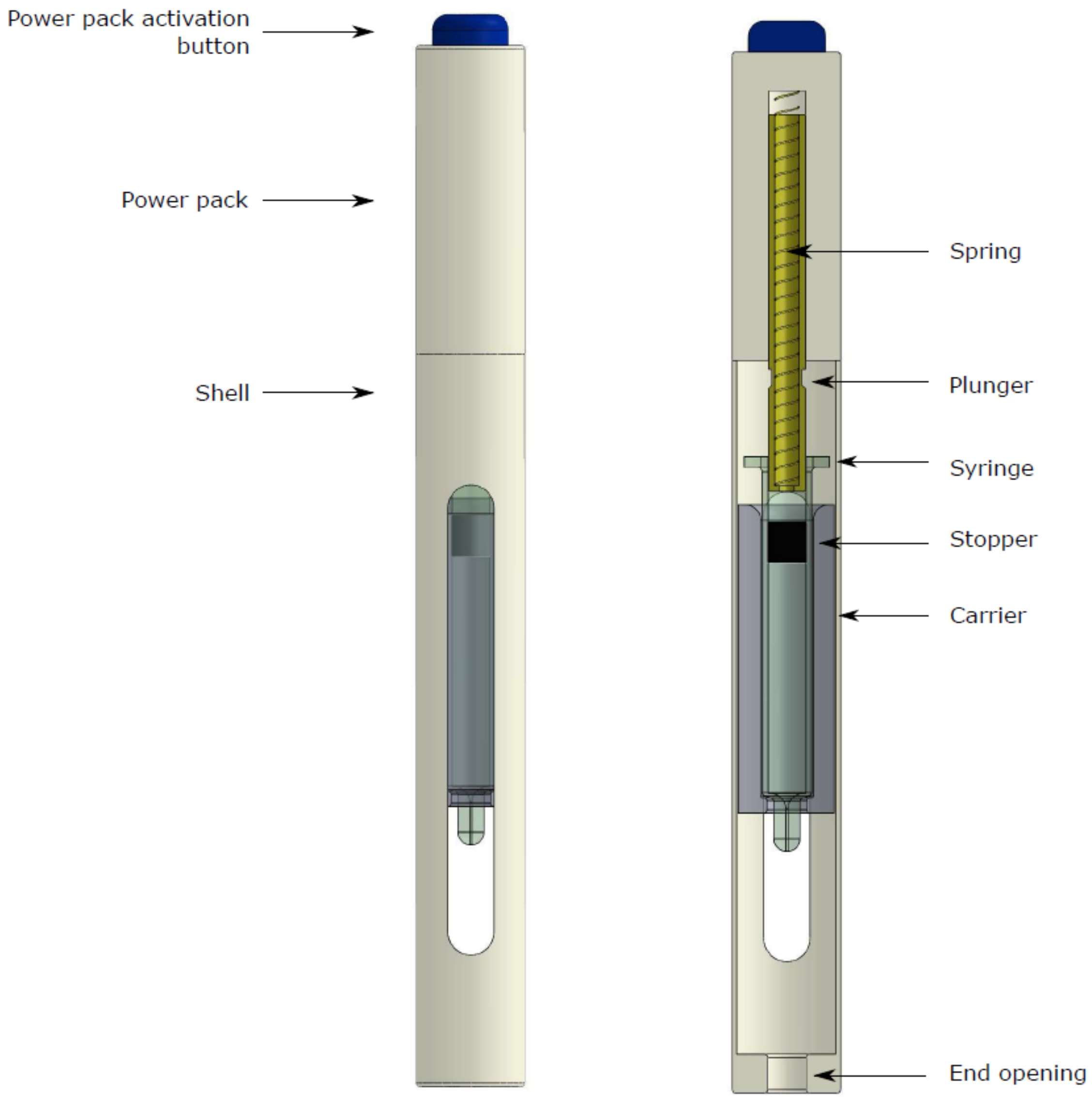
Monoclonal antibodies, biologic drugs, syringes and autoinjectors

Monoclonal Antibodies

- Form of immunotherapy
- Monoclonal antibodies bind to specific cells or proteins and stimulate a patients immune system to attack those cells.
  - Chronic lymphocytic leukemia – Novartis
  - Arthritis – Humira, Enbrel
  - Cholesterol - Repatha
- Created by a cell culture “biologic drugs”
- Has to be taken by injection rather than orally

“Auto or Self-Injectors”

Autoinjectors



Disposable unit used for self-administration of injectable drugs.

