What does biofilm have to do with chronic disease, persistent wounds and recurrent infections?

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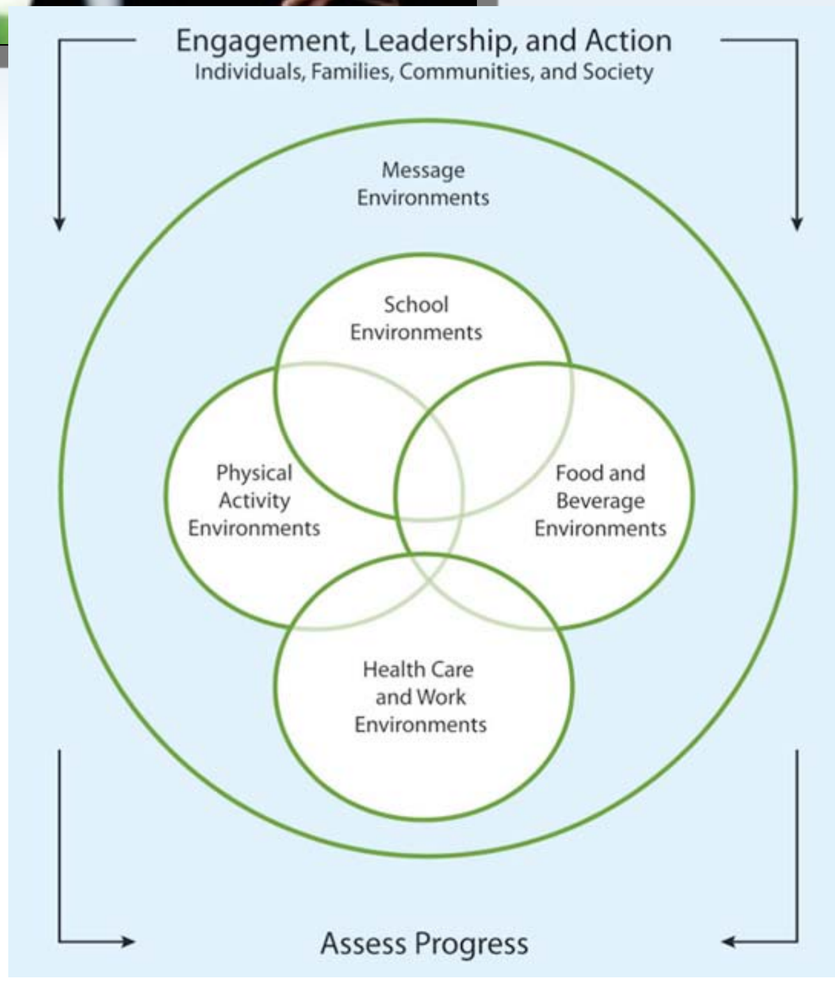
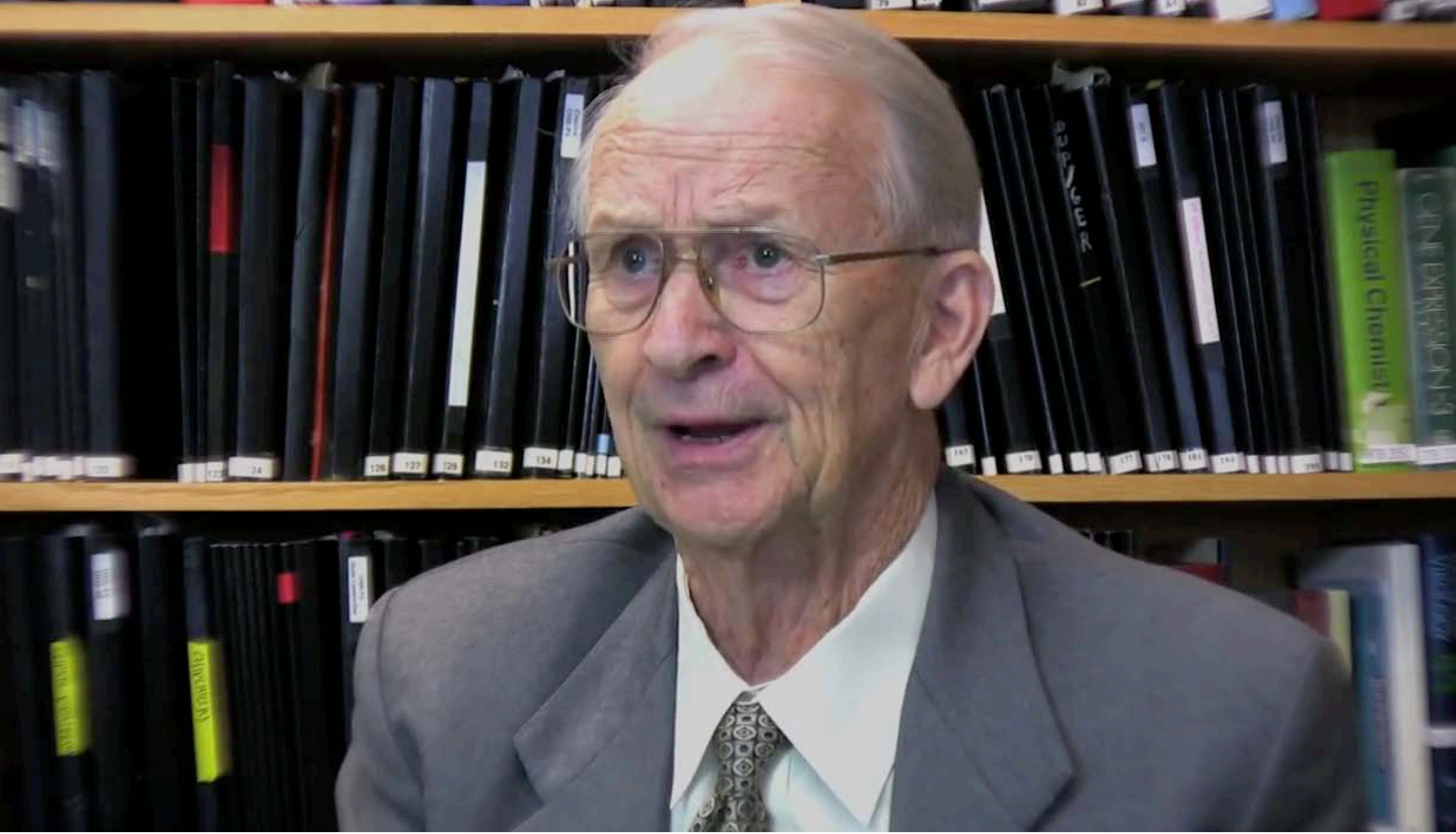
Conversation starters!

oral health to general health

- ★ get the facts
- ★ develop positive energy
- ★ create a legitimate spin
- ★ focus on health benefits
- ★ discuss savings - money, time, comfort
- ★ offer reasonable alternatives
- ★ coaching not scolding



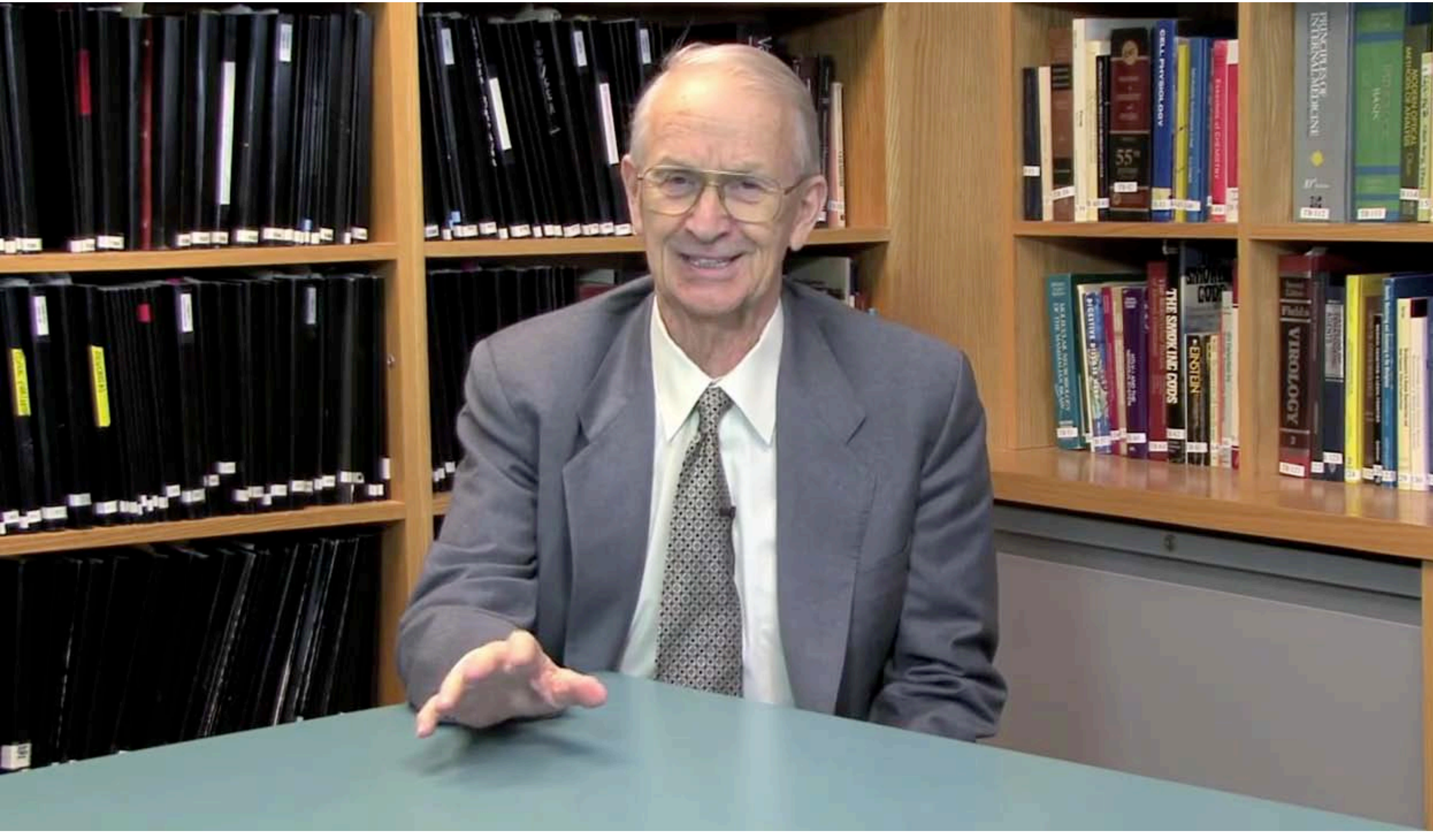
iom.edu/Reports/2012/Accelerating-Progress-in-Obesity-Prevention/Report-Brief.aspx May 12, 2012



Dr. Bill Costerton - The "Father" of Biofims

www.youtube.com/watch?v=M_DWNFFgHbE

Biofilm basics - growing, thriving, surviving



Dr. Bill Costerton - The "Father" of Biofilms www.youtube.com/watch?v=M_DWNFFgHbE

Annu Rev Microbiol. 1995;49:711-45.

Microbial biofilms.

Costerton JW, Lewandowski Z, Caldwell DE, Korber DR, Lappin-Scott HM.

Source

Center for Biofilm Engineering, Montana State University, Bozeman 59717, USA.

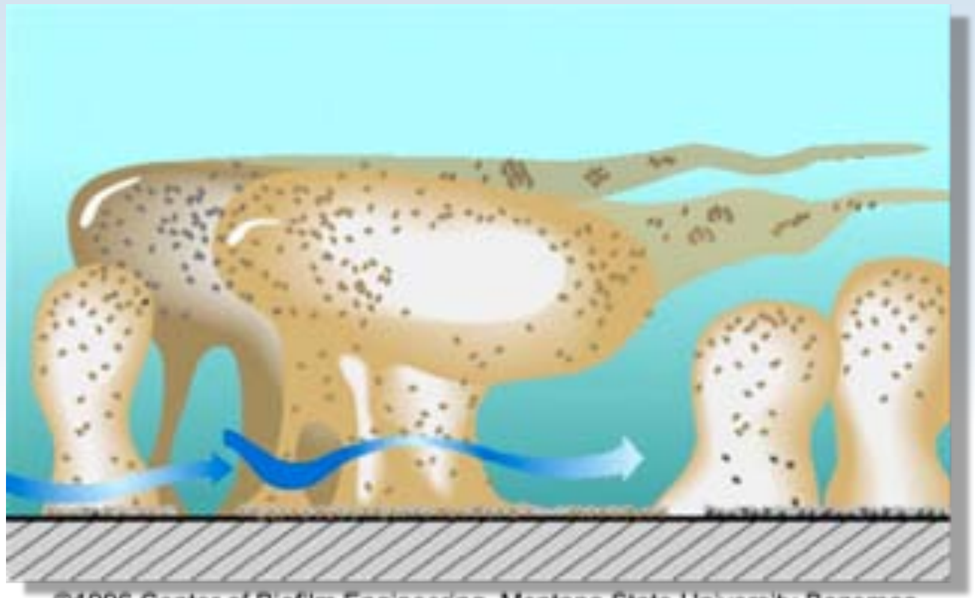
Abstract

Direct observations have clearly shown that biofilm bacteria predominate, numerically and metabolically, in virtually all nutrient-sufficient ecosystems. Therefore, these sessile organisms predominate in most of the environmental, industrial, and medical problems and processes of interest to microbiologists. If biofilm bacteria were simply planktonic cells that had adhered to a surface, this revelation would be unimportant, but they are demonstrably and profoundly different. We first noted that biofilm cells are at least 500 times more resistant to antibacterial agents. Now we have discovered that adhesion triggers the expression of a sigma factor that derepresses a large number of genes so that biofilm cells are clearly phenotypically distinct from their planktonic counterparts. Each biofilm bacterium lives in a customized microniche in a complex microbial community that has primitive homeostasis, a primitive circulatory system, and metabolic cooperativity, and each of these sessile cells reacts to its special environment so that it differs fundamentally from a planktonic cell of the same species.

