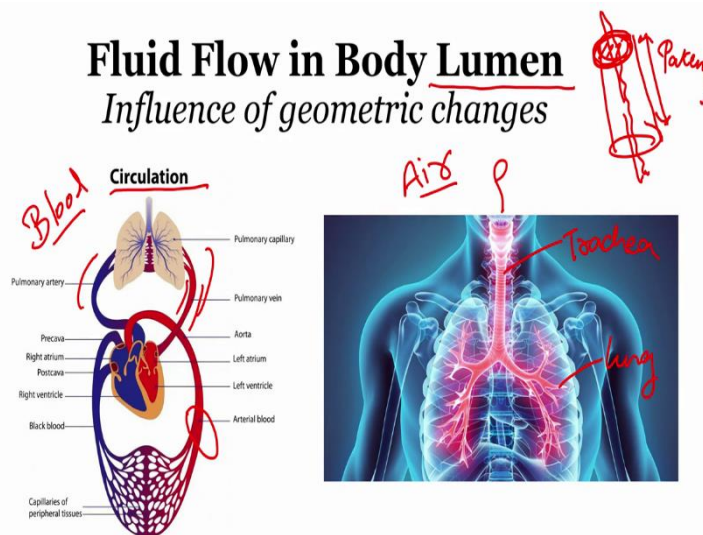


**Mathematical Aspects of Biomedical Electronic System Design**  
**Lecture 05**  
**Fluid Flow in Body Lumen**

Hello, everyone, welcome to another TA session. Today we will be discussing about mathematical modeling about fluid dynamics in Body Lumen.

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So, presenting the first slide, when we are talking about body lumen, the first thing that comes to my mind is the lung, the circulation system, the heart and how blood flows through the human body. So, what we, what does it mean when we say lumen? So, lumen is nothing but any tubular structure that has, that is hollow and then fluid flows through this channel.

So, this would have dimension, say length, diameter and the opening of this that is the cross-section area that is open for the fluid to flow through this channel is called patency. A few terminologies, so that as we proceed through, it will become easier for you to understand, how the derivation goes on.

So, here this is the circulatory system that through the heart, the blood flows through the atrium, aorta, the arteries, and the veins and these are called the lumen or the channels through which the blood flows in. Another example, what I can give because here blood is the fluid that is flowing through the channel, this is another body lumen through which air is being exchanged, that is, this is the upper airway, the trachea and the lungs.

The reason for taking two different examples is the type of fluid that flows through these channels are different. So, the parameters what you need to consider would be different, the density of blood is different from the density of air and how does these influence healthy and

in case there is a disease, how does the fluid flow change and what does the role of geometry play in these, the normal and the healthy and the disease condition.

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## Parameters that govern flow in vessel

- All blood vessels have certain lengths (L) and internal radii (r) through which blood flows when the pressure in the inlet and outlet are unequal ( $P_i$  and  $P_o$  respectively); there is a pressure difference ( $\Delta P$ ) between the vessel ends, which supplies the driving force for flow.
- Friction develops between moving blood and the stationary vessel walls, this fluid movement has a given resistance (vascular), which is the measure of how difficult it is to move blood through a vessel.
- Relative relationship between vascular flow, the pressure difference, and resistance (i.e., the basic flow equation):

$$Q = \frac{\Delta P}{R} \quad \text{or} \quad \Delta P = QR$$

where Q = flow rate (volume/time),  $\Delta P$  = pressure difference (mm Hg), and R = resistance to flow (mm Hg  $\times$  time/volume). WSS

- It is known that the resistance to flow through a cylindrical tube or vessel depends on several factors (described by Poiseuille) including: 1) radius, 2) length, 3) viscosity of the fluid (blood), and 4) inherent resistance to flow, as follows:

$$R = \frac{8L\eta}{\pi r^4}$$

where r = inside radius of the vessel, L = vessel length, and  $\eta$  = blood viscosity.

- It is important to note that a small change in vessel radius will have a very large influence (**4th power**) on its resistance to flow; e.g., decreasing vessel diameter by 50% will increase its resistance to flow by approximately **16 fold**.

$$R \propto \frac{1}{r^4} \quad \Delta P = QR$$

So, as we proceed, what are the parameters that govern the fluid flow through the channel, like I mentioned previously, the channel would have a certain length and the radii from this we talk about the patency that is the cross-section area that is available for the fluid to flow through the channel, the tubular structure and then here considering blood that is the case one we have difference in pressure that is inlet and outlet pressure, that is when the fluid flows through the tubular structure.

And when does the fluid flow? The differential pressure plays an important role here and that is how we see, how through the blood vessels, the force through which the fluid can flow through the channel. Now, the relationship between the fluid flow, the pressure difference, and the resistance. Now, this is a new topic here, resistance which is offered because of the fluid that is flowing through the channel.

Flow here is nothing but the volumetric flow. Why do we call it volumetric? Because it is the entire through the complete volume that is the cross-section area, the inlet flow is the volumetric flow and then it is governed by the pressure difference and here the resistance. Now, when the fluid is flowing through a channel it assumes a flow something like this, the flow is parabolic, a structured flow like this because the walls of the channel has something called as stress, wall shear stress, which offers resistance to the fluid flow.

Considering this parameter, the volumetric flow can be calculated as the ratio of pressure difference to the resistance that the walls of the fluid channel, of the tubular structure or the structure offers resistance and that is what is R here. Now, it is known that the resistance to the flow through a cylindrical tube depends on several factors, one we have already considered length as one parameter, radius, viscosity of the fluid, here it is blood.

And in case you are considering an airway channel or the trachea bronchial tree, then you will have to consider the viscosity and density of air as a medium. So, the medium plays an important role and the inherent resistance to the fluid flow. Here, all the parameters put together we have something called as the Reynolds number  $R$ ,  $L$  here is the length,  $\delta$  is a constant which is derived because of when you go to the Reynolds number derivation, you can see how the parameter comes this depends on the geometry of the structure and the viscosity here it is the blood viscosity, the vessel length and the inside radius.

Now, here how is the radius dependent on the fluid flow? It is inversely proportional to  $r^4$ . This plays an important role because the parameter that is the Reynolds number talks about the fluid flow through a channel. The fluid can be laminar that is, there is no disturbance in the channel and the Reynolds number corresponding to a laminar flow would be something less than 2000.

And if the fluid flow is turbulent that is the direction of the fluid flow cannot be controlled through a channel due to various reasons and why the flow becomes laminar or there is a transition from laminar to turbulence we will see in the coming slides. So, when there is turbulence the Reynolds number is greater than 4000, anything between 2000 and 4000 is called a transition.

Now, this is the resistance to a fluid flow the equation that governs and what are the different parameters, the radius, the length of viscosity of the fluid. So, what happens if there is a change in the vessel radius, because of many parameters, maybe due to a compression, the vessel was supposed to be like this and because of external force, the channel will have constriction to the fluid that is flowing.