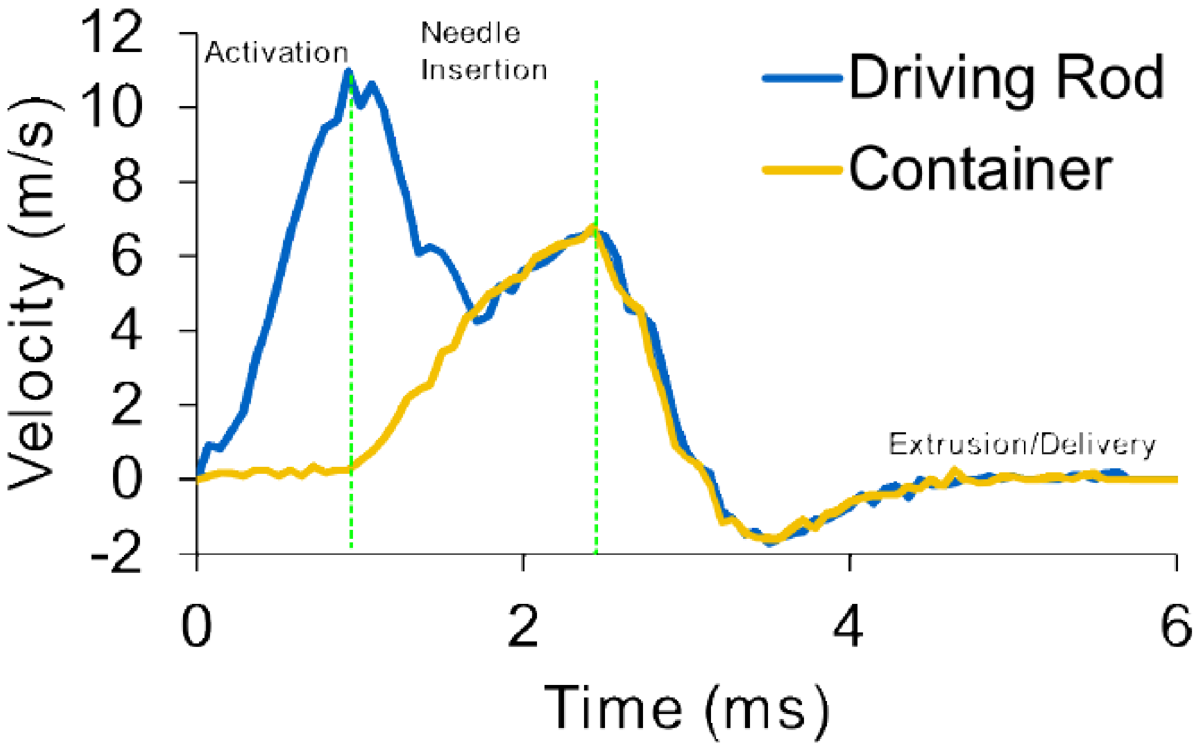
Consists of prefilled syringe and mechanical power pack.

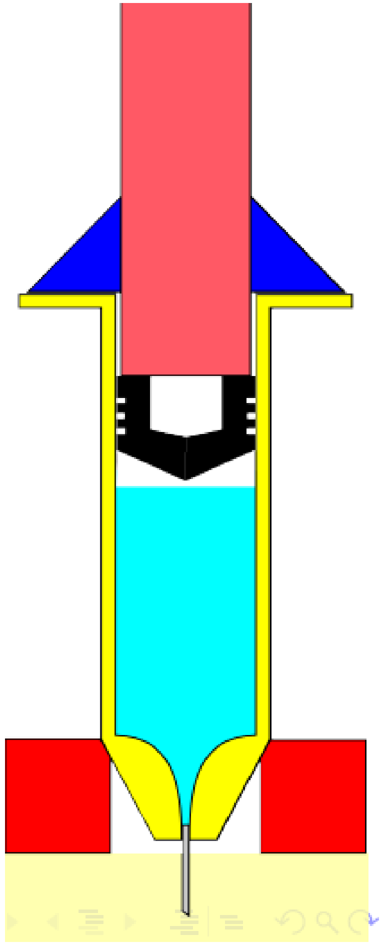
Release of spring in power pack actuates motion of needle and injection of drug solution into tissue.

How drug delivery devices work

To minimize device design complexity, often times the drive mechanisms responsible for drug delivery are also responsible for the events at device activation making the activation process an extremely transient series of events.

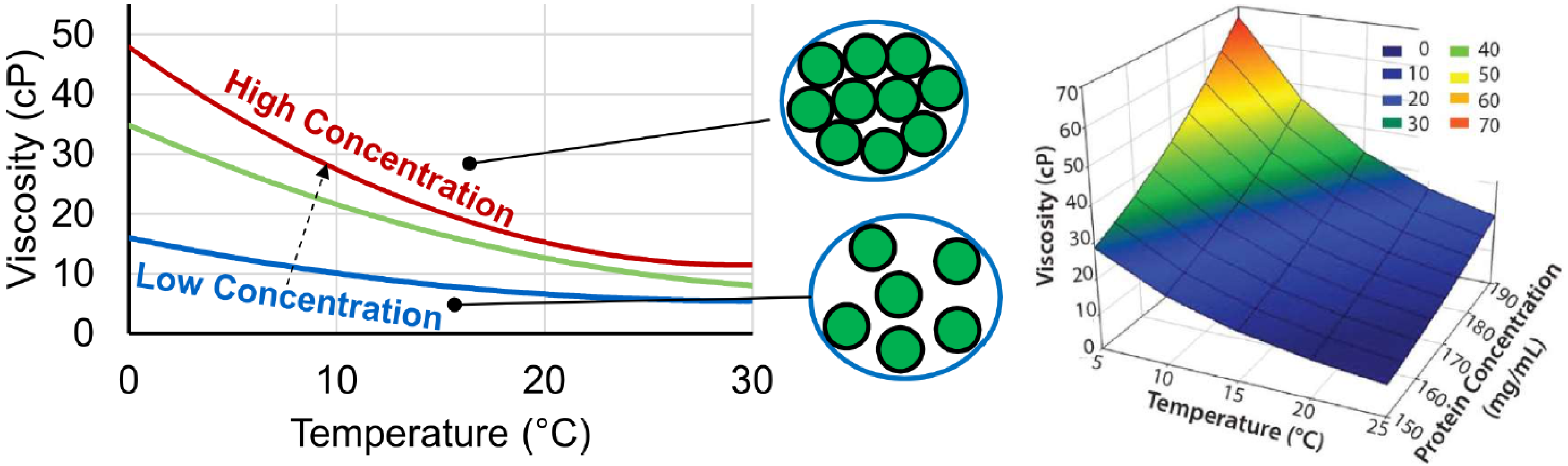
These highly transient events can lead to impulsive forces that may compromise container integrity.