What is a "Biofilm"?

A 3-Dimensional "community" of microbes attached to a surface

- Fluid interaction
- Channels / pores
- Complex structure



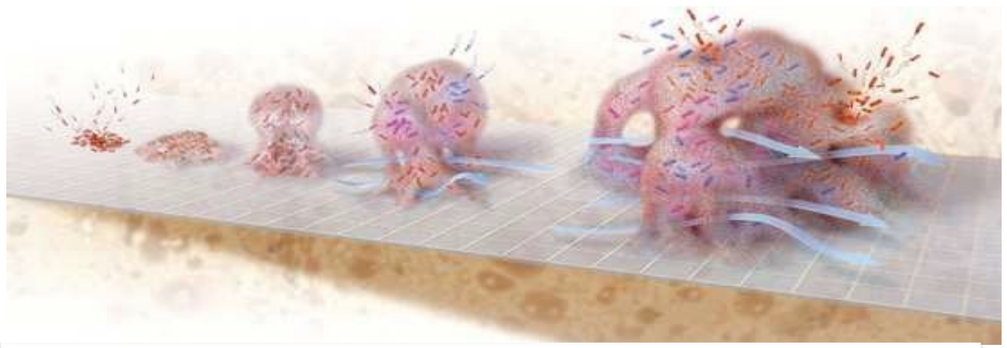
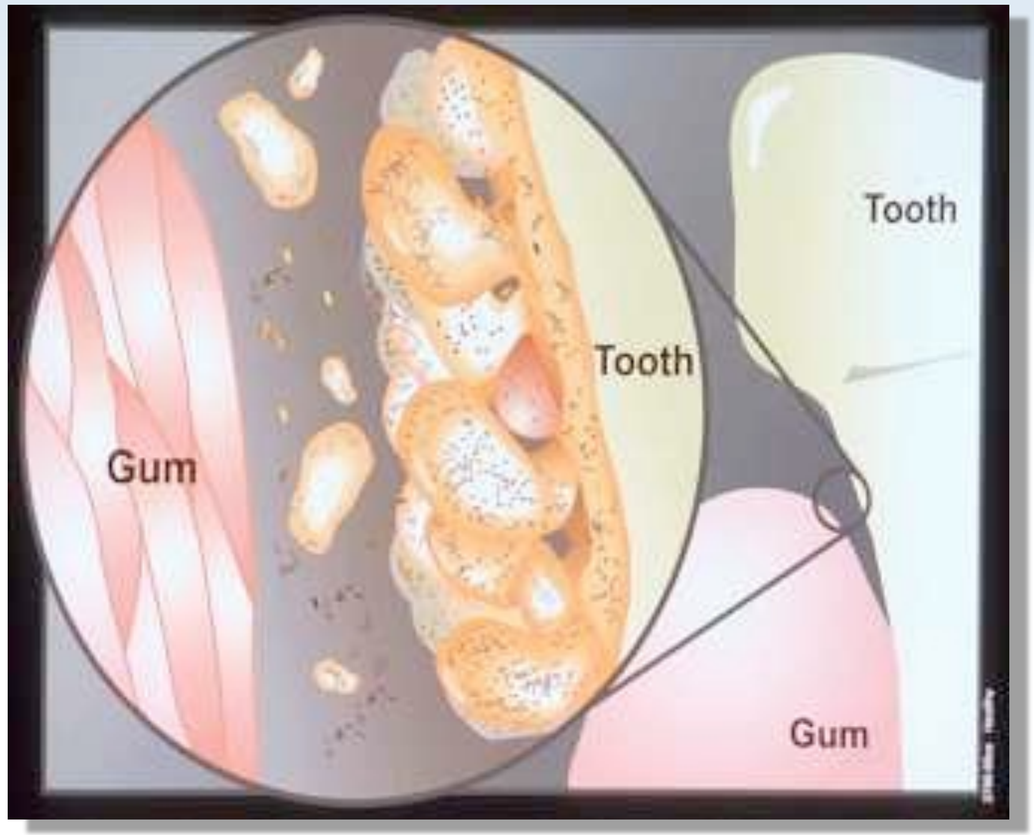


Illustration by Keith Kasnot,: *Scientific American*, July 2001

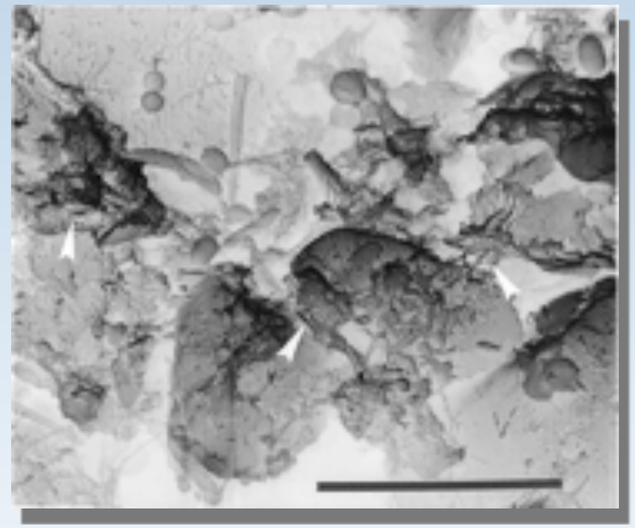
Plaque biofilms

- Complex biofilm
- Hundreds of species
- Adherent to tooth
- Irritates tissue
- Grows / Matures / Calcifies
- Influenced by fluid forces



Emerging Trends in Oral Care - Philips Oral Healthcare Symposium 2003

Biofilm facts



- ✓ millions of interacting micro-organisms
- ✓ bacteria, spirochetes, protozoa, fungi, viruses
- ✓ properties not seen in isolated micro-organisms
- ✓ rapid regeneration via signaling
- ✓ *tenacious - Difficult to remove mechanically*
- ✓ biofilms - higher adhesion to saliva-coated enamel than planktonic

The biofilm primer. J.W. Costerton 2007

Maddi A, Scannapieco FA. Oral biofilms, oral and periodontal infections, and systemic disease. Am J Dent. 2013 Oct;26(5):249-54.

Wessel SW, Chen Y, et al. forces and composition of planktonic and adhering oral microbiomes. J Dent Res. 2014 Jan;93(1):84-8.

Forming a biofilm

✓initiated by planktonic bacteria or fragment

✓attaches to appropriate surface (wound, implant)

✓divide - form micro-colonies

✓critical density - release pheromones

✓quorum sensing

✓altered environment - phenotypic alterations in microbes

Biofilms in wounds:management strategies. Rhodes DD, Wolcott RD, Percival SL. J Wound Care. November 2008.17(11).

Biofilm formation

- ✓ multi species communities
- ✓ EPS - extracellular polysaccharide - slime
- ✓ EPS - polysaccharides, proteins, nucleic acids
- ✓ 80% of the biofilm is EPS
- ✓ 20% of biofilm - microbes encased in EPS matrix
- ✓ h*eterogenous, dynamic and recalcitrant to antimicrobials and immune system*

Biofilms in wounds:management strategies. Rhodes DD, Wolcott RD, Percival SL. J Wound Care. November 2008.17(11).

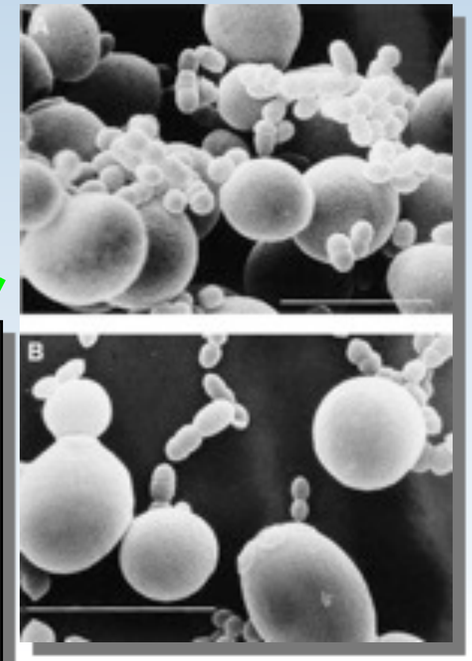
Mixed biofilm community development -

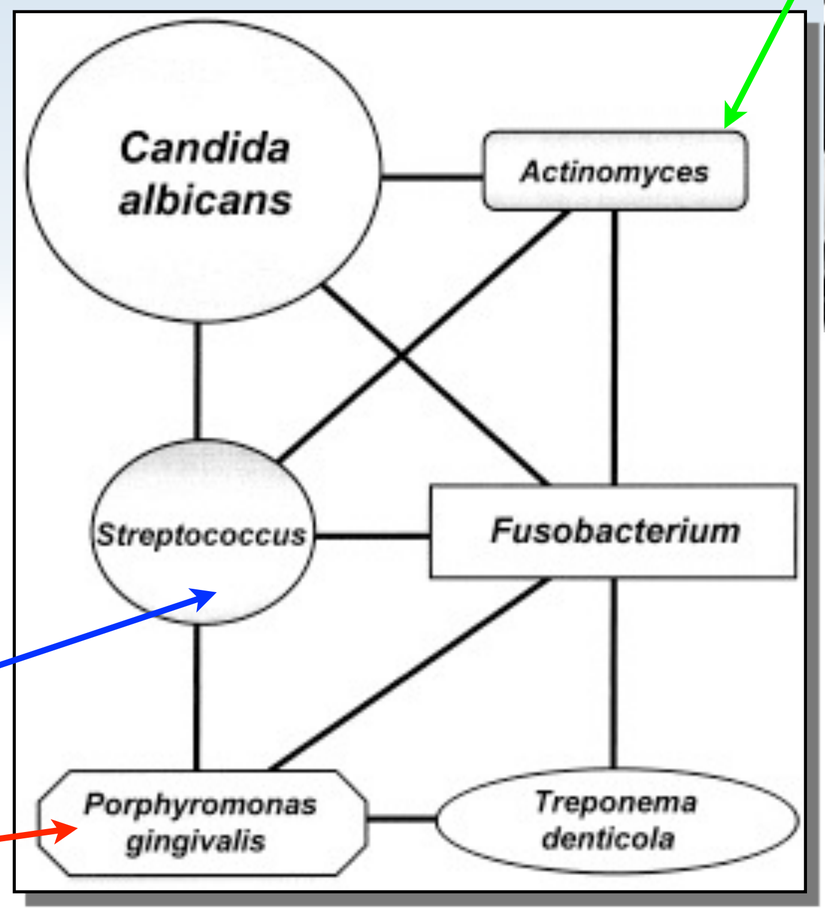
Candida albicans

(opportunistic fungal pathogen)

- coaggregation
- coadhesion
- modified by pH, nutrient supply salivary factors

✶Creates a highly acidic pH





Jenkinson HF and Douglas LJ. Interactions between Candida Species and Bacteria in Mixed Infections. www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=pmd&part=A2773#A Accessed 7/25/2009

Falsetta ML1, Klein MI, Symbiotic relationship between Streptococcus mutans and Candida albicans synergizes virulence of plaque biofilms in vivo. Infect Immun. 2014 May;82(5):1968-81.

Bonnie Bassler: The secret, social lives of bacteria 4/8/2009 http://www.youtube.com/watch?v=TVfmUfr8VPA