What does this construction contribute towards the fluid flow? That is because the radius here drops compared to the original like the healthy radius, what would happen to the fluid? As we have seen the influence is really high that is the resistance that is offered is inversely proportional to 4th power. Now, this has a greater impact. So, when we have, as you see as the diameter decreases just one example to quote and if it reduces by 50 percent.

Now, this is a healthy vessel and when the diameter drops to 50 percent that is the area up to 50 percent the resistance that it offers to the flow increases by 16-fold. Now, this pressure difference radius, now this year is the volumetric flow, how do we relate volumetric flow to the pressure difference, the length, the viscosity, and the radius. This is one equation which relates the different parameters.

And here this is the resistance offered to the fluid flow through a channel, these parameters play an important role because if there as of today, there is no diagnostic tool, which can be just inserted through the organ and then you determine, what is the alteration in the fluid flow.

So, based on these parameters, it can be estimated you can calculate them, but now there are several computational studies, CFD Computational Fluid Dynamics studies based on which you can assume all of these parameters based on the geometry and then you do perform simulation to understand how these parameters are affecting the fluid flow through the given medium.

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### Influence of geometric changes

Laminar flow < 2000

R1 < R2

Tube diameter (µm)	Tube length (cm)	Range of pressure drop (MPa)	Reynolds number range
16.6	1.0	27.6-213.6	400-3400
19.7	2.0	55.8-228.1	900-3100
19.7	2.9	41.3-241.9	400-2800
26.3	2.0	24.1-137.8	700-3200
26.3	2.5	68.9-137.8	2000-3100
32.2	2.0	13.8-107.0	600-3400
32.2	3.0	9.0-106.8	300-2900

Turbulent flow

P1 → ΔP → P2    Q

Rands, C., Webb, B.W. and Maynes, D., 2006. Characterization of transition to turbulence in microchannels. *International Journal of Heat and Mass Transfer*, 49(17-18), pp.2924-2930.

Like I mentioned geometry plays a significant role. This is how the fluid flows, the fluid flows something like this and this is called as a Laminar flow, where the Reynolds number would be less than 2000. So, what happens when the fluid is flowing in a laminar? The resistance offered would be low, there is no the chaotic movement in the channel, all of them throughout the length tend to move in a similar fashion, each of them do not criss-cross like there is no such factor, because of which the fluid flows from one end to the other end, this is why it is laminar flow.

And when it is turbulent, as you can see the turbulence occurs one because of the obstruction. There could be external, the constriction or the obstruction could be because of many reasons, one such as maybe there is an external organ which is compressing on the vessel or there could be something that is interior inside the vessel there could be a formation of inflammation, because of which again the reduced diameter here can cause turbulence.

That is when the fluid is flowing consistently here, but because of this sudden reduction in the radius, it gains additional velocity here and then it transits to a turbulent flow. Now, there is one study here, just to understand the characterization of how the fluid transits, there is a transition from laminar to turbulence in microchannel. Here they have considered parameters such as the tube diameter, the length, that is the channel length, the pressure drop.

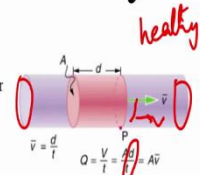
As I said the fluid flow is  $\Delta P$  that is the pressure at the inlet and pressure at the outlet plays a significant role for the fluid flowing through this channel and then the Renault number range, as you can see as the diameter of the channel increases, so this is the smallest diameter here 16 micrometre and this is a 32 micrometre, but they have also increased the length through the different studies 1, 2, 3, and 4.

So, they have increased the length gradually and what happens to the pressure, the pressure drop decreases. So, pressure and velocity are inversely proportional. As the channel diameter increases here, this is the range in pressure drop what they have observed and then the Reynolds number. This is just one case study, but then how these parameters affect can be understood based on few mathematical equations.

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## Flow Rate and Its Relation to Velocity

- Flow rate  $Q$  is defined to be the volume of fluid passing by some location through an area during a period of time
- The precise relationship between flow rate  $Q$  and velocity,

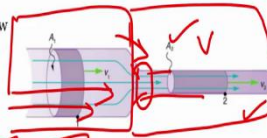


Compressible  $\rightarrow$  density

$$Q = A\bar{v}$$

$$\bar{v} = \frac{d}{t}$$

- An incompressible fluid flowing along a pipe of decreasing radius.
- Because the fluid is incompressible, the same amount of fluid must flow past any point in the tube in a given time to ensure continuity of flow.
- In this case, because the cross-sectional area of the pipe decreases, the velocity must necessarily increase.



1) Re  
2) Newton  
3) =

$$\begin{cases} Q_1 = Q_2 = Q, \text{ Boundary} \\ A_1 v_1 = A_2 v_2 \end{cases}$$

## Parameters that govern flow in vessel

- All blood vessels have certain lengths ( $L$ ) and internal radii ( $r$ ) through which blood flows when the pressure in the inlet and outlet are unequal ( $P_i$  and  $P_o$  respectively); there is a pressure difference ( $\Delta P$ ) between the vessel ends, which supplies the driving force for flow.
- Friction develops between moving blood and the stationary vessel walls, this fluid movement has a given resistance (vascular), which is the measure of how difficult it is to move blood through a vessel.
- Relative relationship between vascular flow, the pressure difference, and resistance (i.e., the basic flow equation):

$$\text{Flow} = \frac{\text{pressure difference } \Delta P}{\text{resistances}} \text{ or } Q = \frac{\Delta P}{R}$$

where  $Q$  = flow rate (volume/time),  $\Delta P$  = pressure difference (mm Hg), and  $R$  = resistance to flow (mm Hg  $\times$  time/volume).

- It is known that the resistance to flow through a cylindrical tube or vessel depends on several factors (described by Poiseuille) including: 1) radius, 2) length, 3) viscosity of the fluid (blood), and 4) inherent resistance to flow, as follows:

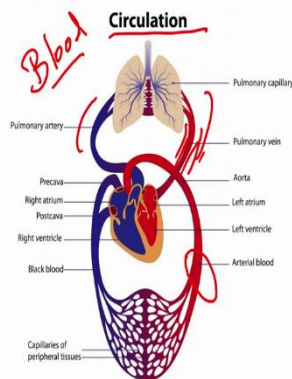
$$R = \frac{8L\eta}{\pi r^4}$$

where  $r$  = inside radius of the vessel,  $L$  = vessel length, and  $\eta$  = blood viscosity.

- It is important to note that a small change in vessel radius will have a very large influence (**4th power**) on its resistance to flow; e.g., decreasing vessel diameter by 50% will increase its resistance to flow by approximately **16 fold**.

## Fluid Flow in Body Lumen

### Influence of geometric changes



Now, the flow rate and its relation to velocity, what we have seen here is how the resistance changes with respect to the channel geometry that is the length and what is a volumetric flow and how the differential pressure and volumetric flow are related. Here what we see is the velocity?