Monoclonal antibody drugs are viscous

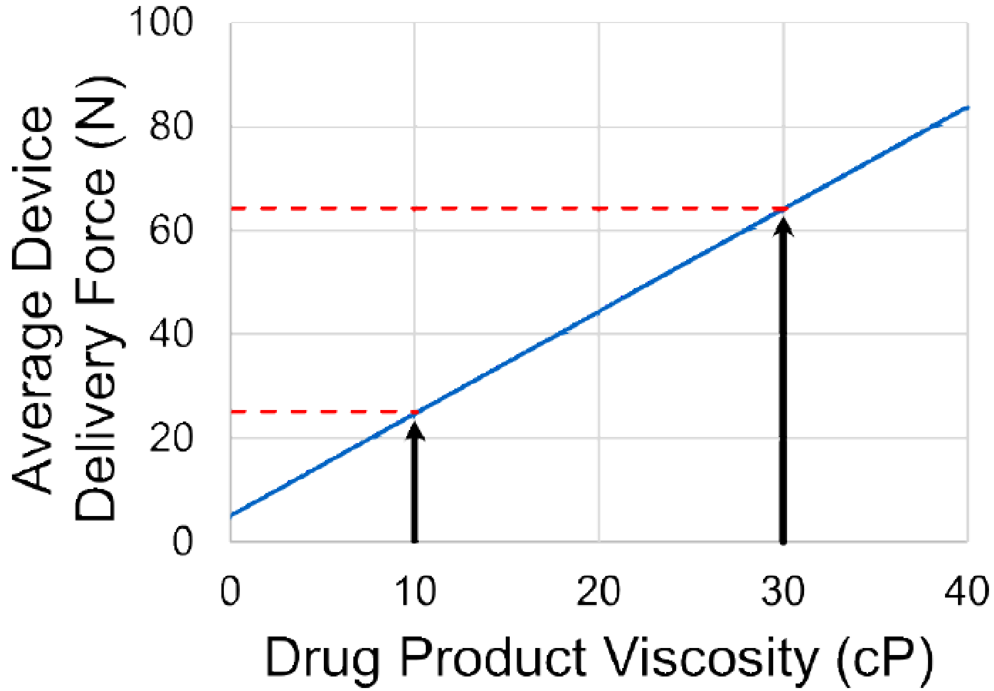
The concentration of monoclonal antibodies and by extension the drug product viscosities have been increasing in order to competitively meet patient needs.

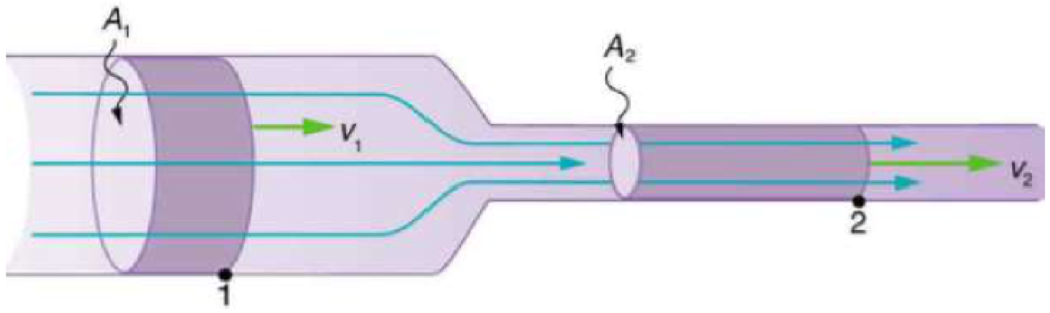


With high concentrations of monoclonal antibodies we can expect large variations in fluid viscosity with environmental conditions.

Performances of delivery systems

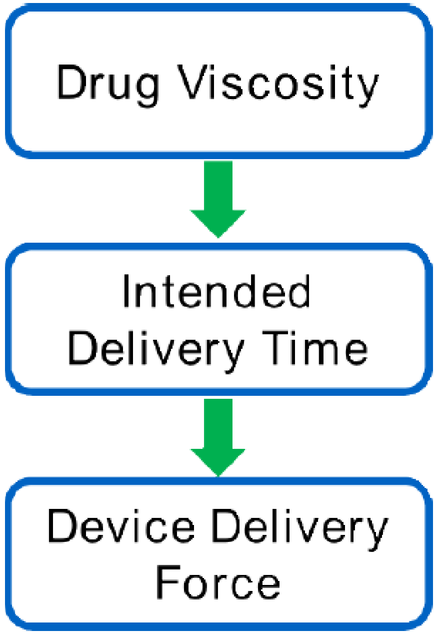
High concentrations of monoclonal antibodies can have a direct impact on the fluid properties of drug products that are relevant to primary packaging and device performances.