Biofilm facts / characteristics

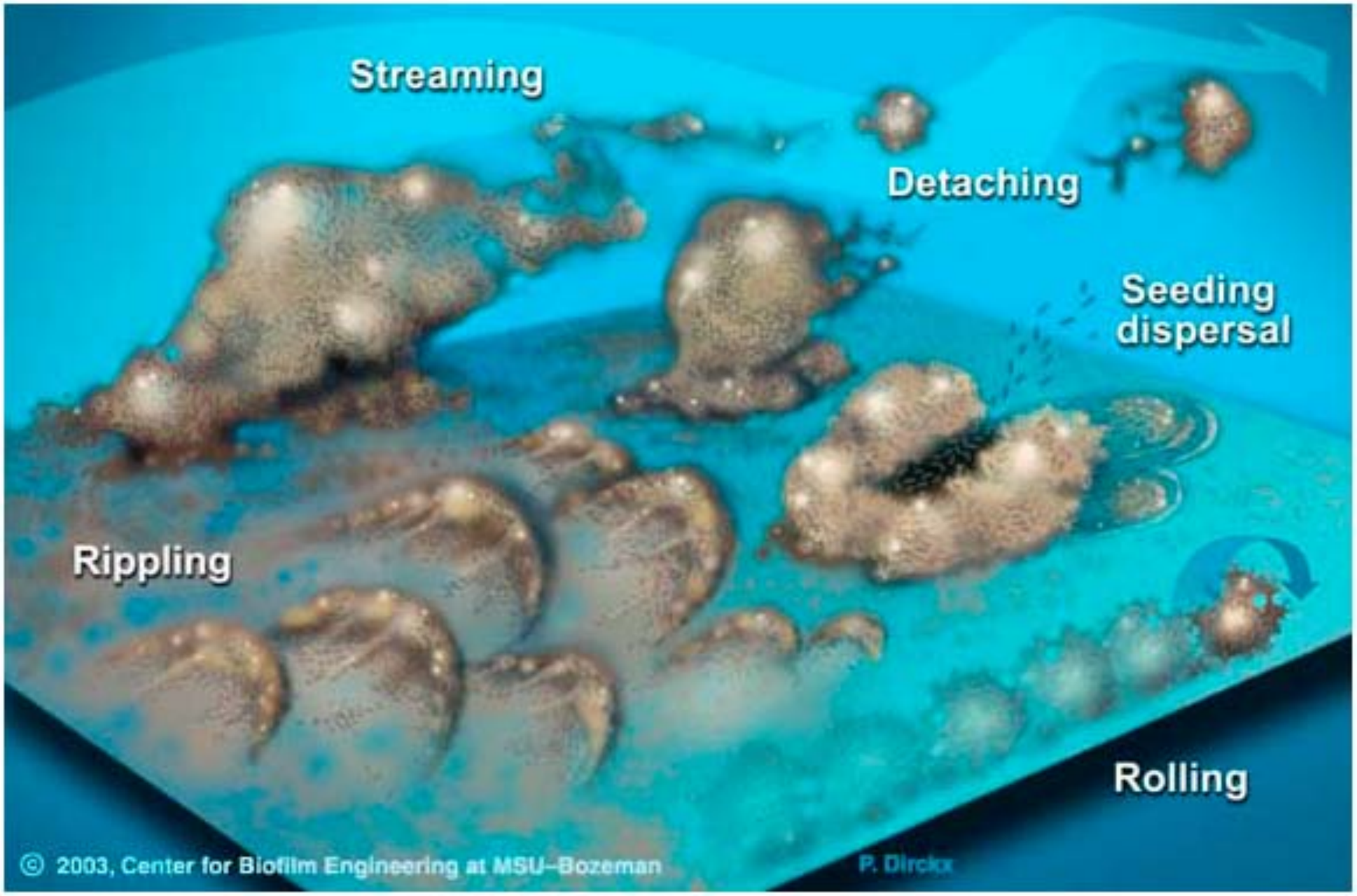
✓Plays a role in otitis media, bacterial endocarditis, cystic fibrosis and Legionnaire's disease, chronic sinusitis, osteomyelitis, catheter infections

✓**80% infectious diseases**

✓**99% of bacteria in nature - stable, persistent biofilms**

http://www.erc.montana.edu/biofilmbook/MODULE_01/Mod01_Blue/Mod01_S04_Blue.htm Image accessed 7/25/09

Biofilms in wounds:management strategies. Rhodes DD, Wolcott RD, Percival SL. J Wound Care. November 2008.17(11).



All materials have certain properties of elastic solids and viscous fluids. Biofilms appear to show aspects of both solids and liquids—much like slug slime—and fall into a category called "viscoelastic." However, as biofilms collect sediment, or become scaled with rust or calcium deposits, they become less fluid and more like a brittle solid.

http://www.erc.montana.edu/biofilmbook/MODULE_01/Mod01_Blue/Mod01_S04_Blue.htm
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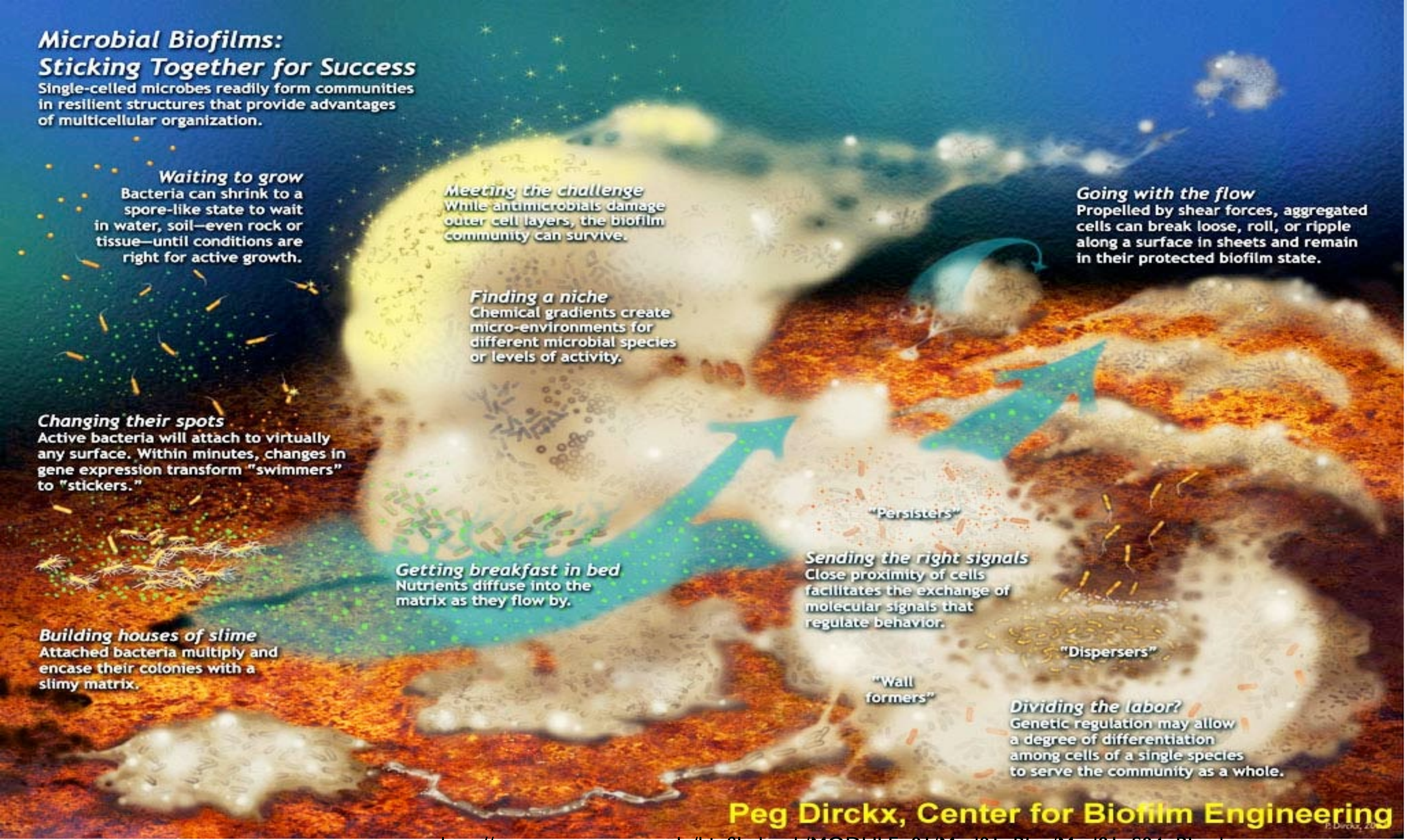

http://www.erc.montana.edu/biofilmbook/MODULE_01/Mod01_Blue/Mod01_S04_Blue.htm
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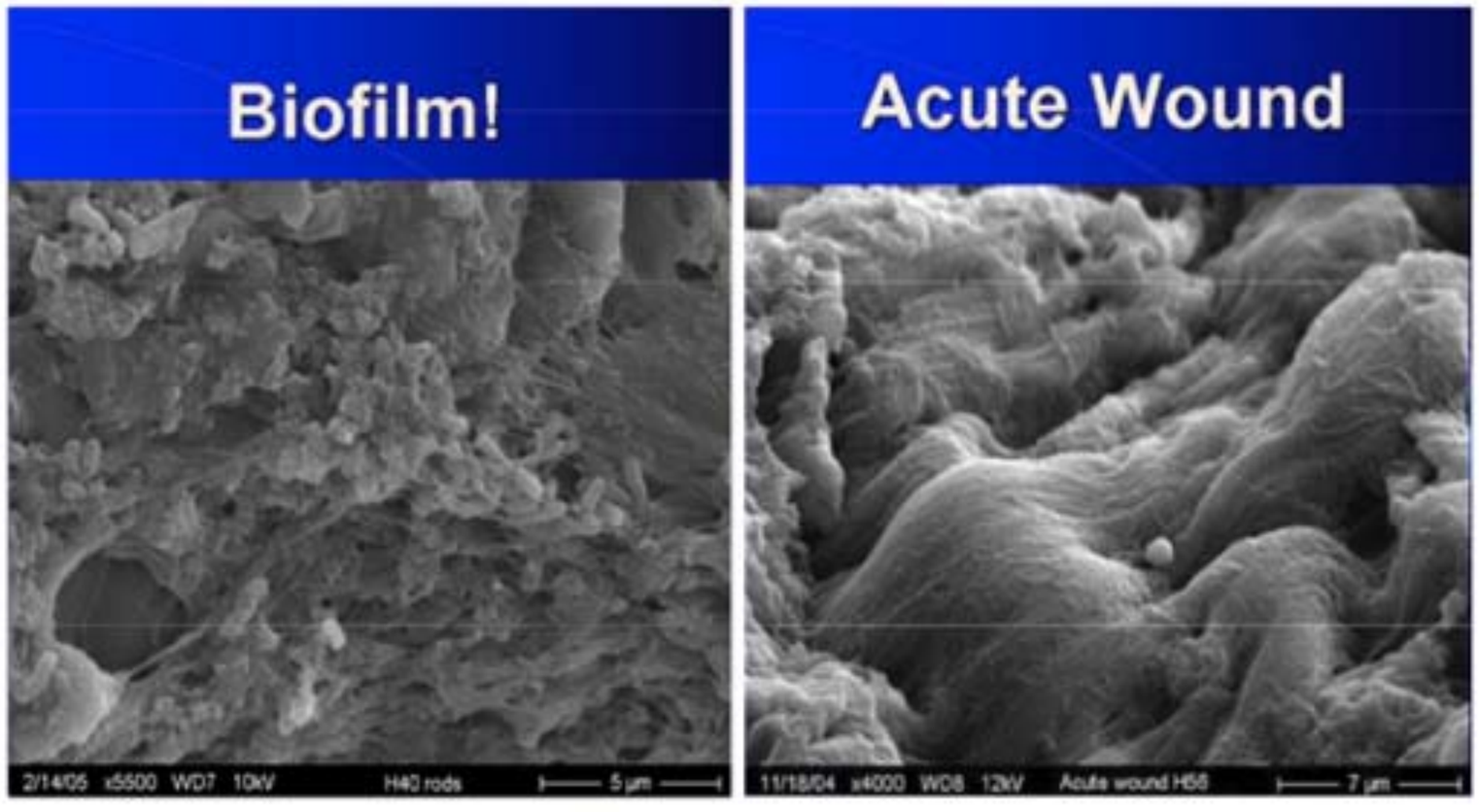
Understanding the trouble makers - microbial defenses that make it hard to treat disease

Biofilms Identified in 60% of Biopsies of Chronic Wounds but in Only 6% of Acute Wounds



Garth James et al, Wound Repair Regen, 2008

Photographs by Randy Wolcott

http://www.npuap.org/NPUAP%20Biofilms%202009%20Schultz%20mod%202%20compressed-1.pdf

Bertesteanu S, Triaridis S, et al. Polymicrobial wound infections: pathophysiology and current therapeutic approaches. Int J Pharm. 2014 Mar 25;463(2):119-26. .