Two parameters what we are to understand is the pressure drop and velocity. If these two parameters can be quantified through the body lumen, then it becomes easier to understand how the fluid is flowing through the channel. Is it laminar or is it turbulent? And why should we understand this property that is the fluid flow is laminar or turbulent, that is it helps us study if there is any change in the geometry, is there a constriction in the channel?

Ideally, when you talk about a healthy organ, say if the channels flow is healthy, then the fluid flow is laminar. So, it is designed to flow in a laminar structure, but if there is an alteration, if there is constriction, if there is a change in geometry for due to several reasons, because of chronic obstruction, then the fluid flow changes to turbulence. So, this transition can be understood and it has to be understood.

So, that you understand what is the root cause for the disease and how do you deal with it? How can be the prognosis? Should you have to operate it, should you insert a stent? So, that it can be brought back to the original diameter or do you have there is something called as resection, the segment will be resected that is removed. So, that when there is this abdominal region can be removed and you have the fluid flow to be laminar.

So, that would be the prognosis, but before that, we have to understand the fluid flow through these channels. Now, this is one such channel assume a vessel through having a cross-section area  $A$  and over the given diameter  $d$  the velocity  $V$ . Now, how are these related? Volumetric flow here  $Q = AV$ ,  $V$  here is the average velocity because  $\bar{V}$  is nothing but again here the velocity.

$$\bar{V} = \frac{\text{distance}}{\text{time}}$$

So, on an average, the velocity into the over a given area will give the volumetric flow. Now, here this line which is incompressible fluid flowing through along the pipe of decreasing radius that is this here. When we are talking about fluid flows, parameters such as Reynolds number needs to be quantified and then you need to know something called as Newtonian and non-Newtonian fluid.



And another thing is compressible flow and incompressible flows. So, these are a few concepts which needs to be understood. Here we are assuming blood to be incompressible fluid flow, when we say incompressible, that is the density remains constant. The details of which, I am just pointing you towards the parameters which has to be understood.

So, you can get into the details about Newtonian, non-Newtonian fluids, compressible and incompressible fluids and these parameters will be helpful when you are, when you have to simulate this in a virtual environment and you have to put something called as Boundary condition. So, that time you have, when you have boundary condition, you should give this the platform inputs such as the inlet pressure, outlet pressure, the type of tissue property and what is the type of fluid is it compressible or not, what would be the density of the fluid all of that comes when you have to do a CFD simulation.

So, here this is something the channel the cross-section area remains the same, consider this to be a healthy environment. But what happens when the diameter reduces that is a cross-section area reduces. So, we know that the mass remains the same. So, from the law of conservation what happens, the velocity gains because of the reduced. I mean, it drastically increases when the cross-section area here drops, the area decreases velocity increases for the same fluid which is being driven through this channel.

Now, we know that the same fluid is flowing through these, so the volumetric flow  $Q_1$  in this region should be equal to the volumetric flow of the fluid in this region. When we equate the two parameters, although the prime cross-section area reduces. How are the other two? How do you, we know that  $Q = AV$ .

So, here you can equate,

$$A_1v_1 = A_2v_2$$

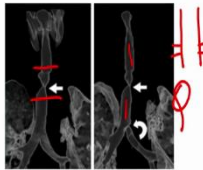
$A_2$  here is in the reduced area that is the area under velocity  $v_2$ . So, not just one channel, the multiple channels could be there and then each of that could have a reduced cross-section area and then there would be a change in velocity all of that can be equated using this principle. So, again when this is in reference to Hagen Poiseuille equation and the Bernoulli's equation, these equations are derived from the two laws.



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## Background o

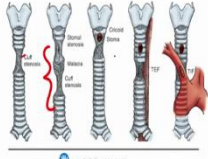
- Chronic upper airway inflammation remains a **diagnostic and therapeutic challenge** for pediatric surgeons.
- Constriction in the small airway geometry requires an individualized approach with **timely diagnosis and treatment**.
- Studies have shown **subjective assessment** (conventional bronchoscopy, CT scan images) is often based on **suspicion index** and has led to **misclassification of airway narrowing**.



3D volume rendered image of 6-year-old boy with history of long-term intubation and tracheostomy placement

## Statistics sum 205

- Acute respiratory infections are a **major cause for morbidity and mortality in young children**, a significant burden to child health both globally and in developing countries like India.
- 85-88% of respiratory infection episodes in young children are **acute upper airway infections**, claiming an estimated **3.9million** deaths annually worldwide (Global Burden of Disease Study)<sup>1</sup>.



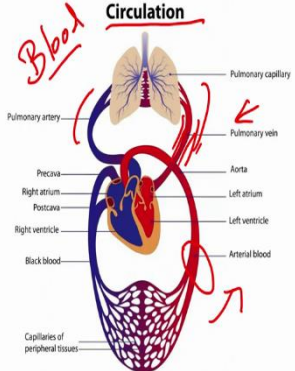
Ann & Robert H. Lane Children's Hospital of Chicago

<sup>1</sup>The Lancet. Infectious diseases. 2018 Nov;18(11):1191

## Fluid Flow in Body Lumen Packing


### Influence of geometric changes

Blood



**Circulation**

Air



**Trachea**  
**lung**

So, as you can see in this image, I was initially talking about I just took two case studies, one is the fluid flow through the blood circulation system and then the airflow through this upper airway. Now, we have seen this and how what are the cases through which there is an alteration in the upper airway geometry. This here on the right side is a CT scan image, it is mostly 2-dimensional and then you make it 3-D.

So, this is a 3-D volume-rendered image long term, of a 6-year-old boy with a history of long-term intubation. What is intubation? So, when you have a patient in a ventilator, we have something called as an endotracheal tube which will be inserted, in the artificial ventilator has is connected to a mechanical system, which can simulate your airflow that is through your lungs inspiration and expiration.

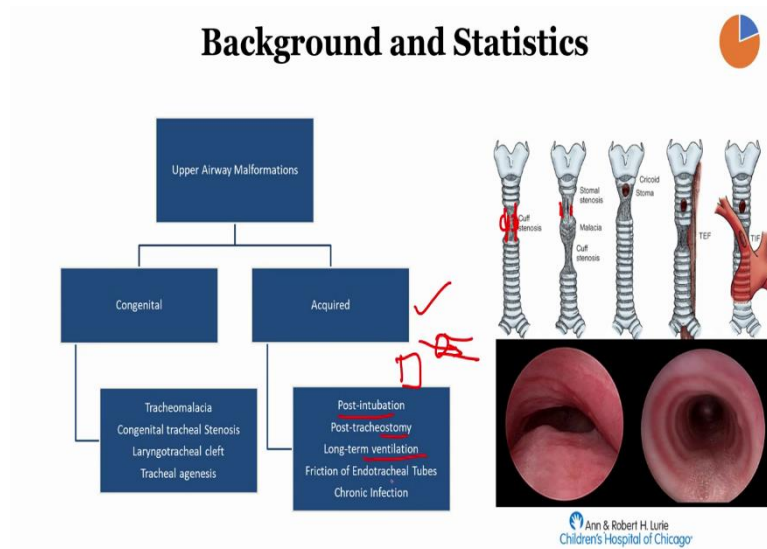
So, this intubation is nothing but when this tube is inserted through your upper airway and tracheostomy placement, that is because here what you see if it is a healthy condition, this is supposed to be a tubular structure, but here what happened is a constriction which was visualized through a CT scan image. Now, because of this constriction, there is a change in the fluid flow that is a transition, there is a transition from laminar to turbulence.