$$F = 8\pi\mu L V_2 \left(\frac{A_1}{A_2}\right)$$

$$F = 8\pi\mu L \left(\frac{A_1}{A_2}\right)\left(\frac{V}{t}\right)$$

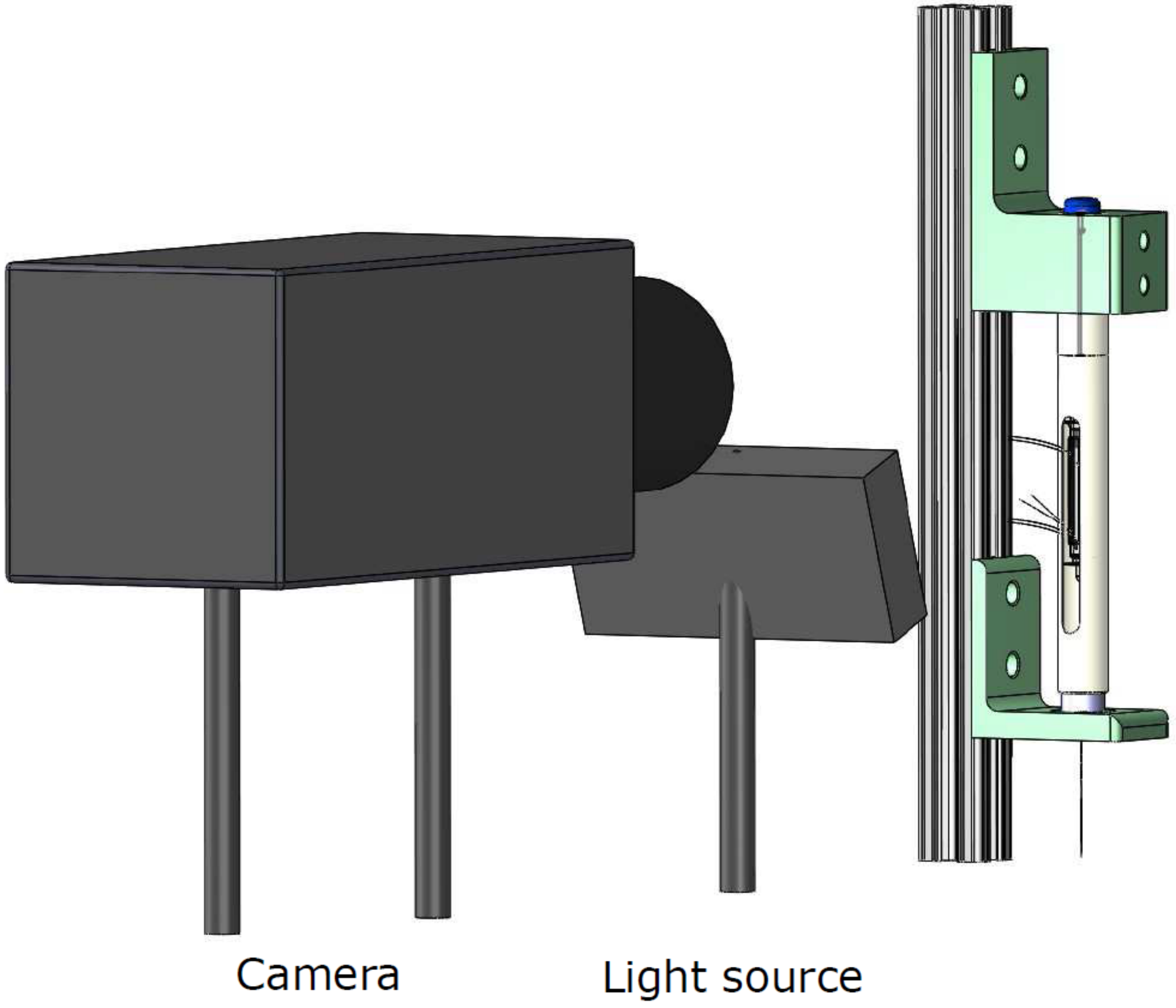


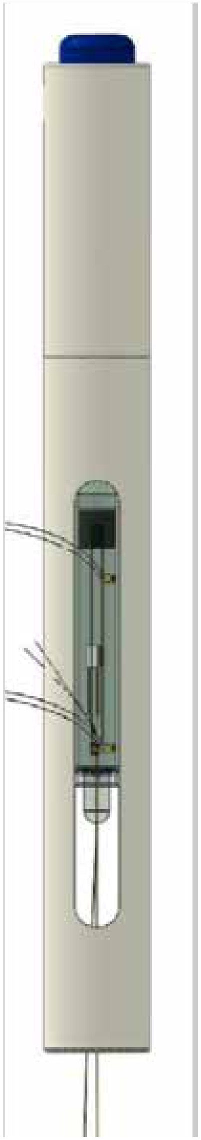
As drug products become more concentrated and viscous, challenges arise with meeting regulatory commitments on dose timing and device delivery forces.

Challenges of Increased Viscosity

- High injection pressures needed to obtain injection times acceptable to patients.
- Injection pressures are increased by using larger spring forces injectors than used for less viscous drugs
- Result: very rare but non-negligible failure through fracture of glass syringe.