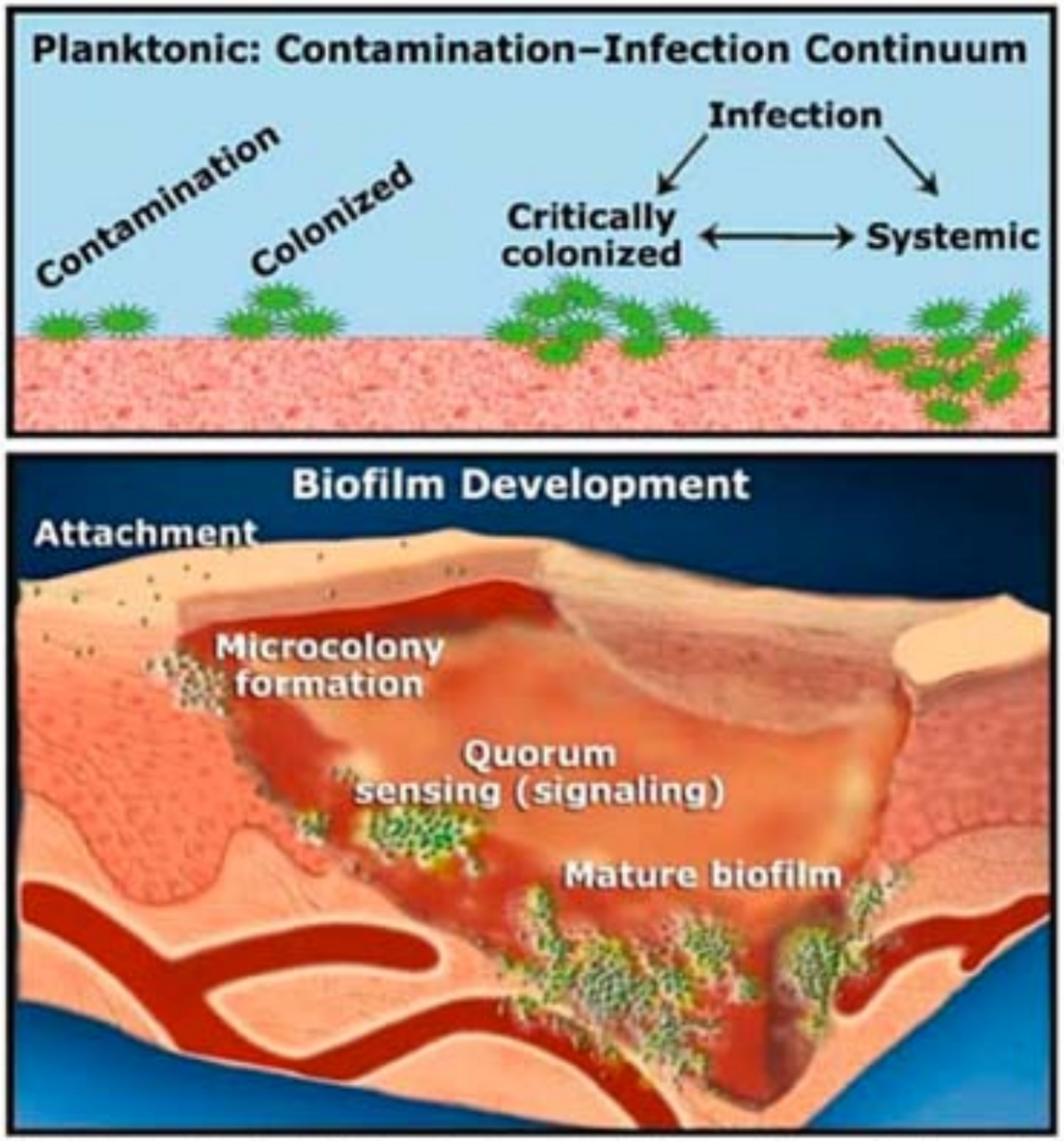
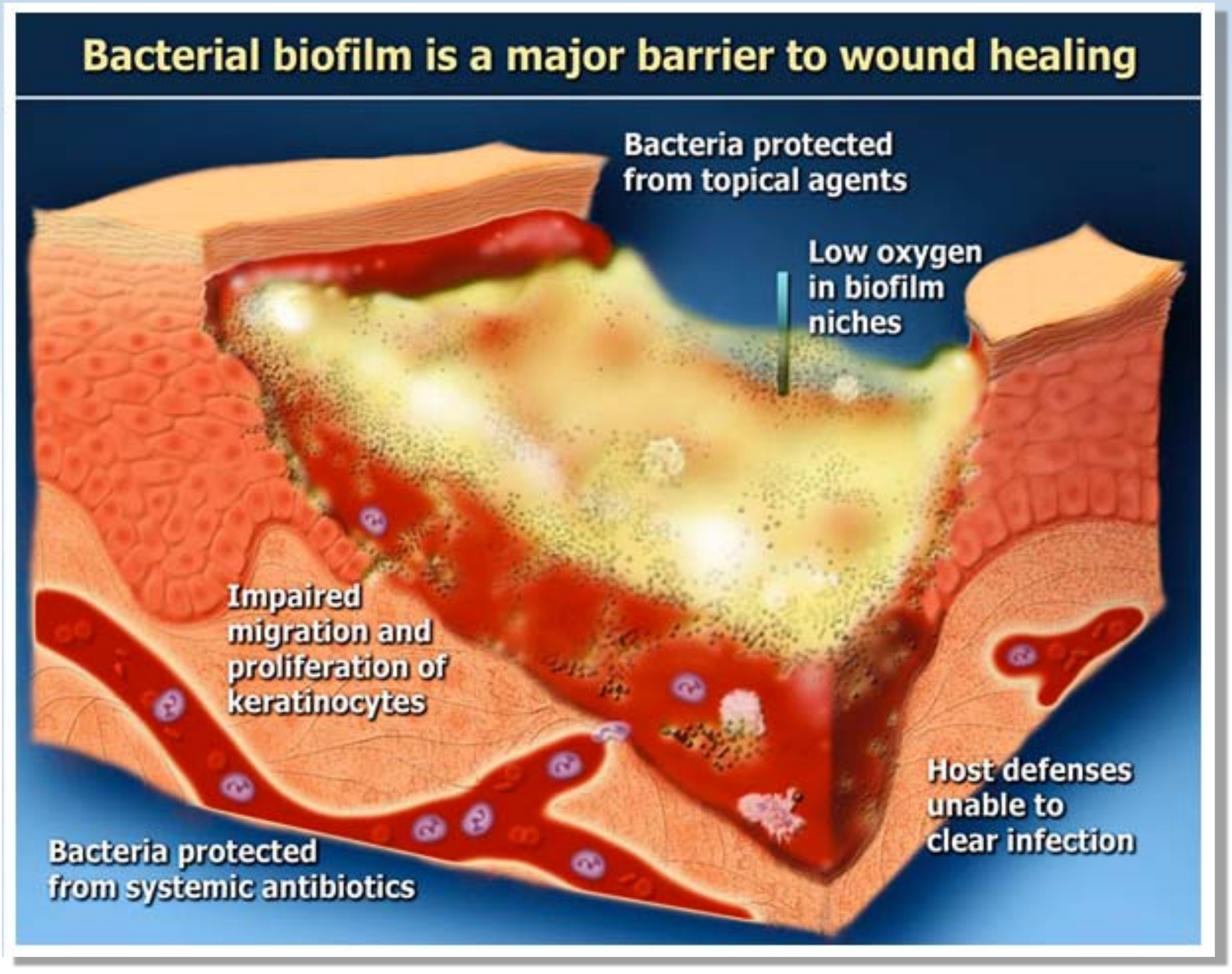


Fig. 1 A planktonic explanation for surface bacteria involved in wounds is not scientifically valid. Planktonic bacteria quickly form into microcolonies and then mature into formidable wound biofilm that evades host defenses and impairs wound healing

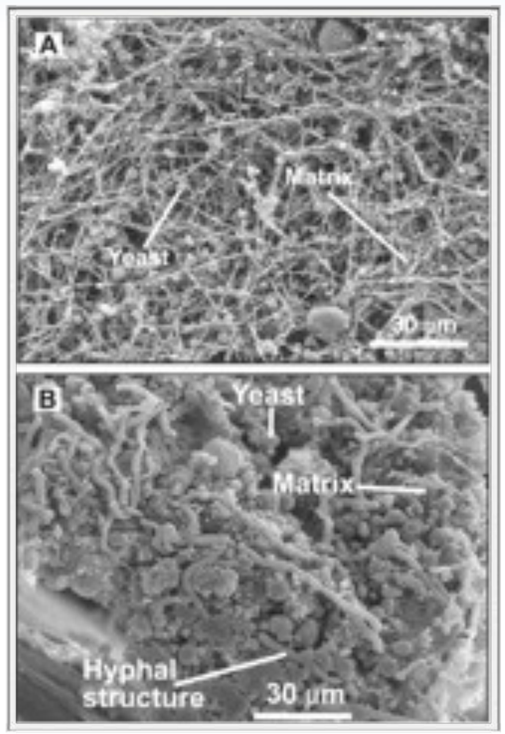
Clinical wound healing using signal inhibitors - Randall Walkout, MD in
2008 - Control of Biofilm Infections by Signal Manipulation - Naomi Balaban, J. William Costerton



http://www.erc.montana.edu/biofilmbook/MODULE_07/Mod07_S03_Blue.htm Accessed 7/25/09

Biofilm layers

- ★ surface microbes - most active -like planktonic
- ★ surface most susceptible to antimicrobials/host defenses
- ★ deeper layers sheltered
- ★ less metabolically active
- ★ more resistant to antimicrobial therapies
- ★ can reconstitute biofilm (persisters)



Biofilms in wounds:management strategies. Rhodes DD, Wolcott RD, Percival SL. J Wound Care. November 2008.17(11).

pH and oxygen levels vary in biofilms

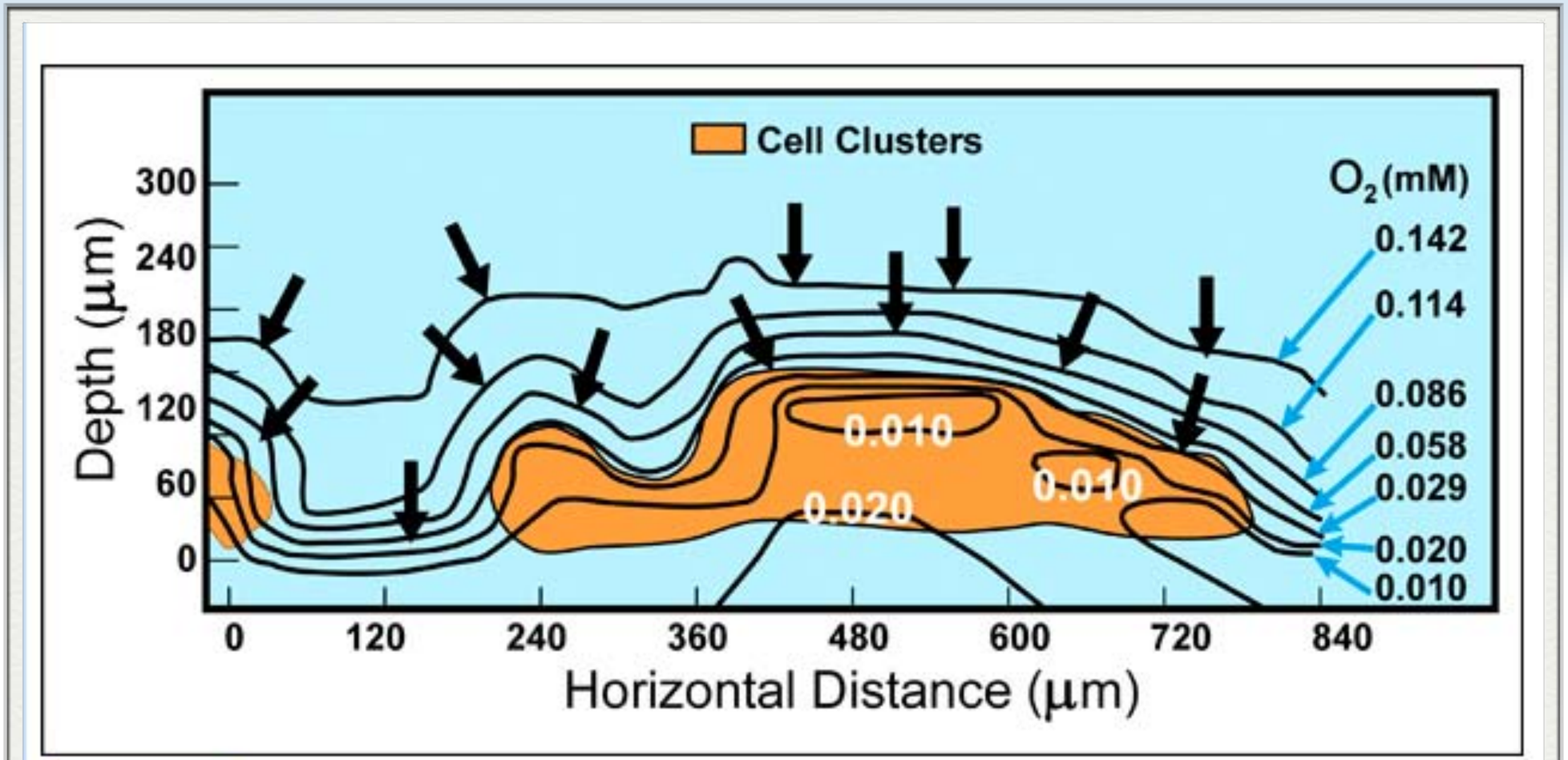
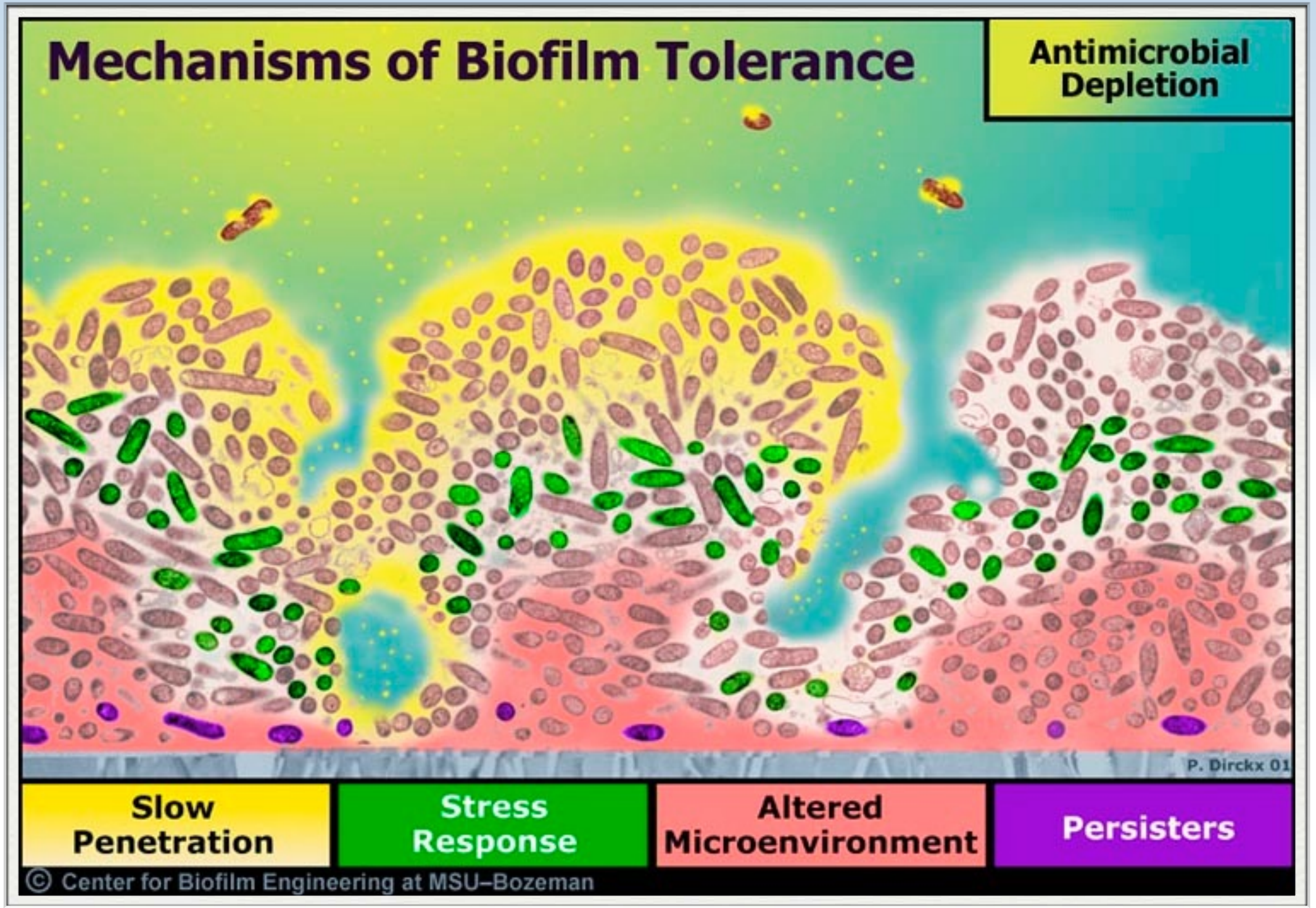


