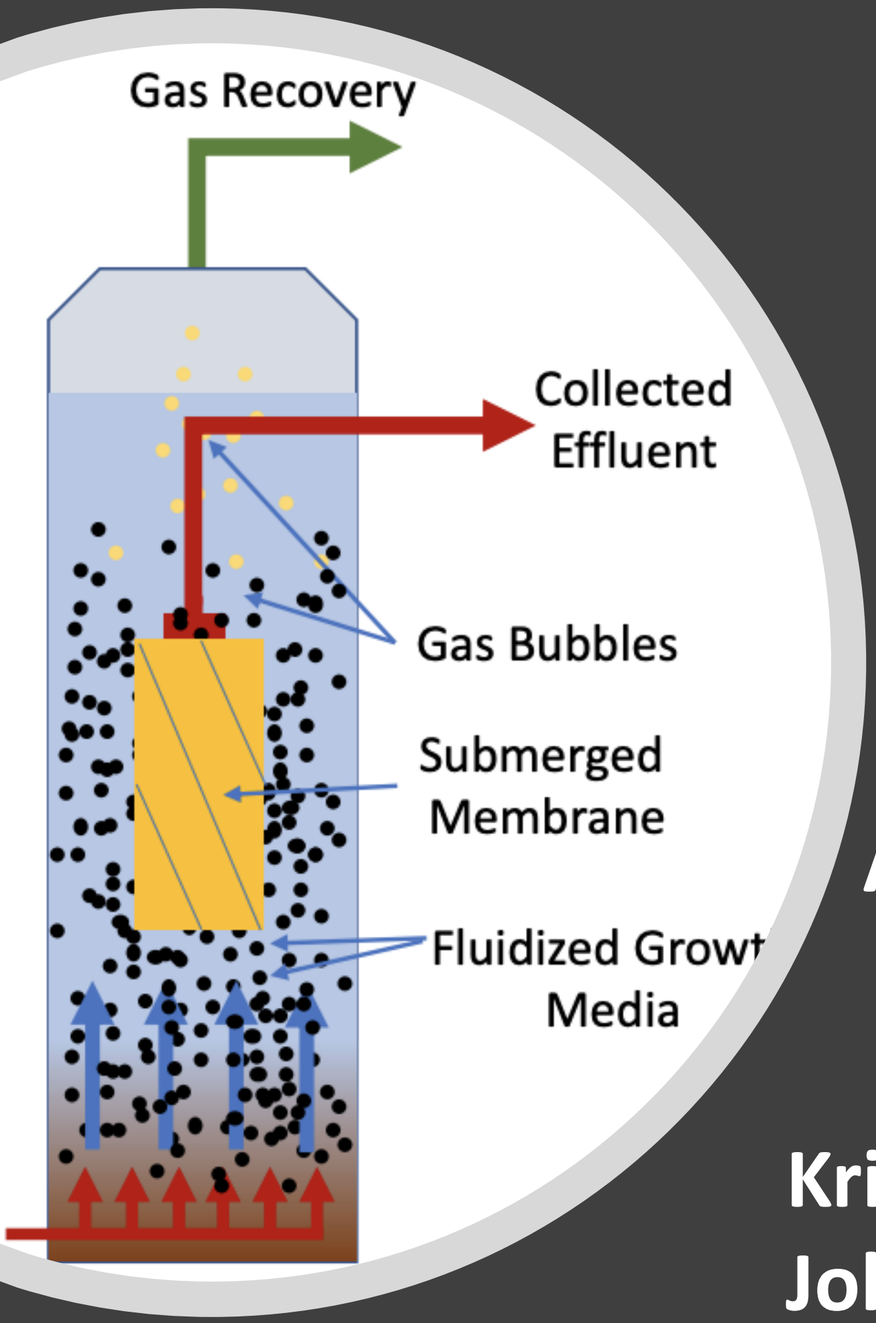