But how do you know, can you quantify this parameter? It would be difficult just by an image, but how do we quantify this and why should you quantify. Now, what is the amount of airway narrowing. So, if you know the percentage of the amount of airway narrowing, you could diagnose it or you could understand what could be the prognosis. Should you resect this segment or should you insert a stent.

So, that you increase the area and then the fluid flow becomes back to normal and all of that becomes important to understand how the disease should be diagnosed. A few statistics about how this can be more severe in young children, that is because the diameter of the structure changes with age. So, in a younger age group, the diameter of these channels are smaller and with increase in age, it increases say from 8 mm the diameter of the tracheal tube increases to 20 mm in adults.

Now, higher the area it is easier compared to this smaller region to deal with how this area can be repaired or reconstructed. So, it is more challenging in younger children. Now, this is one such reference. This constriction can happen through any region of the organ it could be in the proximal or it could be in the distal end or if the segment length can be higher or it could be a smaller region. What causes this? What is the root cause? All of this can be better understood if you quantify what is the velocity of the air that is flowing through this channel.

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Again, a few more details. Now, this could be congenital that is by birth or it could be acquired, I said there is something for every patient who is on an artificial ventilator, they have been introduced through a mechanical ventilator system and they have an endotracheal tube which is inserted through the mouth such that the air flows through this tube in and out of your lungs.

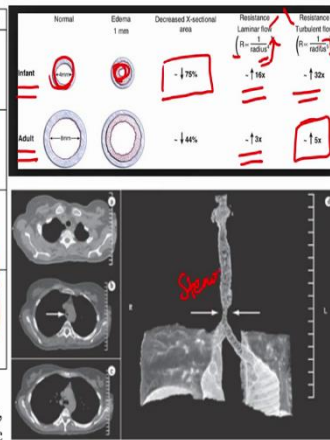
Now, that process is called as intubation. Now, because of intubation, that tube exerts a pressure on this organ here and this loses its mechanical properties. So, that is why post-intubation tracheotomy is a surgical procedure and then long-term ventilation, friction because of the tubes or it could be internal that is chronic infection. So, the root cause are many.

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## Myer-Cotton Classification

Classification	From	To	Endoscopic appearance
Grade I	No Obstruction	50% Obstruction	
Grade II	51%	70%	
Grade III	71%	99%	
Grade IV	No detectable lumen		

Filauro, Marta, Francesco Mazzola, Francesco Missale, Frank Rikki Canevari, and Giorgio Peretti. "Endoscopic preoperative assessment, classification of stenosis, decision-making." *Frontiers in pediatrics* 7 (2020): 532.



So, they came up with something called as a Myer-Cotton classification system based on the obstruction. Now, why are we studying the reduction in geometry. Now, we will see in future how the reduction in geometry can be related to the alteration in the fluid that is flowing through the channel.

So, for that, they have this classification, grade one when the channel is healthy there is no obstruction and if there is 50 percent obstruction anything less than 50 percent, they have classified it to be grade one and grade two between 50 and 70 percent obstruction that is only this much patency is available either for the blood or for the air to flow through this channel.

And then for a 70 to 90 percent, which is grade three and grade four when there is no detectable lumen. Now, these are the images that were obtained using a bronchoscope, bronchoscope it gives, it is a tube which is inserted into the organ and it has a camera which captures the internal structure of the organ, so these are the bronchoscopy or the endoscopic images. I have mentioned earlier why this is more serious in younger that is the infants and it is to handle when it comes to adults.

Because the first thing what we discuss is the resistance is inversely proportional to  $R^4$ . Now, when there is a 4 mm dia that is in children and when there is an obstruction or inflammation and it reduces the available patency is just 3 mm. Now, what happens because of the reduced cross-section area, the resistance to flow is increased by 16 percent, 16 times.

And if it is an adult, the same 1 mm reduction in area, there is just three times increase in reduction only because of this relationship here, the resistance being inversely proportional to

$R^4$  and when the flow is laminar, it is still okay but when it becomes turbulent, the power is, in turn, rising five times.

So, you see how this the channel geometry plays a important role in the fluid flow through these airway structures or the circulation system. This here, we call it the medical terminology is stenosis, that is reduction in the cross-section area when compared to its healthy diameter.

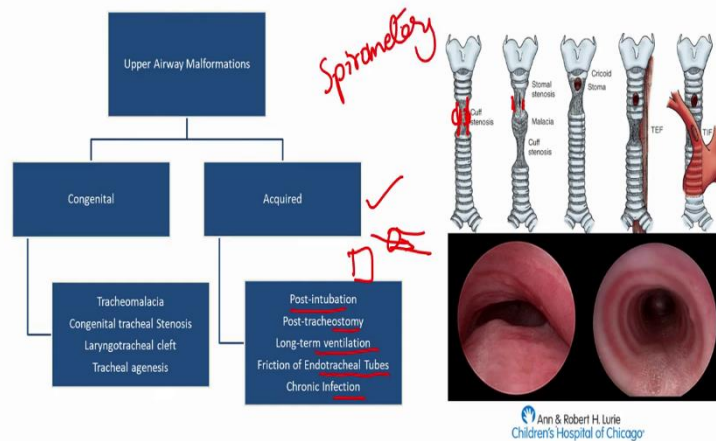
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## Challenges

- Anomalies of upper airway malformation are congenital tracheal stenosis, tracheomalacia, tracheal agenesis, atresia and many more.
- Definitive diagnosis of such anomalies calls for a team of **competent clinicians** and a **sophisticated clinical setting**, which becomes challenging in economically developing nations.
- The **variability in clinical symptoms**, **diversity of the associated anomalies** and **scarcity of resources** present significant challenges towards **effective diagnosis and timely management**.
- High radiation exposure from CT and **long scan times** in both MRI and CT make these modalities sub-optimal for infants.
- **Patient cooperation** in providing inspiration/expiration images.
- Sometimes a child is **incorrectly diagnosed** with severe asthma when they really have tracheomalacia. This is one reason why it's very important that your child's physician has **lots of experience diagnosing** and treating this condition (Source: Boston Children's Hospital)

*Quantity*

## Background and Statistics



*Spiranometry*

*DA*

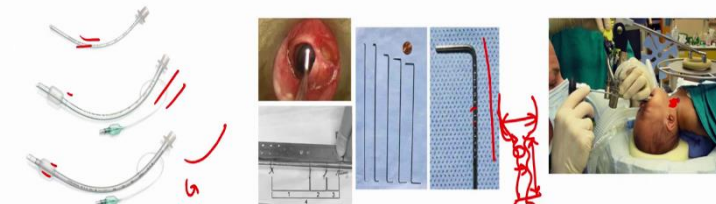
There are several challenges. One is because the disease has diversified anomalies like we have seen here, it could be based on the location again based on the root cause and based on that type, the anomalies are vast, so because of this diversified type of anomalies, it becomes difficult to understand what is the root cause and how can it be effectively diagnosed and by the time you understand, what procedure has to be adopted, there is no enough time.