Figure 7-XX. Oxygen concentration contours mapped around a three-species biofilm cell cluster using microelectrode technology. The substratum on which the biofilm grew was at the bottom and the aqueous medium at the top. Black arrows indicate the direction of the local flux of oxygen.

http://www.cbe.montana.edu/biofilmbook/MODULE_07/Mod07_S01-2_Blue.htm

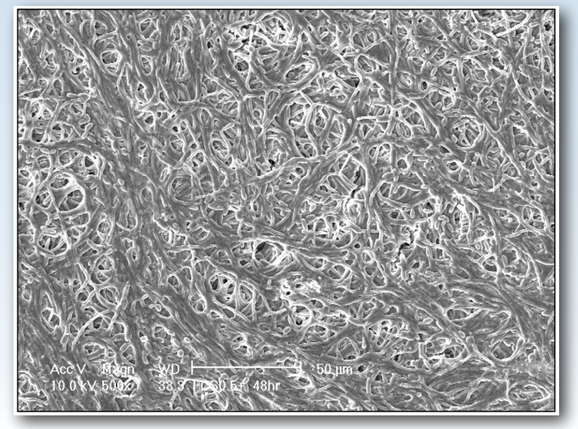


http://www.erc.montana.edu/biofilmbook/MODULE_01/Mod01_Blue/Mod01_S04_Blue.htm Accessed 7/25/09

Biofilm survival - making inflammation a lifestyle

Biofilm – strategies for survival

- attach within minutes
- 2-4 hours - strongly attached micro-colonies
- 6-12 hours - develop initial EPS
- increasingly tolerant to antibiotics, antiseptics, disinfectants
- 2-4 days - fully mature biofilm
- now highly resistant to biocides / shedding planktonic bacteria
- rapidly recover from mechanical disruption
- reform mature biofilms within 24 hours



48 hour old Candida Albicans on denture acrylic

Phillips PL, Wolcott RD, Fletcher j, Schul GS. Biofilms made easy. May 2010. Vol 1. Issue 3. woundsinternational.com

Periodontitis

- requires susceptible host
- dysbiotic microbial communities
- inflammo-phillic
- inflammation-provides nutrients
- fosters growth of dysbiotic communities
- selects for certain pathogens
- dysbiosis and inflamation support each other

control of inflammation is critical

Inflammation

Hajishengallis G. Immunomicrobial pathogenesis of periodontitis: keystones, pathobionts, and host response. Immunol. 2014 Jan;35(1):3-11.

Hajishengallis G. The inflammophilic character of the periodontitis-associated microbiota.Mol Oral Microbiol. 2014 Jun 26.

Dry mouth - a biofilm paradise

Salivary dysfunction – etiology and contributing factors

- dehydration
- stress
- smoking
- systemic disease
- recreational drugs
- chronic renal failure
- autoimmune disorders
- asthma
- mouth breathing
- during exercise
- sleep apnea
- C-Pap machines
- salivary gland pathology
- radiation treatment
- hormone imbalance
- laxative/diuretic abuse
- pharmaceutical and OTC medications (over 1,800 meds)

Mese H1, Matsuo R. Salivary secretion, taste and hyposalivation. J Oral Rehabil. 2007 Oct;34(10):711-23.

Insufficient saliva –
Oral Desert Storm

- Changes can be subtle
- Often unnoticed until 50% decrease
- Sets the stage for demineralization
- pH decreases

Takahashi N, Nyvad B.Caries ecology revisited: Microbial dynamics and the caries process. Caries Res. 2008;42(6):409-18.

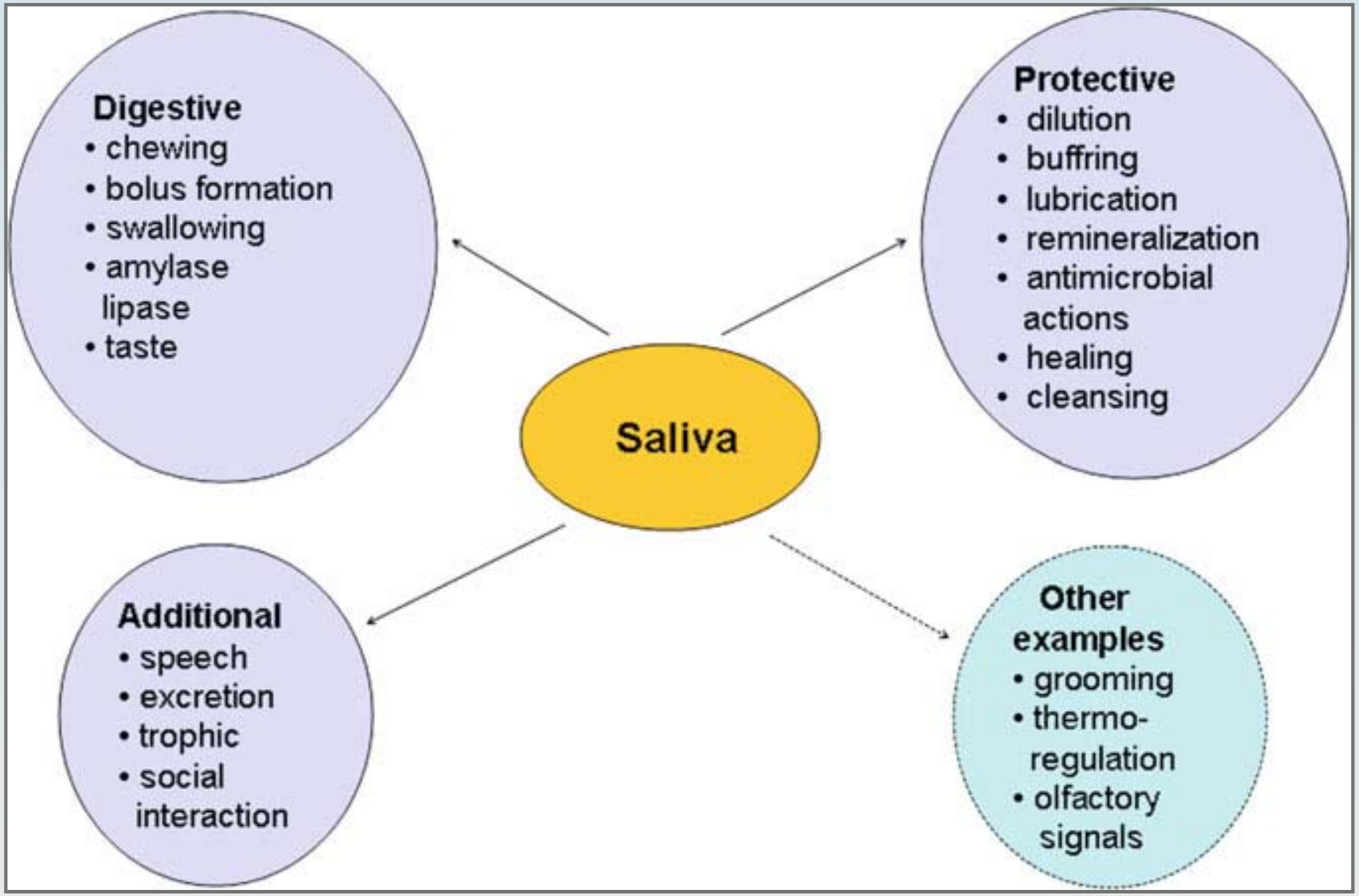
Saliva and the Control of Its Secretion. Ekberg (ed.), Dysphagia, Medical Radiology. Diagnostic Imaging, Springer-Verlag Berlin Heidelberg 2012
Graham I, Mount WH. (2005). Preservation and restoration of tooth structure. 2nd Edition. Queensland, Australia: Knowledge Books and Software.

Insufficient saliva –
Oral Desert Storm

- acidogenic bacteria numbers increase
- buffering capacity decreases
- aciduric bacteria thrive
- plaque biofilm becomes very sticky

Saliva and the Control of Its Secretion. Ekberg (ed.), Dysphagia, Medical Radiology. Diagnostic Imaging, Springer-Verlag Berlin Heidelberg 2012
Graham I, Mount WH. (2005). Preservation and restoration of tooth structure. 2nd Edition. Queensland, Australia: Knowledge Books and Software.

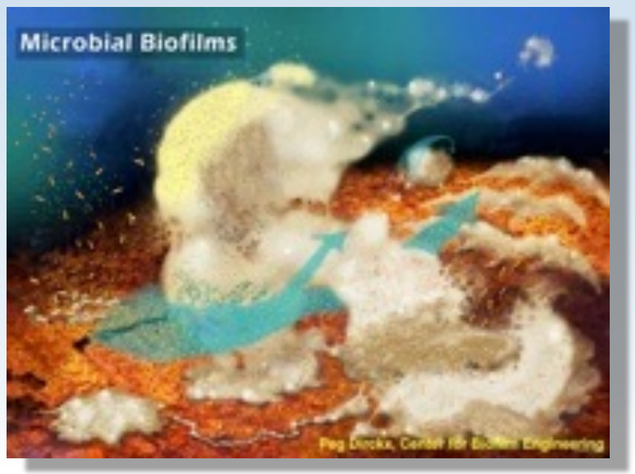
Saliva – The magic fluid



Saliva and the Control of Its Secretion. Ekberg (ed.), Dysphagia, Medical Radiology. Diagnostic Imaging, Springer-Verlag Berlin Heidelberg 2012

New ideas - about caries biofilm

Oral microflora
How fast does it grow?



- 1 mg plaque = 100,000,000 microbes
- Whole mouth = 20,000,000,000 microbes - at any given time
- 1 liter of saliva swallowed daily - 100 billion microbes
- Oral bacteria double every 4.8 hours!

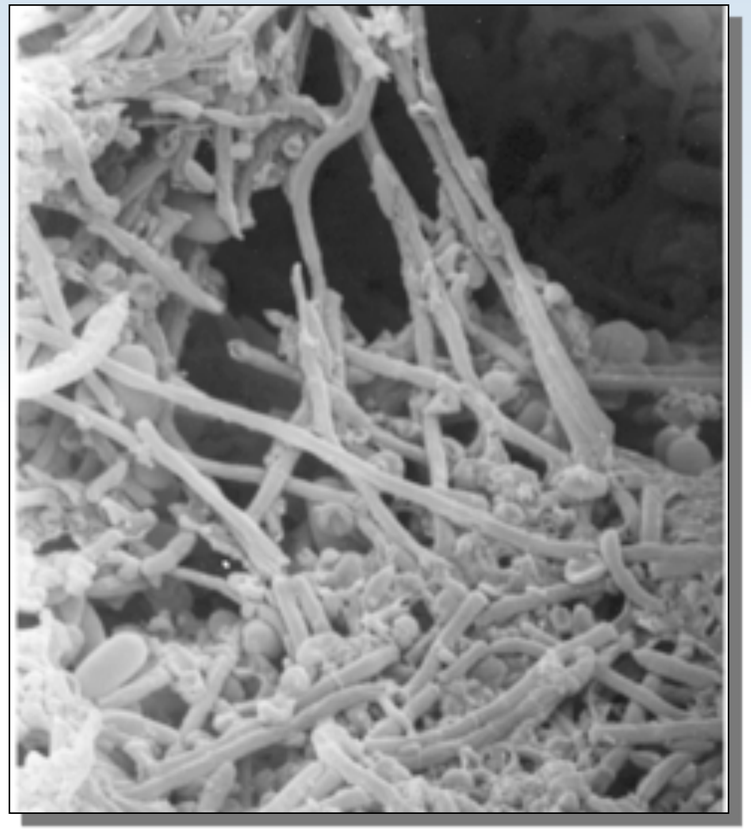
Loesche, WJ. Dental caries: a treatable infection. Springfield, IL: Charles C. Thomas; 1982. p. 558