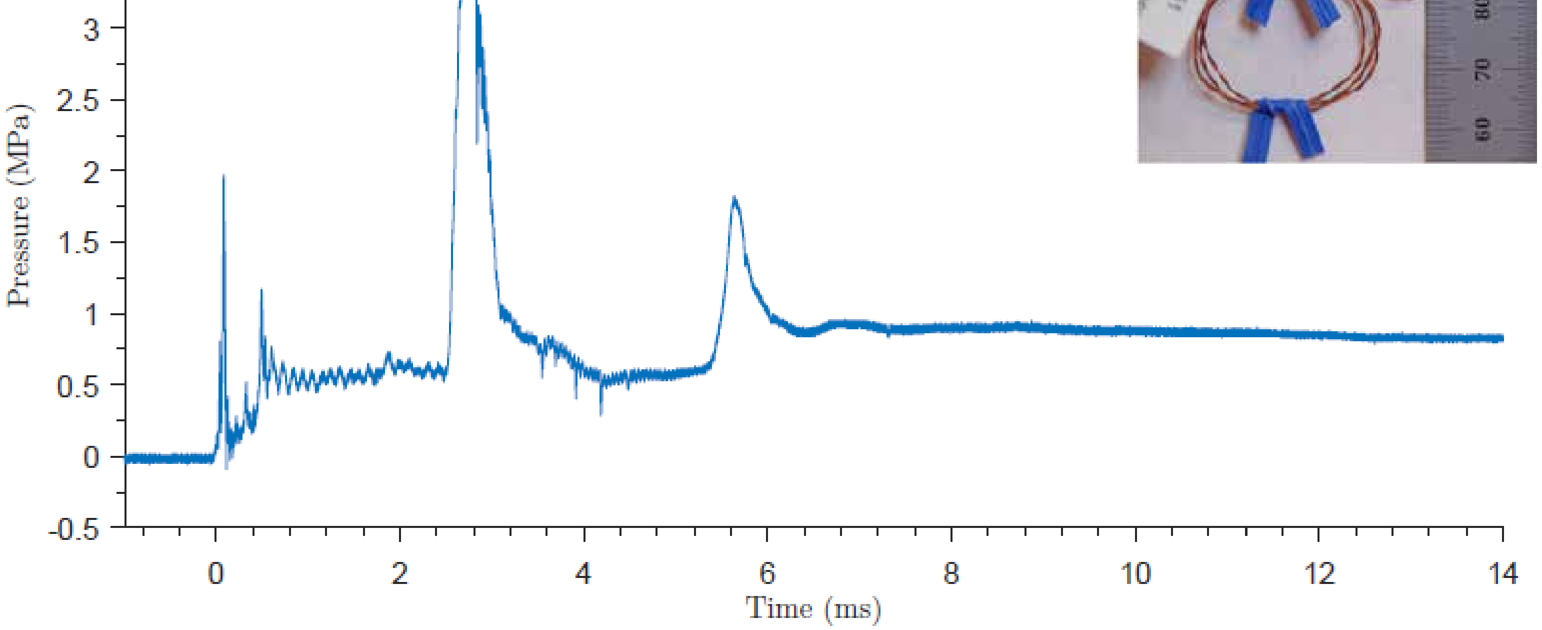
Development of In-situ Diagnostics

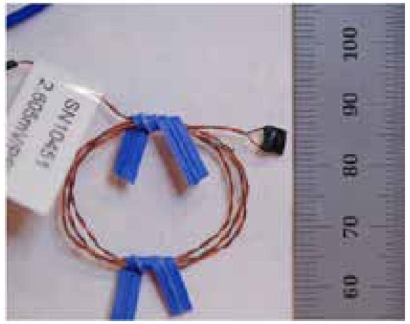


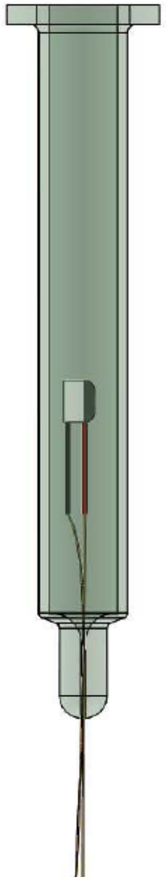


Transparent shell
for visualization

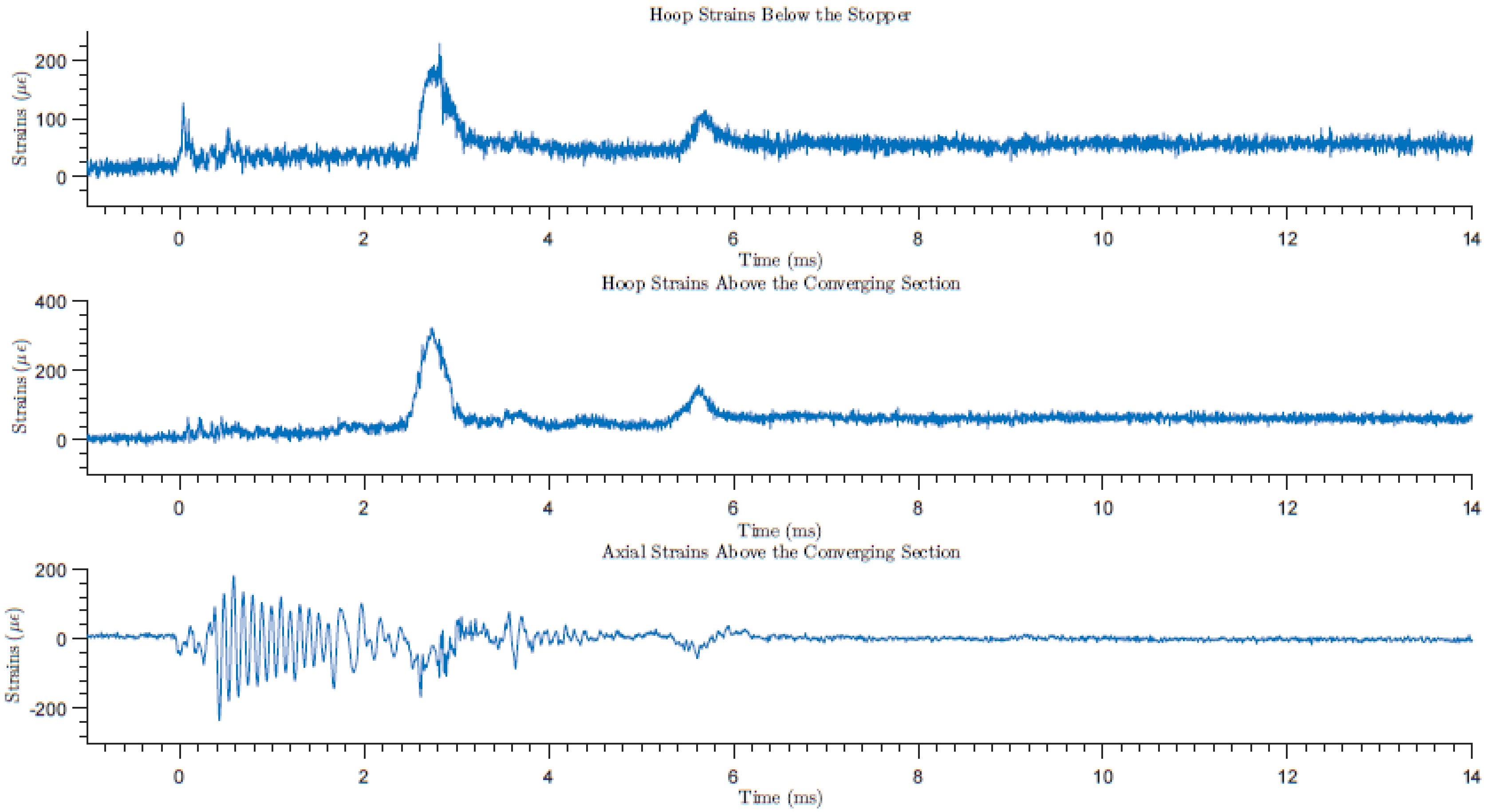
In-situ Pressure Measurement