So, timely management again becomes important. Currently, there is one image what we saw, all of this are nothing but a CT scan images or bronchoscopy images, but what are the challenges with CT scan, that is it has long scan times both in MRI and CT and that is why this sub-optimal for infants and then the patient cooperation.

There are other instead of the radiology scans, there are other methods to understand this something called as Spirometer, but that again requires forced inspiration and expiration that is again not possible when it comes to children or the infant and then because of this, there are a lot of studies which report that all of the grading of stenosis have been incorrect because there is no system which can precisely quantify what is the percentage reduction in the patency.

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## Current Technology



Evaluation and characterization of stenosis using endotracheal tubes.

The most widely used objective method for measuring stenosis in clinical practice

Needs interchanging of tubes multiple times to give crude estimate of degree of stenosis

**Kirschner Wire Measuring Sticks<sup>2</sup>** was proposed by a research group in 2015 for quantifying stenosis

The measuring sticks needs to be swapped until the right fit is determined.

<sup>2</sup>Sharma et al. JAMA Otolaryngology-Head & Neck Surgery. 2015 Apr 1;141(4):377-81

Measurements of tracheal stenosis with a rigid bronchoscope.

Optical distortions may lead to imprecise measurements

**Severity of narrowing often misclassified<sup>3</sup>**

<sup>3</sup>Murgu et al. Interactive cardiovascular and thoracic surgery. 2013 May 1;16(5):655-60


This is the endotracheal tube, what will be inserted into the patient who is on a ventilator. This is most widely used, how do you understand, this is a crude way just to estimate based on the tube size, they estimate what is the trachea diameter of the patient and the diameter changes with age again it is gender-dependent male and female have different size.

So, how do you determine what is the size of the patency or the trachea just by roughly inserting two-three times multiple size they estimate what would be the diameter and this is a very crude way of estimating what the degree of stenosis could be and then another technology came up where they had this metal rods which were inserted and they had markings like these just to understand what would be the stenosis segment length.

If this is the natural or the healthy diameter and if it reduces at what distance would it reduce, what is the stenosis segment length and by how much has it reduced. All of this again a crude

estimate using this tool and here you can see how challenging it is for a surgeon to insert something called as a bronchoscope and visually assess how the diameter inside is reduced or assessing the amount of narrowing becomes difficult and hence it is often misclassified.

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## Need of the hour

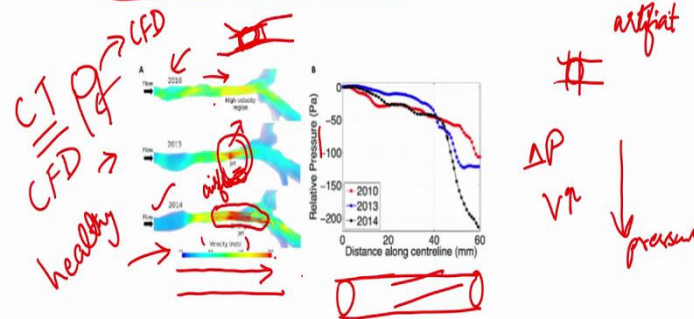
- There is no definitive surgical approach to repair tracheal abnormalities and is an area of **active research**.
- As surgeons lack a real-time estimation of the airway caliber, developing a stenosis measuring tool will be a **valuable guide to pediatric surgical therapy**.
- Deployment of the tool in **clinical setting** will aid in improving assessment of disease severity and its progression.
- The multifunctional, sensor integrated intubation catheter will be a **first-of-its-kind diagnostic tool** developed for monitoring infants and children with chronic airway obstruction.

So, again, what is the need of the hour. We need a tool which can effectively quantify what is the patency or the diameter the cross-section area that is available so that you can efficiently identify the right diagnosis procedure.



(Refer Slide Time: 29:52)

## Tissue-Engineered Tracheal Replacement in a Child: A 4-Year Follow-Up Study



Hamilton, N.J., Kanani, M., Roebuck, D.J., Hewitt, R.J., Cetto, R., Culme-Seymour, E.J., Toll, E., Bates, A.J., Comerford, A.P., McLaren, C.A. and Butler, C.R., 2015. Tissue-engineered tracheal replacement in a child: A 4-year follow-up study. *American Journal of Transplantation*, 15(10), pp.2750-2757.

Now, this is one such research paper, interesting article. So, a field that is emerging today is tissue engineering, if you identify a segment that is diseased, so you could replace that which with an artificial tissue.

So, that is something called another field of study, which is taking a lot of interest among research scientists is tissue engineering. So, if you found this segment to be abnormal, they would cut this and replace it with the healthy tissue once such study was being performed on a child, and then they followed a 4-year study clearly was described how the tissue-engineered segment behaved over 4-years in time.

So, he was initially in 2010, the patient was under a ventilator what was diagnosed is like I said, tracheal stenosis. Now this segment was resected that is removed and they replaced this with a stent. Even before they replace it with a stent. They had engineered a tissue and replaced the engineered tissue and on the safer side also inserted a stent in that region. So, they have performed a CFD, because as of today, there is no diagnostic tool that can be inserted and you understand how is the fluid flowing through this medium.

So, this colour difference is nothing but it talks about the velocity here. The gradient in colour here is to indicate how velocity changes over the length of this trachea bronchial tree. Now, here red is the highest velocity. Year 1, when the child was operated the fluid flow was for more or less laminar.

And it was observed that the velocity is as per the study, however it has to be in a healthy condition, that was observed in year one. But every time the child was again reported back to

the hospital and when they had a CT scan, each of the CT scan was converted into a 3-dimension model.

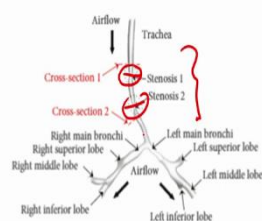
And then again following a 3-dimension model, CFD study was performed, how is the fluid flow changing over the year and 2013 they observed that in spite of the stent, here, there is an airflow jet. When we say this, it means there is a transition from laminar to turbulence, that is the velocity here is increasing, which means the wall here is collapsing. So, what happens as the segment collapses and this became severe in 2014, as you can see, the velocity segment the region, where the velocity increase is higher compared to the previous year.

So, now, that they have understood that the stent or the tissue-engineered trachea is no more working, they had to replace the whole segment and identify what could be the next step. So, that you can have a healthy airflow into the lungs and throughout the channel. This is again a pressure drop. Two parameters which affects the fluid flow like I mentioned, you either understand the pressure drop or you understand the increase in velocity.