New news about caries biofilm

Strep mutans not the only organism -

Different microbes colonize

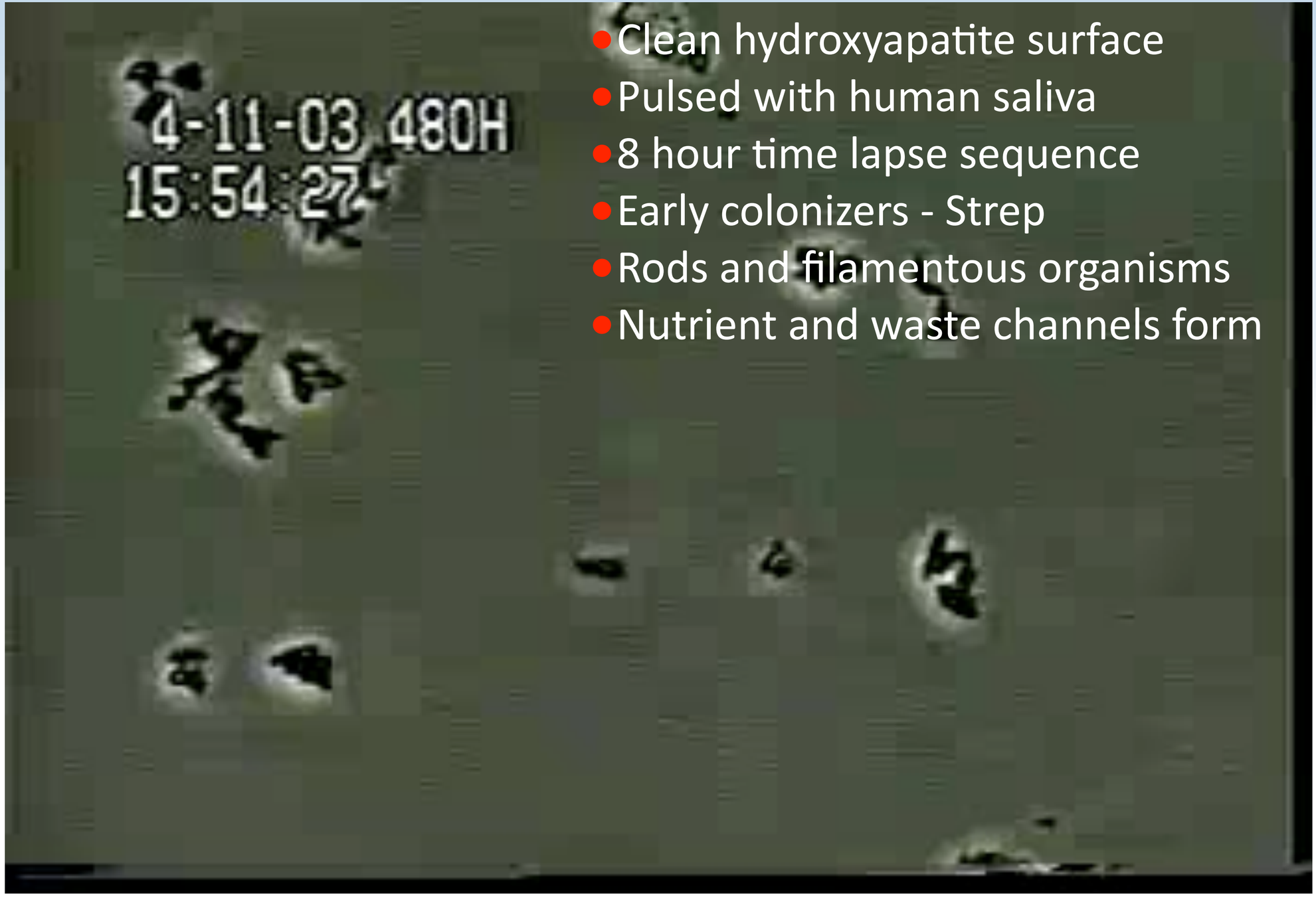
- white spots
- dentin lesions
- root caries
- primary and secondary dentition
- specific tooth surfaces



Asa JA, Griffen AL, et al. Bacteria of dental caries in primary and permanent teeth in children and young adults. J of Clin Microbiol. April 2008. 46(4):1407-17.

Microarray analysis of the microflora of root caries in elderly. Preza D, Olden I, et al. Eur J Clin Infec iDs. May 2009. 28(5).

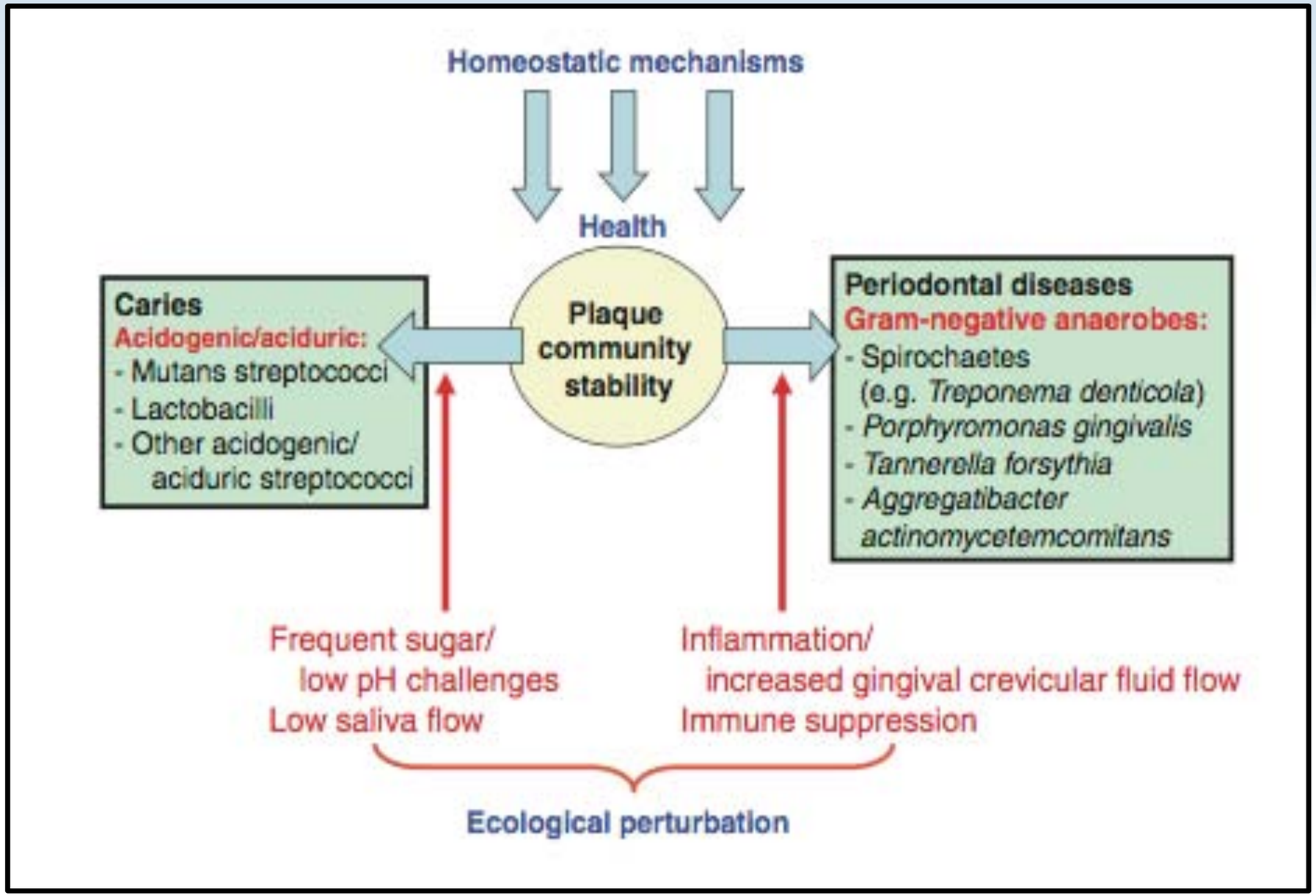
Cavalcanti YW, Bertolini MM, et al. A three-species biofilm model for the evaluation of enamel and dentin demineralization. Biofouling. 2014;30(5)579-88.



- Clean hydroxyapatite surface
- Pulsed with human saliva
- 8 hour time lapse sequence
- Early colonizers - Strep
- Rods and filamentous organisms
- Nutrient and waste channels form

Weiyuan Shi, PhD. - UCLA carifree.com Accessed 10/11/2009

Ecological shifts in dental plaque



Marsh PD, Motter A, Devine D. Dental plaque biofilms: Communities, conflict and control. Periodontology 2000, Vol. 55, 2011, 16–35.

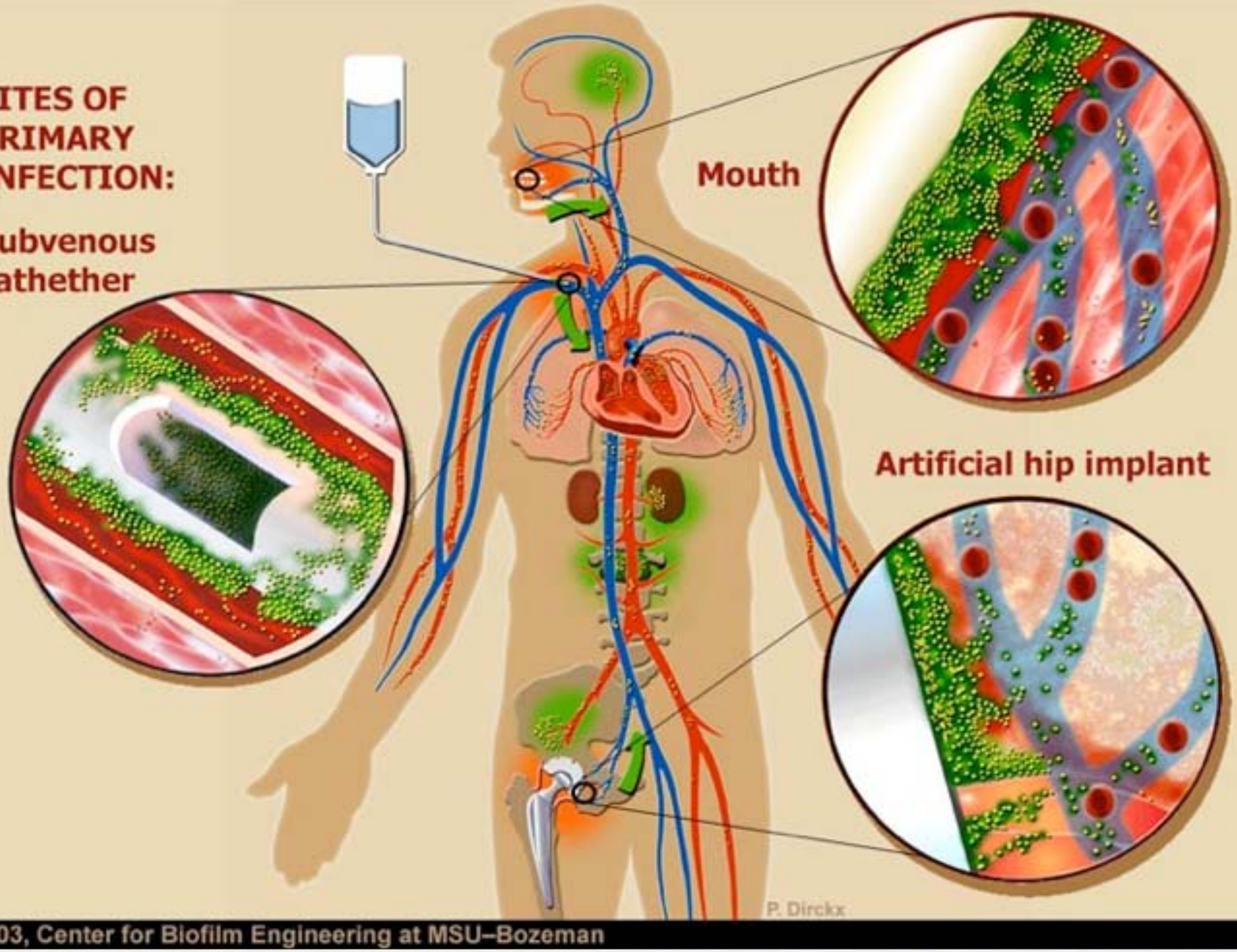
Biofilms - complicated, real life situations