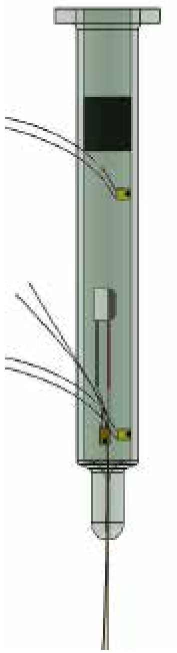




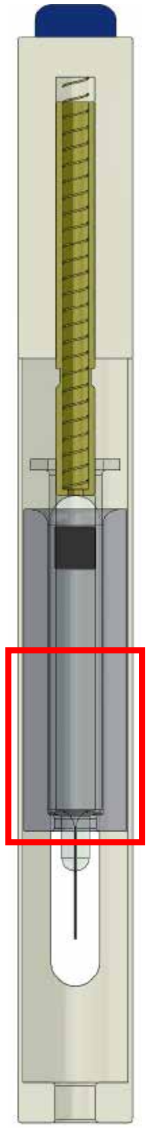


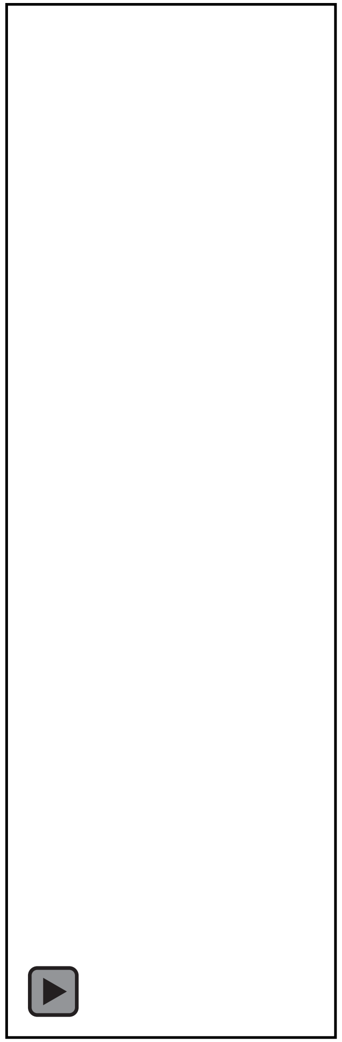
In-situ Strain Measurement

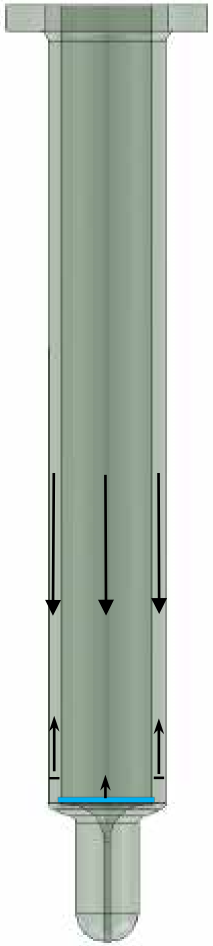




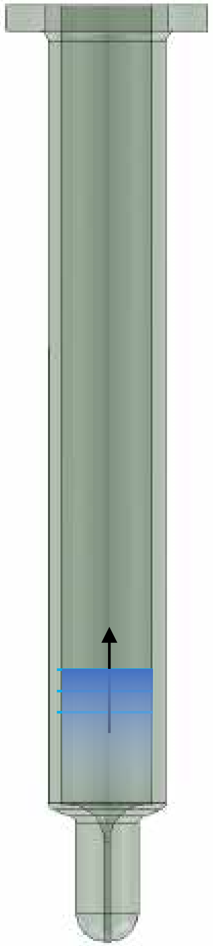
High-Speed Video of Cavitation