Now, this simulation talks about increase in velocity, the colour contour here was clearly used so that we understand where is the change in velocity and this plot here across the tracheal length. What was the change in pressure drop? An increase in velocity corresponds to a significant decrease in pressure drop, which means there is something abnormal happening with the organ here.

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## Multisegmental Complex Congenital Tracheal Stenosis

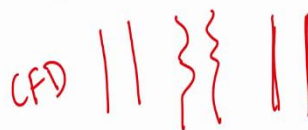


To evaluate the degree of stenosis, the stenosis ratio ( $r$ ) is described mathematically as follows:

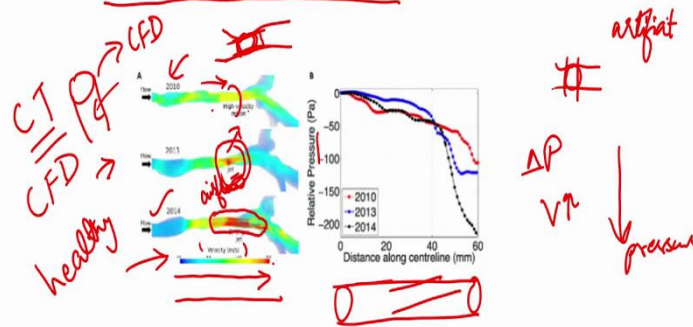
$$r = \frac{S_{TE} - S_{SP}}{S_{TE}} \times 100\%$$

Where:

$S_{TE}$  represents the cross-sectional area of the tracheal entrance  
 $S_{SP}$  denotes the minimal cross-sectional area of the stenosis.



# Tissue-Engineered Tracheal Replacement in a Child: A 4-Year Follow-Up Study

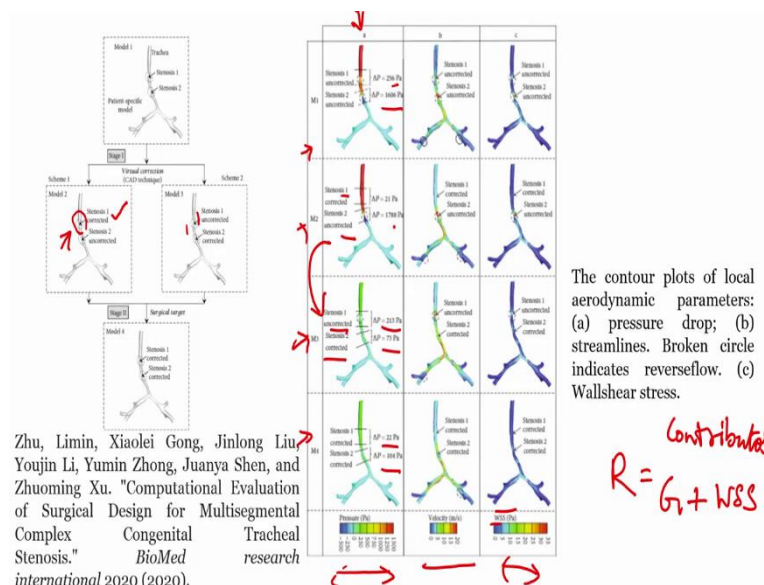


Hamilton, N.J., Kanani, M., Roebuck, D.J., Hewitt, R.J., Cetto, R., Culme-Seymour, E.J., Toll, E., Bates, A.J., Comerford, A.P., McLaren, C.A. and Butler, C.R., 2015. Tissue-engineered tracheal replacement in a child: A 4-year follow-up study. *American Journal of Transplantation*, 15(10), pp.2750-2757.

Another study, Multisegmental Complex Congenital Tracheal Stenosis. Congenital which means it is by birth, complex, that is what we studied here is just stenosis at one region. And I said the aetiologies are vast. Here, there is another study which talks about stenosis at two regions.

So, again, based on the geometry, CFD was being performed and then the challenge here was should you operate this region first or should you operate this region first, so that you bring back the trachea from two stenosis to a normal healthy segment. Why does this become challenging? When you, the next slide talks in detail about why this parameter multisegmental stenosis and which has to be operated first becomes important here.

(Refer Slide Time: 35:14)



Zhu, Limin, Xiaolei Gong, Jinlong Liu, Youjin Li, Yumin Zhong, Juanya Shen, and Zhuoming Xu. "Computational Evaluation of Surgical Design for Multisegmental Complex Congenital Tracheal Stenosis." *BioMed research international* 2020 (2020).

# Parameters that govern flow in vessel

- All blood vessels have certain lengths (L) and internal radii (r) through which blood flows when the pressure in the inlet and outlet are unequal ( $P_i$  and  $P_o$  respectively); there is a pressure difference ( $\Delta P$ ) between the vessel ends, which supplies the driving force for flow.
- Friction develops between moving blood and the stationary vessel walls, this fluid movement has a given resistance (vascular), which is the measure of how difficult it is to move blood through a vessel.
- Relative relationship between vascular flow, the pressure difference, and resistance (i.e., the basic flow equation):

$$Q = \frac{\Delta P}{R}$$

where Q = flow rate (volume/time),  $\Delta P$  = pressure difference (mm Hg), and R = resistance to flow (mm Hg  $\times$  time/volume).

*Handwritten notes: WSS, OR*

- It is known that the resistance to flow through a cylindrical tube or vessel depends on several factors (described by Poiseuille) including: 1) radius, 2) length, 3) viscosity of the fluid (blood), and 4) inherent resistance to flow, as follows:

$$R = \frac{8 L \eta}{\pi r^4}$$

where r = inside radius of the vessel, L = vessel length, and  $\eta$  = blood viscosity.

*Handwritten notes: Re, 1/r^4, Ha, 1/r^4*

- It is important to note that a small change in vessel radius will have a very large influence (**4th power**) on its resistance to flow; e.g., decreasing vessel diameter by 50% will increase its resistance to flow by approximately **16 fold**.

$$Q = \frac{\Delta P \pi r^4}{8 L \eta}$$

*Handwritten notes: CFD, simulation, 16 fold*

# Multisegmental Complex Congenital Tracheal Stenosis

To evaluate the degree of stenosis, the stenosis ratio (r) is described mathematically as follows:

$$r = \frac{S_{TE} - S_{SP}}{S_{TE}} \times 100\%$$

Where:  
 $S_{TE}$  represents the cross-sectional area of the tracheal entrance  
 $S_{SP}$  denotes the minimal cross-sectional area of the stenosis.

*Handwritten notes: CFD, 11, 11, 11*

As you can see, this was the initial model, they have performed a CAD and then the CFD to understand the fluid flow. What if you correct this first segment first and then they leave the second one uncorrected? What if it is the vice versa that is the first one is not corrected and the second one is corrected?

This is something critical they were two options that was left that is because they had to understand this because there is a change in pressure and if this segment is corrected assuming and this segment is not corrected, there is a significant drop in pressure here and the velocity rises, the sharp peak could collapse the entire airway.