Characteristics of biofilm infections

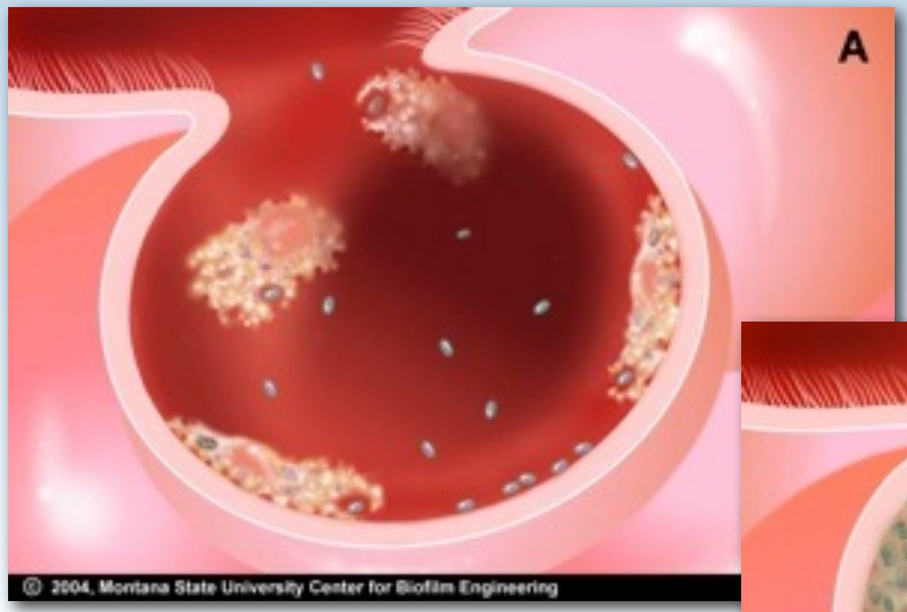
CHARACTERISTIC	CYSTIC FIBROSIS	PERIODONTITIS	CENTRAL VENOUS CATHETER INFECTION	CHRONIC WOUNDS
Form preferentially on foreign bodies, dead or damaged tissue	The genetic defect in the chloride ion channel predisposes the lung to infection	The tooth surface is not as well-defended as are vascularized tissues	Indwelling plastic and metal surfaces are very vulnerable to microbial colonization	Necrotic tissue could provide nidus for biofilm formation
Slow to develop	Persistent infection takes years to establish	Typically manifests gradually, later in life	Symptoms may take weeks to manifest	Symptoms such as pain, exudate and size wax and wane over weeks to months
Respond poorly or only temporarily to antibiotics	Lung is never cleared of bacteria despite aggressive chemotherapy	Tetracycline, antiseptic mouthwashes have little efficacy	Preferred therapy is removal of the infected catheter	Marginal response to antibiotics; may deteriorate when antibiotics are stopped
Collateral damage to neighboring healthy tissue	Massive neutrophil invasion contributes to gradual loss of lung function	Host responses and bacterial virulence factors lead to progressive bone loss; teeth fall out	Infection may disseminate to blood and other locations in body	Normal healing process of cell differentiation and migration is arrested

www.erc.montana.edu/biofilmbook/MODULE_07/Mod07_S04-2_Blue.htm Accessed 11/11/09

Sites of Primary and Secondary Biofilm Infection



Health implications
Aspirated biofilm



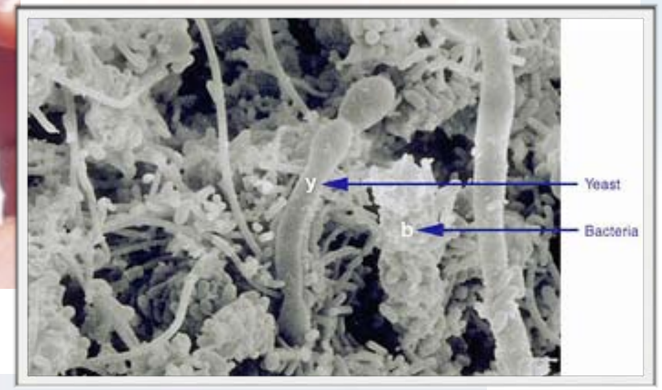
Health Implications of Aspirating Biofilm Fragments

(Above) People with strong immune systems in normal circumstances are protected from infection by inhaled bacteri because single bacteria are readily phagocytized by activated white cells in alveoli of the lung.

(Below) If biofilm fragments are inhaled or aspirated in environments like hospital wards, "sick" buildings or space vehicles, these slimy aggregates are not cleared by phagocytosis. Mild or severe infection can ensue. Such biofilm aggregates were implicated in the sometimes fatal cases of Legionnaire's disease, emanating from hotel air conditioning and ventilation systems.

http://www.biofilm.montana.edu/Res-Lib99-SW/Image_Library/Medical%20&%20Health/default.htm Accessed 7/25/09

Oral appliances



- ★ surface roughness
- ★ Strep and Candida both adhered
- ★ even small scratches reduce cleansability
- ★ retained microorganisms proliferate when appliance is reinserted

Verran J, Jackson S, The effect of dentifrice abrasion on denture topography and the subsequent retention of microorganisms on abraded surfaces. J Prosthet Dent. 2014 Jul 3. pii: S0022-3913(14)00253-4.

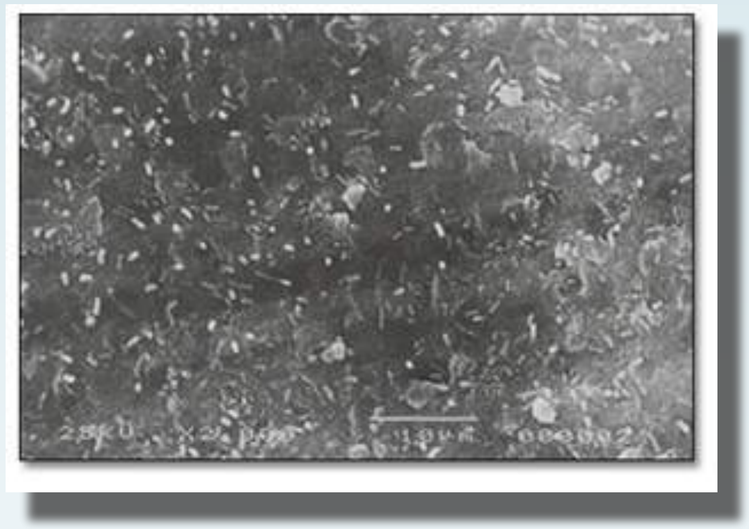
Health history clues

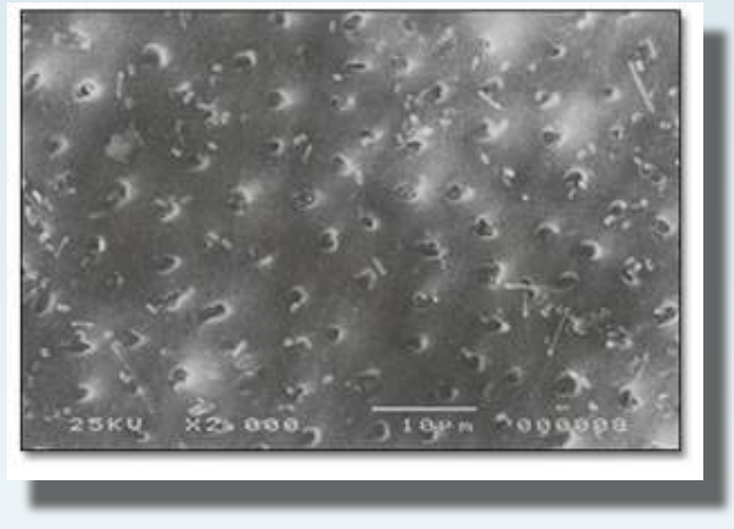
- medications - poly pharmacy

  antibiotics - prolonged use compromise intestinal flora

- acid reducers - alter intestinal tract pH

Structural differences between sensitive and non-sensitive dentin*



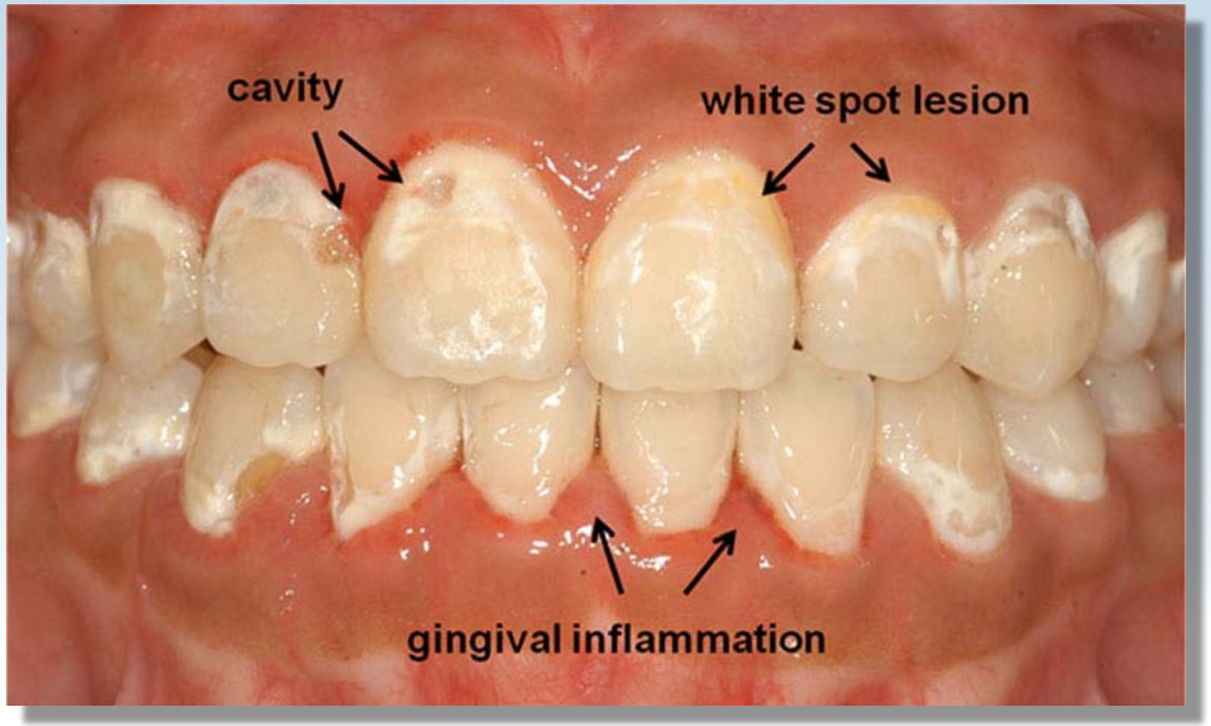


	Non-sensitive	Sensitive
No of open tubules	x	8 x
Diameter of tubules	0.43	0.83
Fluid Flow (Poisseuille's law)	y	16 y

*Absi *et al, J Clin Periodont* 1987; pictures from http://www.thejcdp.com, Sept 2006

Effective home care – mechanical and chemical

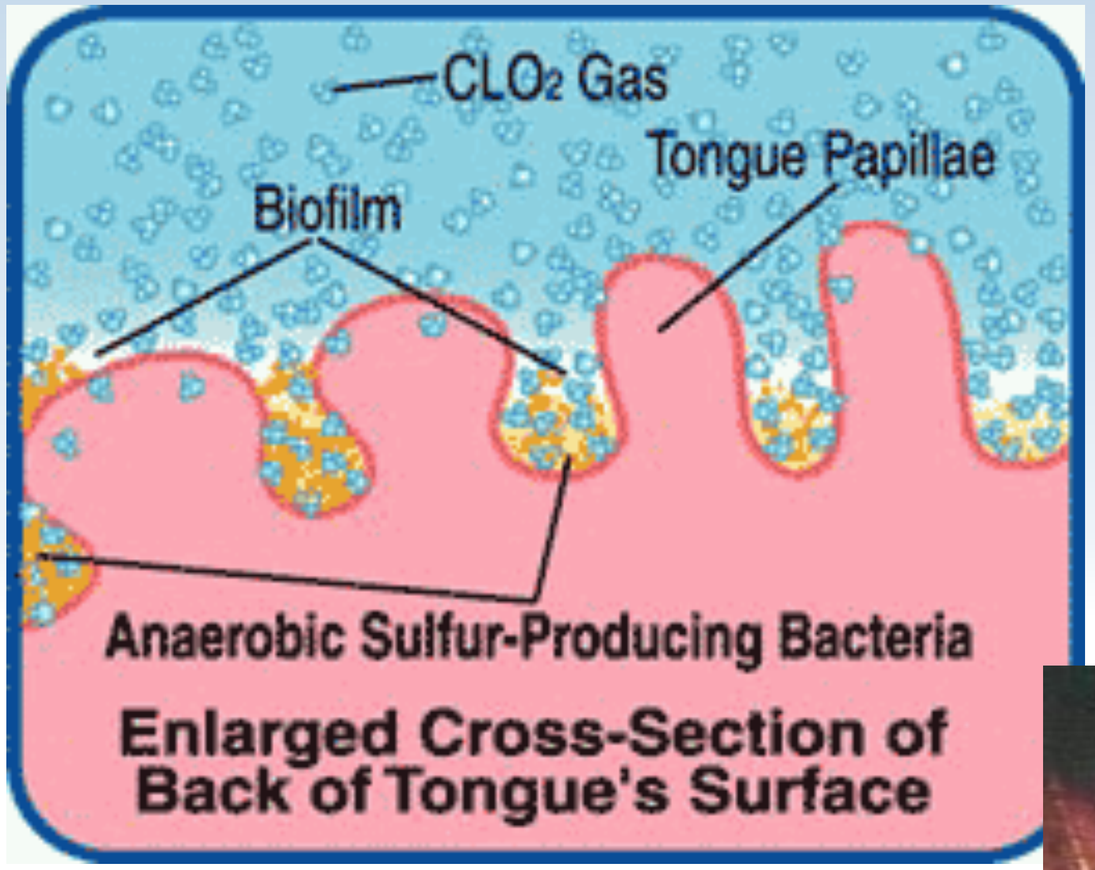
Goal is to reduce pathogenicity, disrupt biofilm, stimulate salivary flow and increase pH

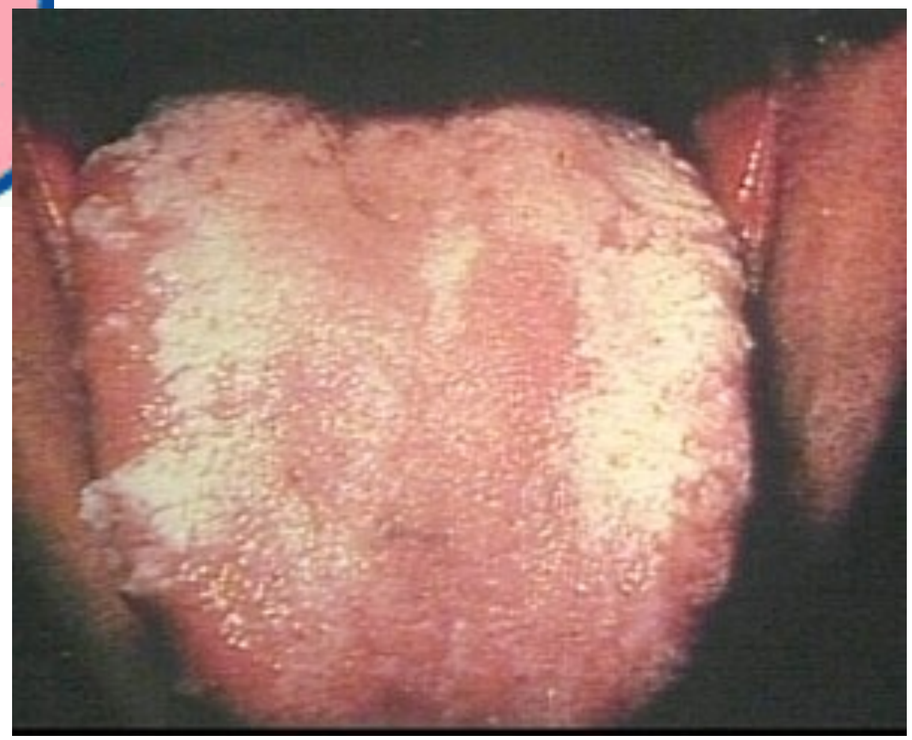


- brushing - power and manual
- site specific activities – interdental devices, floss
- irrigation
- therapeutic rinses and paste
- xyylitol – gum, mints, wipes, spray

Kawasaki A, et al. Effects of plaque control on the patency and occlusion of dentine tubules in situ. J Oral Rehabil. 2001 May;28(5):439-49.