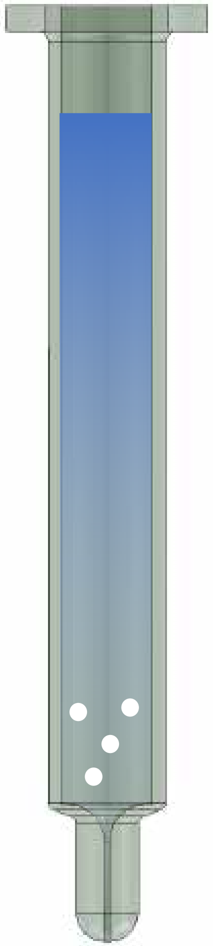




Downward motion of syringe creates acoustic waves in liquid

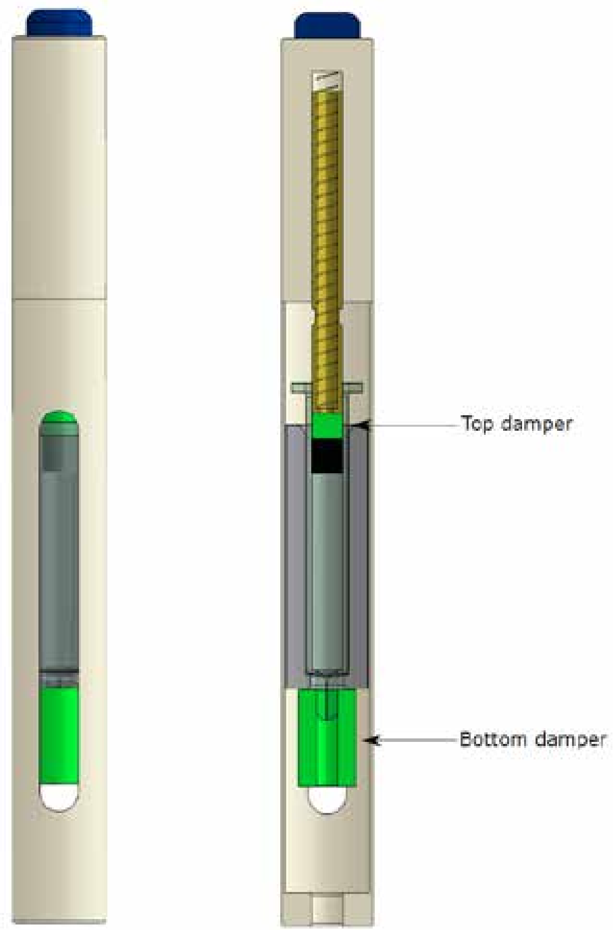


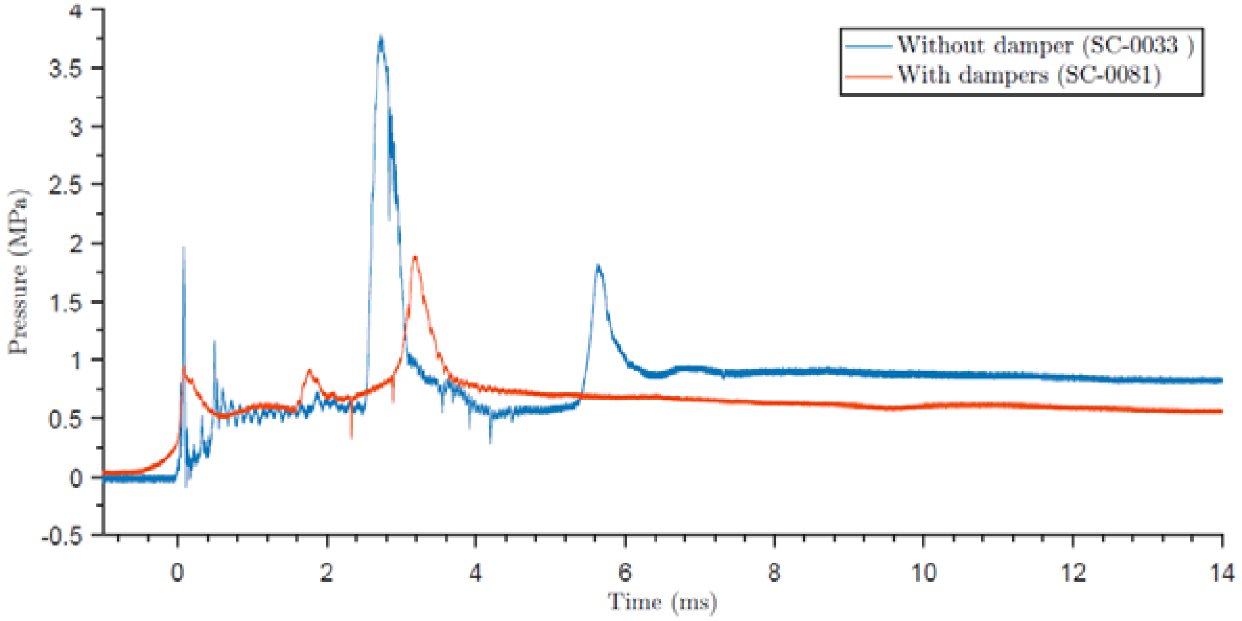
Propagation of acoustic wave and creation of negative pressure region