So, again this correction procedure was being understood using a CFD simulation, here the colour contour here in a, talks about the pressure difference and they have considered four different cases. So, stenosis one is not corrected and both of them if they are not corrected that

is the ideal the original condition, what is the pressure that is observed and if either one of it is corrected, how is the pressure drop changing?

And this is the vice versa of this case scenario. This is the pressure drop which was obtained using the CFD. However, this may not be exactly close to the natural or something in C2 what might happen, but this can give a clear estimation as to what the surgeon can do and when both are corrected, how is the pressure drop changing?

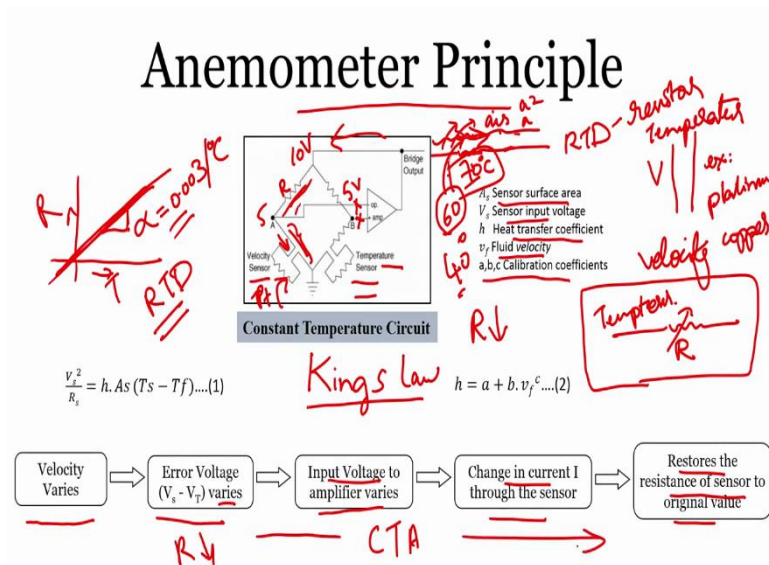
And here again, velocity has been analyzed and this here wall shear stress from equation one the resistance, but we had understood in our first slide, how R plays a significant role here the resistance to the fluid flow talks about the length, the channel radius and also the viscosity of the fluid flow. So, here what offers the resistance here, not just the change in geometry, but also the wall shear stress.

So, this is one such simulation. The residence is nothing but the change in geometry, two contributors here. One is because of the geometry, the other one is the wall shear stress. All of this simulation has been done just to understand the change in fluid flow through this channel, how we have already seen the Meyer cotton grading system. So, here the degree of stenosis can be calculated as the ratio of.

Now, this is the difference between the cross-section area at the entrance, assuming the entrance is normal and as we proceed, there is a reduction in area. So, this here can be calculated as STE and this area is SSP that is the cross-section area of the stenosis. So, this can tell you about what is this stenosis ratio.

And this is important so that you correlate this with the change in fluid flow through the channel. Now, these were the two studies based on computational fluid dynamics, just to estimate how the velocity or the pressure drop changes through this medium that is the trachea bronchial tree.

(Refer Slide Time: 39:14)



However, there is another method to quantify, how the fluid flow the velocity through the channel can be determined. This we call it as an anemometer principle assuming we have an RTD, that is RTD here is a resistor that changes with temperature and examples for these metals such as platinum, copper can be used as resistors where the resistance can change because of the change in temperature.

Now, so how can we integrate this mechanism to understand the fluid velocity inside a channel. Now, assume this is your sensor, the Platinum-based sensor again why I chose platinum, there is something called as the temperature coefficient of resistance R versus T. So, how is your resistance changing with increase in temperature, if this is linear and you have this coefficient here alpha that is the temperature coefficient is excellent for platinum that is it is around 0.003 ohms per change in resistance for every per degree rise in temperature and it is different for copper and other materials.

So, there are different metals and you can again look for what are the different types of RTDs and what is their temperature coefficient and what you need to prefer is the one which has linear curve. Now, assuming one such RTD is here, in a bridge, in a Wheatstone bridge here, this is your resistor and here is a temperature compensation. We will get to the details about why you need to have a compensation sensor here.

Now, what happens is, so here the whole anemometer principle is based on Kings law, the clear derivation is in the next slide. So, I am just showing how the sensor can be integrated in a bridge circuit like this and you can force it to operate at constant temperature. So, assume this is my sensor and I am driving the sensor at 70 degrees Celsius. But when the fluid flows through



this heater, what happens is because of convection, the heat is taken away from the heater to the fluid here, assuming air is a fluid here.

The convective heat transfer from the heater to the air or the medium because of the fluid flowing above it what happens is it tends to decrease the temperature that is it drops from 70 to say 60 and if you drive the fluid at even higher speeds from what it is in case a and you increase it to a higher velocity that is a square.

So, when the velocity increases again because of the increase in convection, the temperature might drop as low as 40. These are not the exact numbers but I am just telling you how they are related to the fluid flow with the increase in velocity, how the temperature drops. Now, with an increase fluid flow, the temperature is dropping.

However, when you have it in a loop like this, when you put it integrate into a bridge structure, it is forced to operate at constant temperature that is any difference, because say you are having an input voltage of 10 volts and at a given resistance there is 5 volts across each of this arm. But because the resistance decreases, there is a decrease in voltage the potential drop here decreases.

However, this year is always compared to a reference 5 volt and a decrease will force fully have a feedback such that the additional voltage is pumped in and the increase in current because of the pumping of voltage here is the higher I or the current flow through this is going to bring it back working to the 70 degrees Celsius.

Again, this may be a little complicated to understand at one instance, but then it is very simple R drops because of the convective heat transfer, R drops and then what happens is here the velocity, the fluid velocity increases. Error voltage, error voltage rise because the RTD's R is dropping and that is when the differential voltage increases and to balance it the input voltage to the amplifier varies and this is compensated by an increase in current through this segment.

And now, because of the high inrush of current, you are restoring the resistance of the sensor to its original value. Now, this whole thing is called a constant temperature anemometer. Now, based on this principle, how can you determine the velocity of the fluid flowing through a channel? Several parameters your sensor area, what is the input voltage? What is the heat transfer coefficient fluid velocity and then you have a few calibration coefficients? Now, how are all these interrelated we will see in the next slide.

(Refer Slide Time: 45:45)



The power driven into the sensor is equal to the power loss due to convective heat transfer

$$\frac{V_h^2}{R_h} = h A_h (T_h - T_f)$$

where  $V_h$  is the voltage across the microheater with resistance  $R_h$  and surface area  $A_h$ ,  $h$  is the thermal coefficient,  $T_h$  and  $T_f$  are the temperature of the microheater and fluid, respectively

From King's law, the equation governing thermal coefficient ( $h$ ) and fluid velocity ( $V_f$ ) is

$$h = a + b V_f^c$$

where  $a$ ,  $b$  and  $c$ , constants obtained from calibration experiments.