Tongue





Oral malodor. JADA, Vol.134, February 2003

Getting national press

Slots J, Jorgensen MG. Efficient antimicrobial treatment in periodontal maintenance care. JADA, Vol.131, September 2000

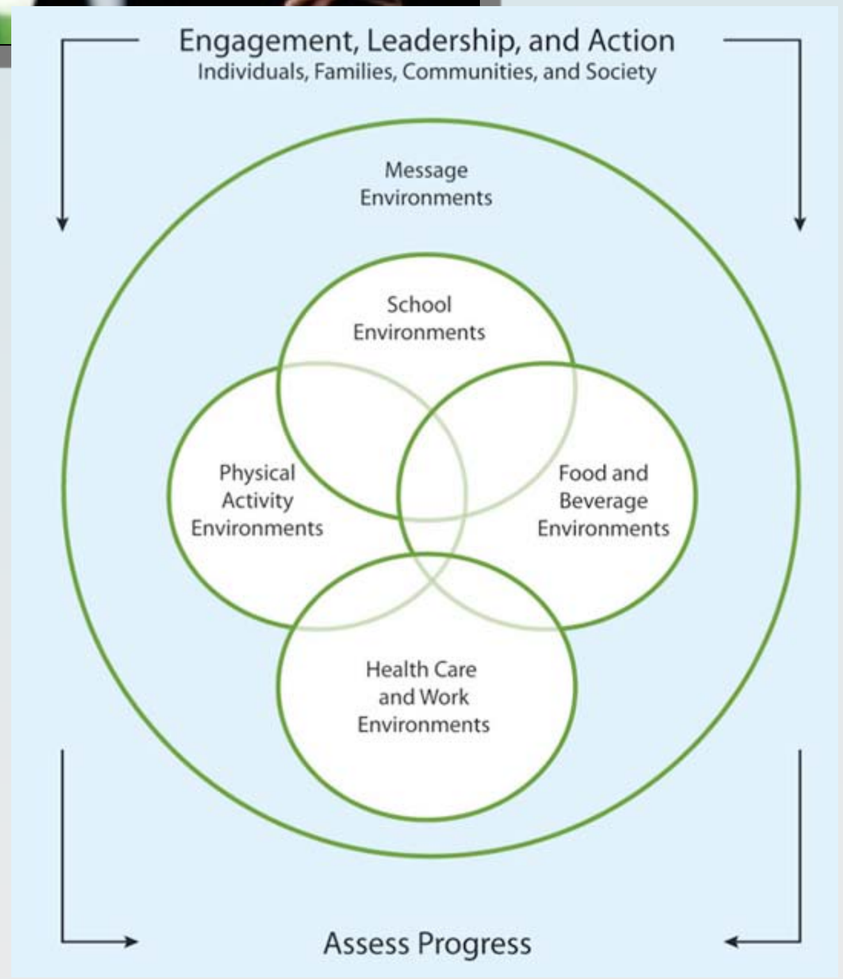
Rupesh S, Winnier J, et al. The comparative evaluation of the effects of tongue cleaning on salivary levels of mutans streptococci in children. Int J Dent Hyg. 2011 Jul 29.

Improving saliva,
neutralizing acids

Conversation starters!

oral health to general health

- ★Get the facts
- ★Develop positive energy
- ★Create a legitimate spin
- ★Focus on health benefits
- ★Discuss savings - money, time, comfort
- ★Offer reasonable alternatives
- ★Coaching not scolding

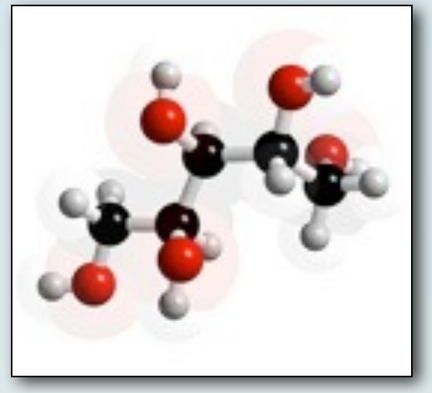


iom.edu/Reports/2012/Accelerating-Progress-in-Obesity-Prevention/Report-Brief.aspx May 12, 2012

The magic of xylitol

xylitol.org

- interferes with Strep Mutans metabolism
- disrupts biofilm integrity
- promotes neutral pH
- stimulates saliva flow
- shifts equilibrium to enhance remineralization
- increases available calcium and phosphate



Can be fatal to dogs and ferrets

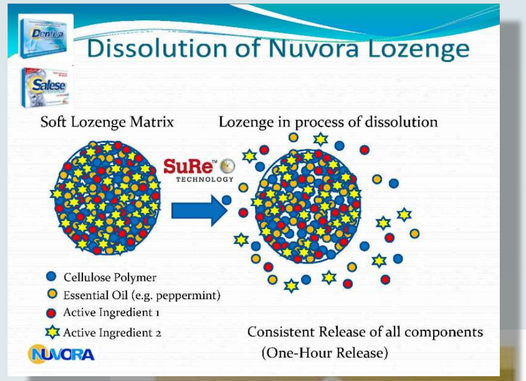
Avoid fructose for up to one hour after use

Policy on the use of xylitol in caries prevention. American Academy of Pediatric Dentistry - Oral health policies – Adopted 2006.

Ribelles Llop M, Guinot Jimeno F, et al. Effects of xylitol chewing gum on salivary flow rate, pH, buffering capacity and presence of Streptococcus mutans in saliva. Eur J Paediatr Dent. 2010 Mar;11(1):9-14.

Burt BA. The use of sorbitol- and xylitol-sweetened chewing gum in caries control. J Am Dent Assoc. 2006 Feb;137(2):190-6.

Novel xylitol products



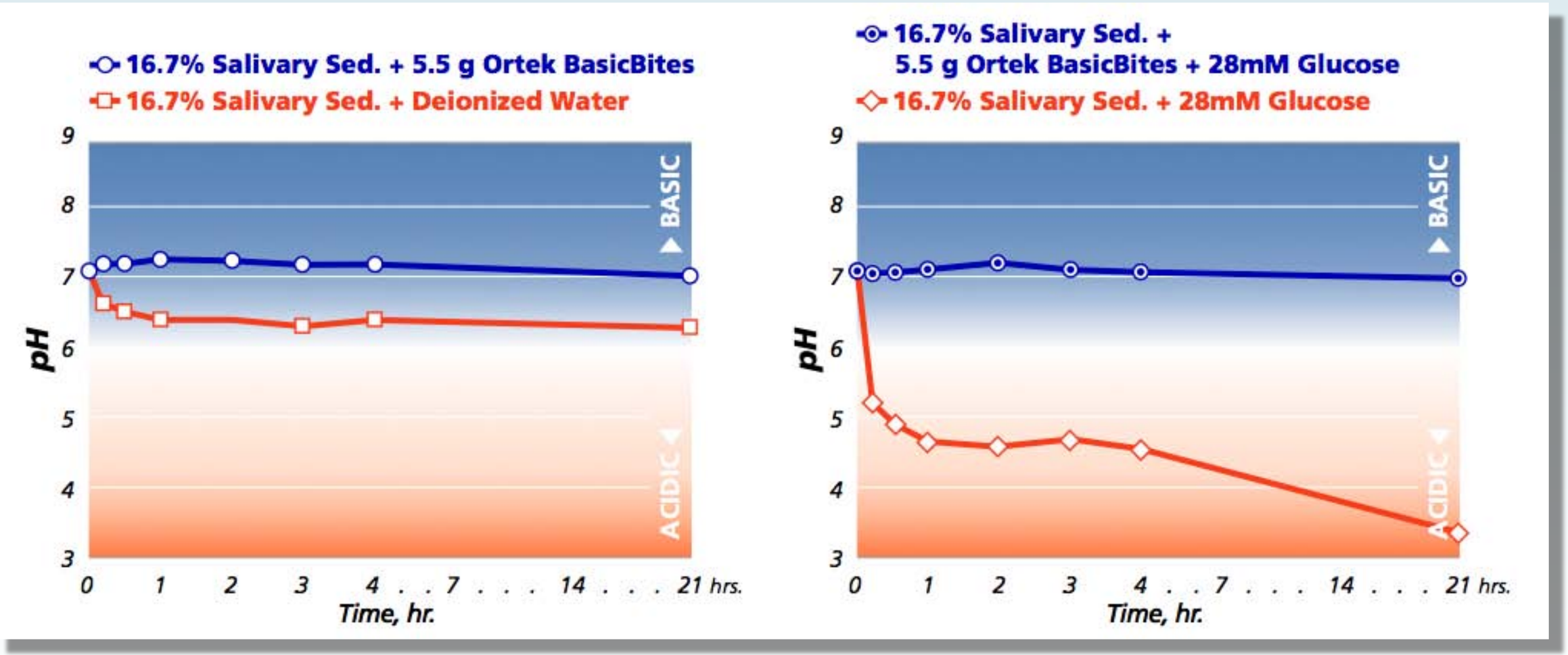
García-Godoy F, Hicks MJ. Maintaining the integrity of the enamel surface: the role of dental biofilm, saliva and preventive agents in enamel demineralization and remineralization. J Am Dent Assoc. 2008 May;139 Suppl:25S-34S.

Arginine - mode of action

- exogenous source of arginine - toothpaste
- enhances alkaline pH in saliva and plaque
- 4 weeks - arginine toothpaste
- alkali production higher - plaque samples caries active (CA)subjects
- CA subjects - shift in bacterial composition - healthier

Nascimento MM, Browngardt C, et al. The effect of arginine on oral biofilm communities. Mol Oral Microbiol. 2014 Feb;29(1):45-54.

Arginine bicarbonate calcium carbonate - keeping saliva neutral



Understanding biofilm – impacting lives

The Dental-Systemic Link: Managing Biofilms and Getting Well - Jeffrey Corbett, DDS Lynnfield,MA
http://www.youtube.com/watch?v=cGWKbroDh78

Medical biofilm based wound care

- Debridement- frequent and aggressive
- Selective biocides
  Silver, Iodosorb, Hydrofera Blue
- Antibiofilm agents
  Lactoferrin, Xylitol, Farnasol
  Plant Products, Fatty Acid Gel
- Antibiotics (25-32% effective)
  Adjunct
  Strong and long

Multiple Concurrent Strategies

Biofilms in wounds:management strategies. Rhodes DD, Wolcott RD, Percival SL. J Wound Care. November 2008.17(11).

Wound healing anti-biofilm agents

7-26-04

1-13-05

5-25-05

Biofilms in wounds:management strategies. Rhodes DD, Wolcott RD, Percival SL. J Wound Care. November 2008.17(11).

Wound healing antimicrobial agents

- ionic silver - minute concentrations / broad spectrum / used in dressings

- iodine - prevents wound infection / aids healing / povodone iodine preferred

- medicinal honey antibacterial activity

Rhodes DD, Wolcott RD, Percival SL. J Biofilms in wounds:management strategies. Wound Care. November 2008.17(11).

Percival SL, Cutting KF, Williams D(2010) Biofilms: possible strategies for suppression in chronic wounds. Nursing Standard Supplement.

Wound healing anti-biofilm strategies

- lactoferrin - bacteriocidal / block surface attachment / works with PMNs /binds iron even at a low pH
- xylitol - interferes with biofilm formation
- enzymes - Dispersin B - causes biofilm detachment
- gallium, EDTA, hyperbaric oxygen, bacteriophages, glucose oxidase, pulsed electric fields
- ultrasound / ultrasonics
- no more amputations

Rhodes DD, Wolcott RD, Percival SL. J Biofilms in wounds:management strategies. Wound Care. November 2008.17(11).

Percival SL, Cutting KF, Williams D(2010) Biofilms: possible strategies for suppression in chronic wounds. Nursing Standard Supplement.

Dr. Bill Costerton - The "Father" of Biofilms http://www.youtube.com/watch?v=lbLFOUHvAJg

What do we owe our patients?

- Current, in-depth health history
- Assess a patient's total needs
- Tell them the truth
- Provide all options
- Patients must make the final choice
- Current scientific information
- Understand technology

What's the take home message? Understand.....

- Biofilms are complex
- Mother Nature rules
- Better health is possible
- Take responsibility for your role
- New information about biofilms emerges every day