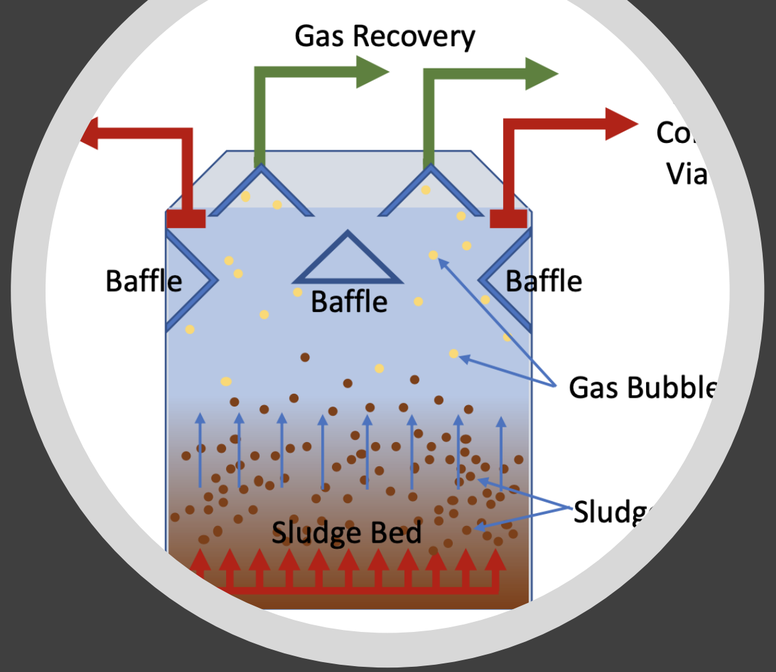
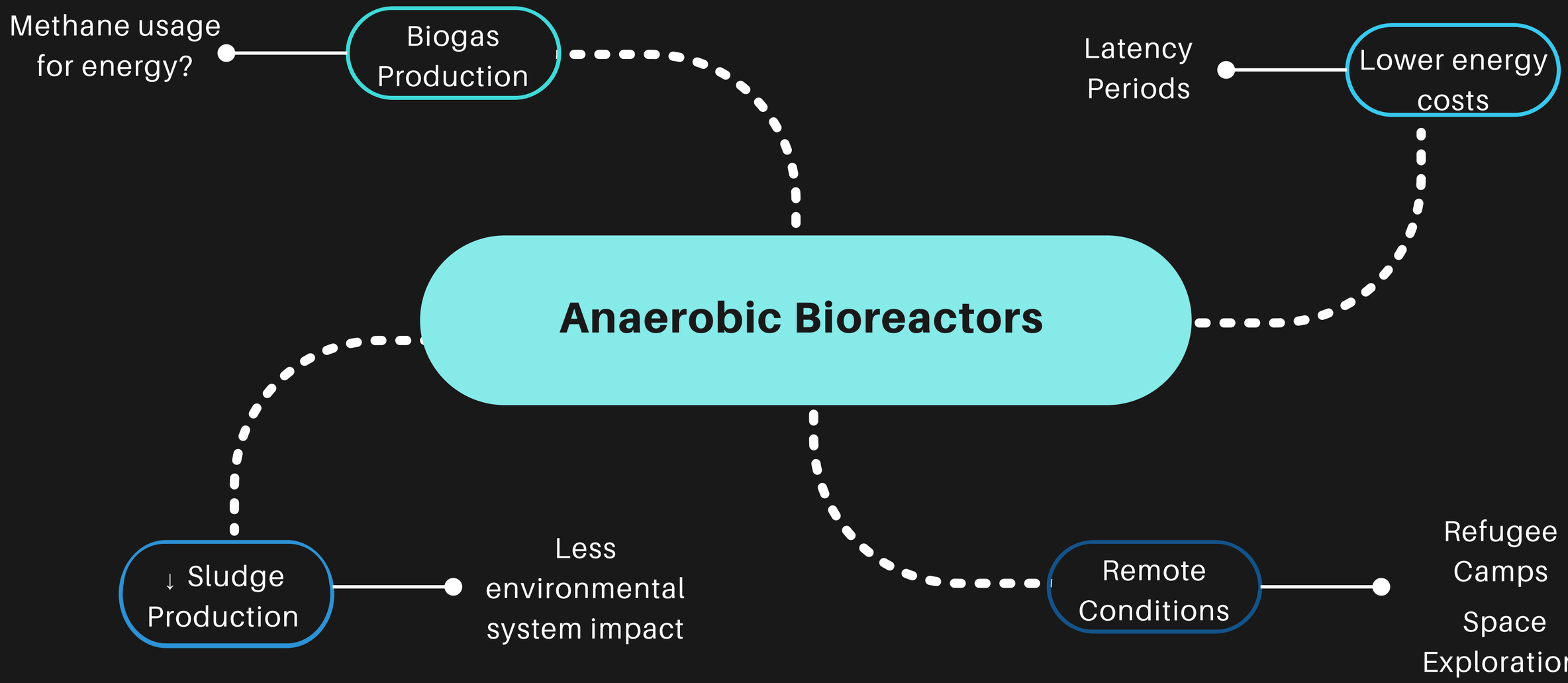