Negative pressure creates cavitation bubbles

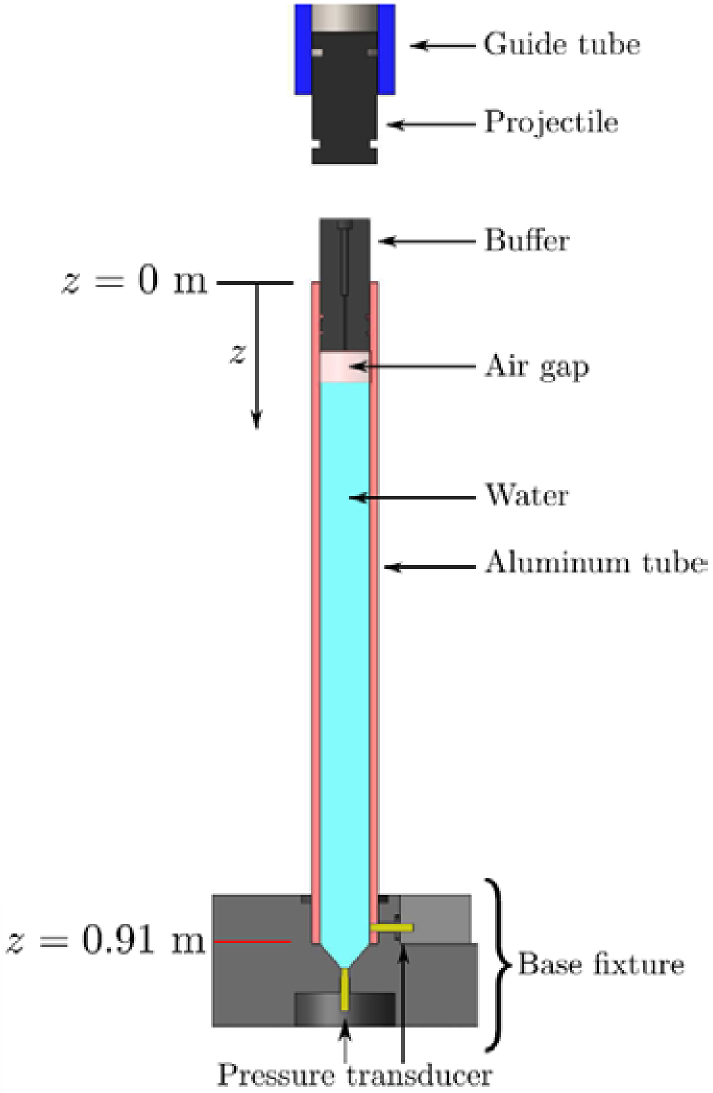
Mitigating Impulsive Pressures

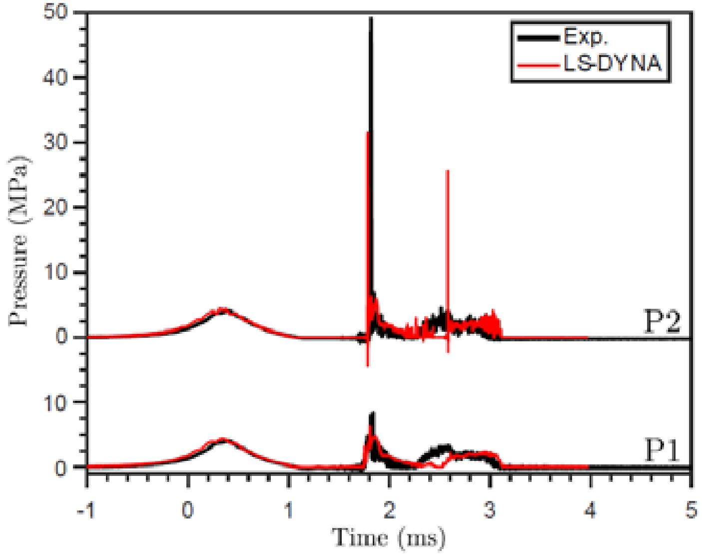


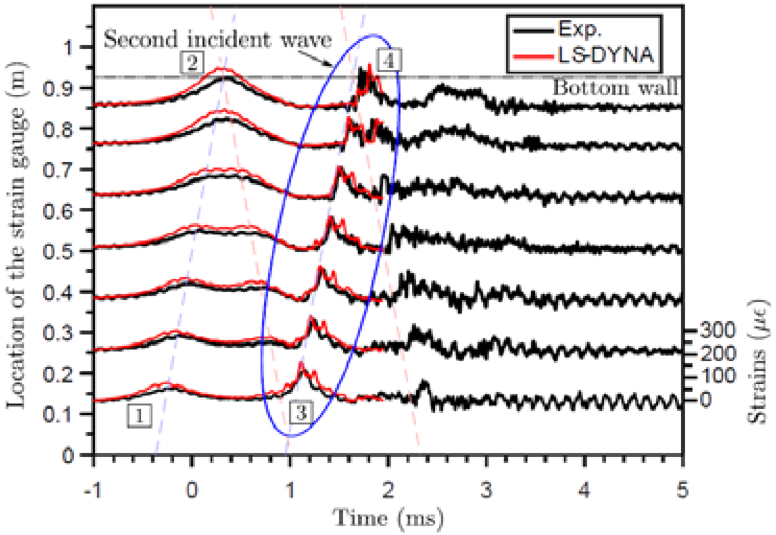


Reduction of peak pressures and strains by 75% while maintaining injection time.

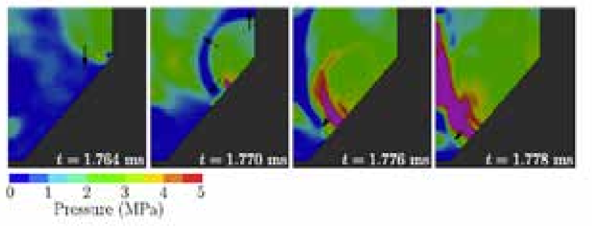
Scale Modeling and Simulation



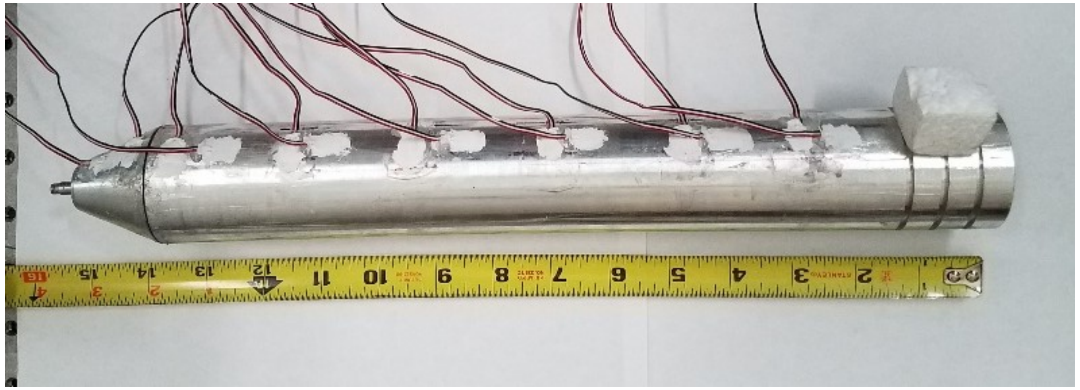




12 mm air gap
Converging section



Super-scale Model of Syringe



- Enables detailed measurements of strain
- Fixture can simulate first and second impact
- Fluid-solid coupling and impact dynamics scaled

Thank you.

- Amgen: Bruce Eu, Julian Jazayeri
- DHS, ONR, LANL, DOE
- Marco Beltman, Raza Akbar, Chris Krok, Florian Pintgen, Tony Chao, Macro Arienti, Patrick Hung, Jim Karnesky, Rita Liang, Kazuaki Inaba, Jason Damazo, Neal Bitter, Jean Christophe Veilleux, Tim Colonius, Ravi Ravichandran.

E D L