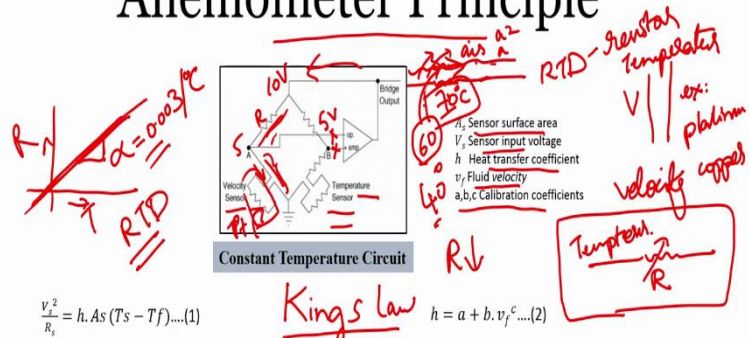
For a balanced Wheatstone's bridge with driving voltage  $V_d$  and resistance  $R_1$  connected in series to  $R_h$

$$V_h = V_d R_h / (R_1 + R_h)$$

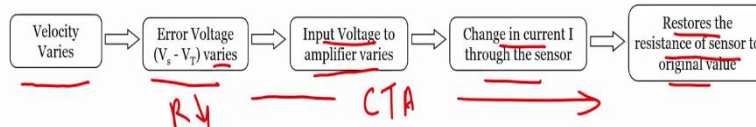
From the above equations, fluid velocity ( $V_f$ ) can be determined using driving voltage  $V_d$  as shown below,

$$h = \frac{V_h^2}{R_h A_h (T_h - T_f)}$$

## Anemometer Principle



$$\frac{V_h^2}{R_h} = h \cdot A_h (T_h - T_f) \dots (1)$$



I told you about this mechanism. Once this is understood, let us go step by step. Now, the power that is driven into the sensor is equal to the power loss due to convective heat transfer. Now, there is convection the fluid flow here, the fluid is flowing at a velocity we say  $v_f$  is a fluid velocity and this is your sensor which is having a cross-section area resistance  $R_h$  and the voltage across this  $V_h$  is a voltage across the heater and  $h$  is the heat transfer coefficient,  $A$  is a cross-section area of the sensor which is here.

$T_h$ , which is the temperature of the heater here and this is the temperature of the fluid. In our case, I said we are driving this at 70 degrees Celsius, and assuming this is a normal healthy breathing condition the temperature would be around 36 or 37 degrees Celsius. So, this is the fluid temperature the heater temperature, the coefficient here and this is a cross-section area  $V_h$  here is the voltage across the heater and this is your  $R_h$ .

Same parameters which has been described here. As I mentioned we will be using something called as Kings law and from here the heat transfer coefficient  $h = a + bv_f^c$ ,  $v_f$  here is a fluid flow and  $c$  what are these  $a$ ,  $b$ , and  $c$  constants? How do you get these values?

So, you have to perform experiments considering this is a channel volumetric flow was introduced to you in the beginning, say you know the volumetric flow of the fluid, you know it by using another, you are using a pitot tube or their multiple mechanisms several mechanisms can be adopted. So, that you know what is the volumetric flow of the fluid which you are pumping through this channel.

Now, you drive the fluid through this channel and you have this your sensor here or the heater here through this channel. After multiple say you perform 10 such experiments you will find the relationship between the voltage, the sensor voltage and the volumetric flow  $Q$ . Now, from these plots, multiple plots, there is a relation  $Q = a + bV^c$ . From these multiple experiments you can get these constants, these are calibration constants.

So, when you try to fit these two by knowing the, for the known volumetric flow, what is the change in voltage. So, for this, you have this relation  $Q = a + bV^n$  or it can be called as  $c$ . Now, from all of this, you have  $a$ ,  $b$ , and  $c$ . Once you have these constants, we know that from the bridge circuit the voltage that is across the heater.

Now, what you are pumping in is called as the driving voltage  $V_d$ . So, how is  $V_d$  related to the voltage across the heater  $V_h$ ,  $V_h$  is equal to from the voltage divider circuit you can come to a conclusion with how  $V_h$  can be written. So,  $V_h$  is  $V_d$  our residence of the heater divided by  $R_1$ , assuming this is  $R_1$  here the resistance of the other branch divided by  $R_1 + R_h$ , and then how do you substitute for this in this and then you have the heat transfer coefficient.

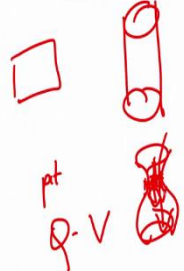
We want to eliminate this parameter  $h$  because it remains unknown and it again depends on the type of fluid. So, eliminating this becomes easy for calculation. This is again from the first equation here. We know  $h$  in terms of the heater voltage, but how can you substitute  $V_h$  in terms of driving voltage because we know the  $V_d$  here from this output. So, again eliminating  $V_h$  from this equation, we substitute  $V_h$  as this in terms of  $V_d$  in this equation.

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# Velocity vs Driving Voltage

$$h = \frac{V_d^2 R_h}{A_h (T_h - T_f) (R_1 + R_h)}$$

$$V_f = \left\{ \frac{1}{b} [h - a] \right\}^{\frac{1}{c}}$$

$$V_f = \left\{ \frac{1}{b} \left[ \frac{V_d^2 R_h}{A_h (T_h - T_f) (R_1 + R_h)} - a \right] \right\}^{\frac{1}{c}}$$


And so, now you have  $h$  and this  $h$  is replaced in this equation here fluid flow  $V_f$  is and how did we get this  $\left(\frac{1}{V_f} - a\right)^{\frac{1}{c}}$  from here. We need fluid flow and we have  $\left(\frac{h-a}{b}\right)^{\frac{1}{c}}$  and we want to eliminate  $h$  we already know the heat transfer coefficient from here substituting all of this we have this fluid flow relation in terms of the heater resistance the driving voltage, the sensor cross-section area, the temperature of the heater, the temperature of the fluid, the resistance across the bridge.

And these calibration constants can be determined from an experiment in prior either using a pitot tube or any other anemometer principle, where the volumetric flow, so that you know  $Q$  and  $V$  and from there you get the values of  $a$ ,  $b$ , and  $c$ . So, this was about how you can derive the velocity of a fluid flowing through a channel and if the channel cross-section area changes, how can you determine the velocity of the fluid at this point without even knowing the geometrical parameters, because it becomes difficult to quantify, what is the reduction in this area.

So, when you have a sensor that can be introduced and you already know the parameters of the sensor that is the cross-section area of the sensor, the resistance all of this would be the signal conditioning circuit outside. So, all of these parameters can be known and the driving voltage of this changes only because of the change in fluid flow and this way, it becomes easier to quantify the velocity of the fluid in say to just by having a sensor of this kind. So, this was a mathematical model to understand how the fluid flow can be derived using MEMS space sensor. Thank you.