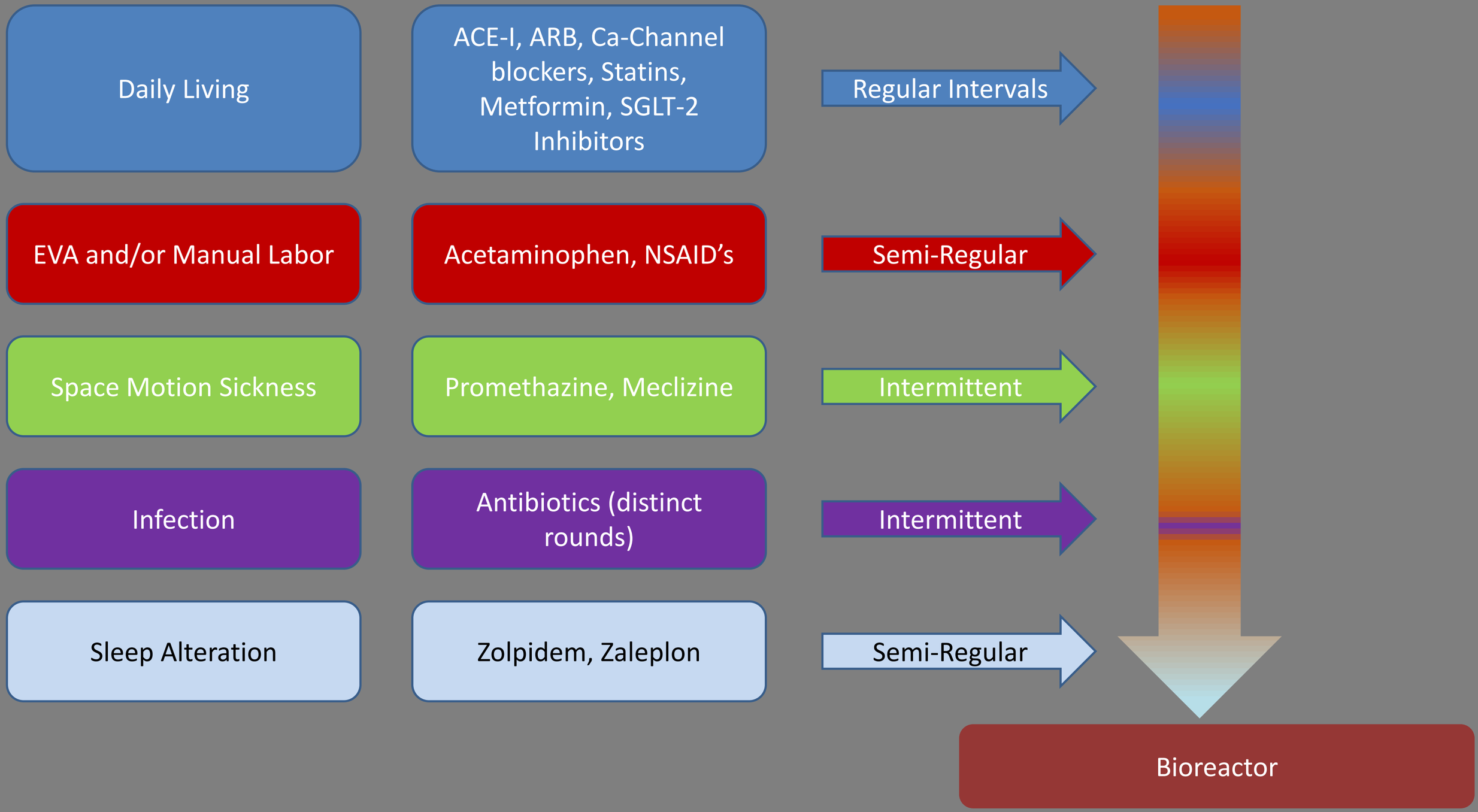




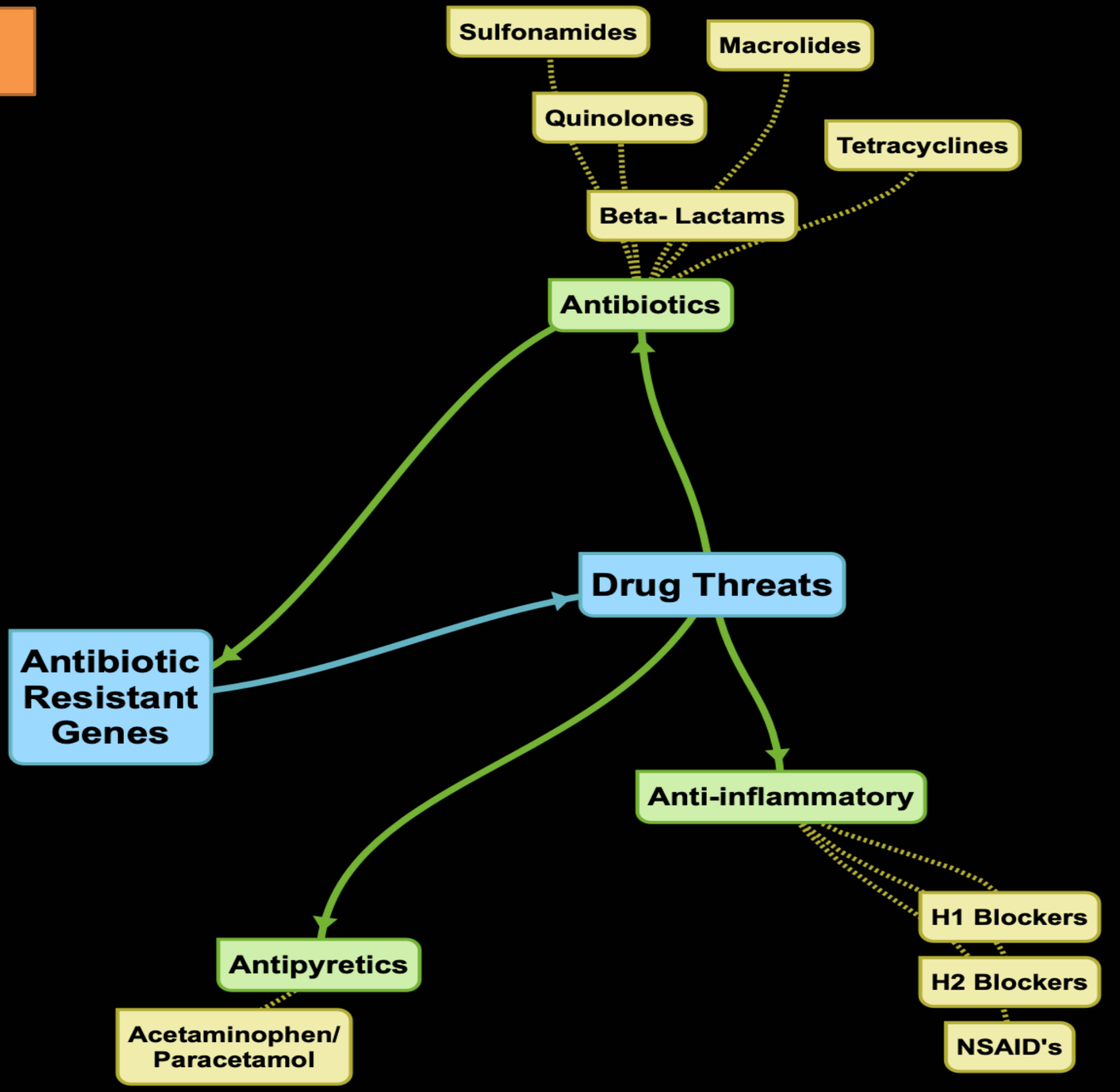
Anaerobic Bioreactors for Refugee Health and Long Duration Space Missions

Kristi Ray DO/MPH
John Marshall MD/ MPH


Anaerobic Bioreactors
Biogas Production
Methane usage for energy?
Lower energy costs
Latency Periods
↓ Sludge Production
Less environmental system impact
Remote Conditions
Refugee Camps
Space Exploration

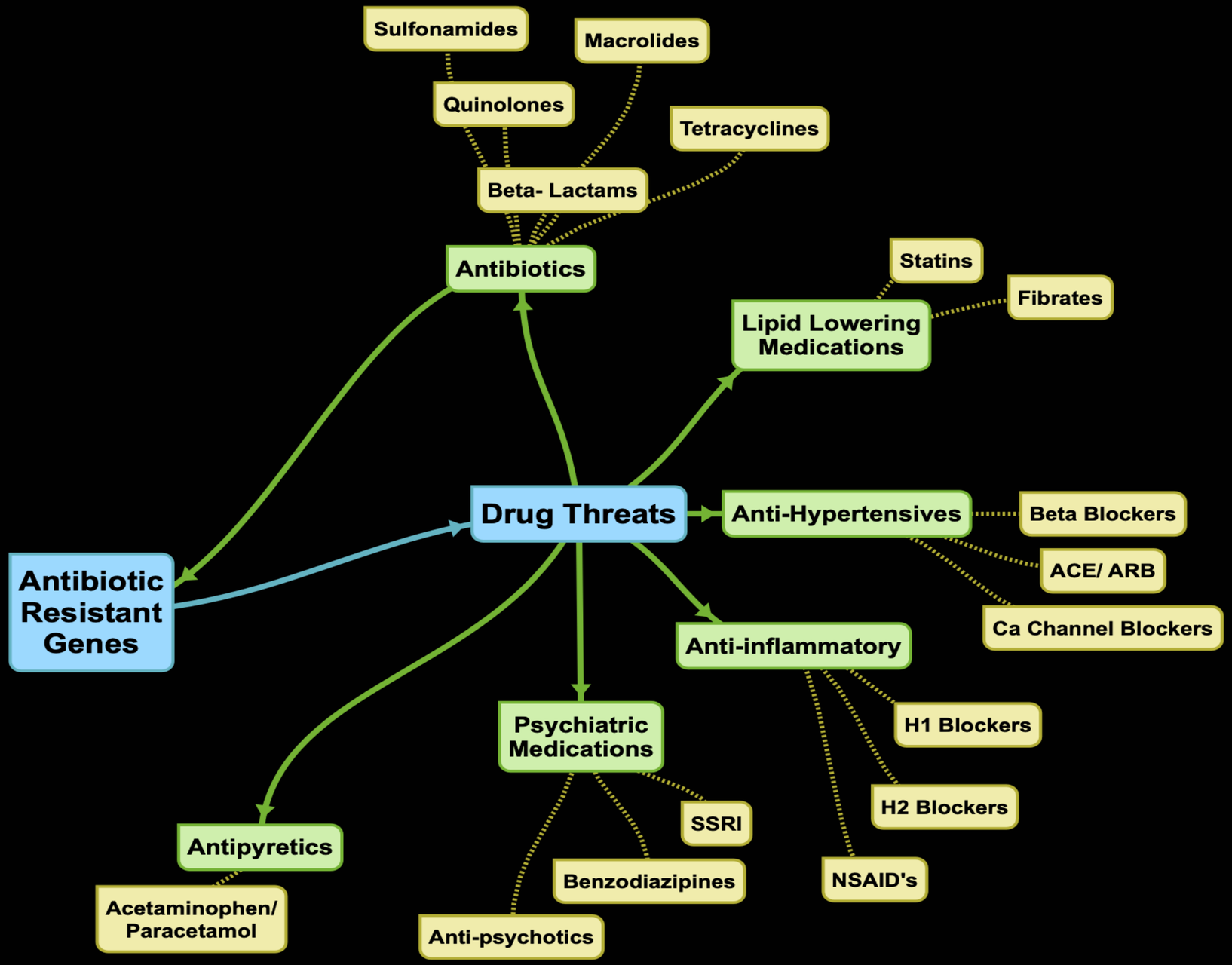

Daily Living
ACE-I, ARB, Ca-Channel blockers, Statins, Metformin, SGLT-2 Inhibitors
Regular Intervals
EVA and/or Manual Labor
Acetaminophen, NSAID's
Semi-Regular
Space Motion Sickness
Promethazine, Meclizine
Intermittent
Infection
Antibiotics (distinct rounds)
Intermittent
Sleep Alteration
Zolpidem, Zaleplon
Semi-Regular
Bioreactor

Refugee Health



Space Exploration

- Some pharma classes used more than others
- Effects possibly magnified
- Space pharma landscape shifting



Drug Wastewater

- Biological systems can be cost-effective for treating pharmaceutical wastewater compared to physio-chemical processes.
- High COD and total suspended solids with wide pH range.
- Can be highly bioactive and persistent.

Example: Wasting Antibiotics

- Antibiotics in environment known to alter prevalence of antibiotic resistance genes (ARG’s) and antibiotic resistant bacteria (ARB’s).

- Presence of ARG’s has negative influences on public perceptions of wastewater reuse and its economic viability

Drugs and Anaerobic Bioreactors

Bioreactor Chemistry/Mechanisms

- Chemical properties
- Removal mechanisms

Challenges

- Toxicities/Inhibition
- Altered biomes
- Altered chemical process
- ARG’s

AnMBR Experiences

- Drugs studied
- Representative classes
- Aerobic system comparison

Questions

- Which drugs/classes
- Removal efficiencies
- ARG degradation
- Pre-treatment
- Configuration methods

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Anaerobic Bioreactor Chemistry/Mechanisms:

Excretion in Excrement

- Substantial concentration of parent drug
- 30-90% Abx excreted as parent drugs
- Anaerobic bioreactors capable of treating many pharmaceuticals in wastewater.

Chemical structures

- Electron donating functional groups (EDG)
- Electron withdrawing functional groups (EWG)
- Hydrophobicity versus hydrophilicity
- Sulfur or nitrogenous structural elements

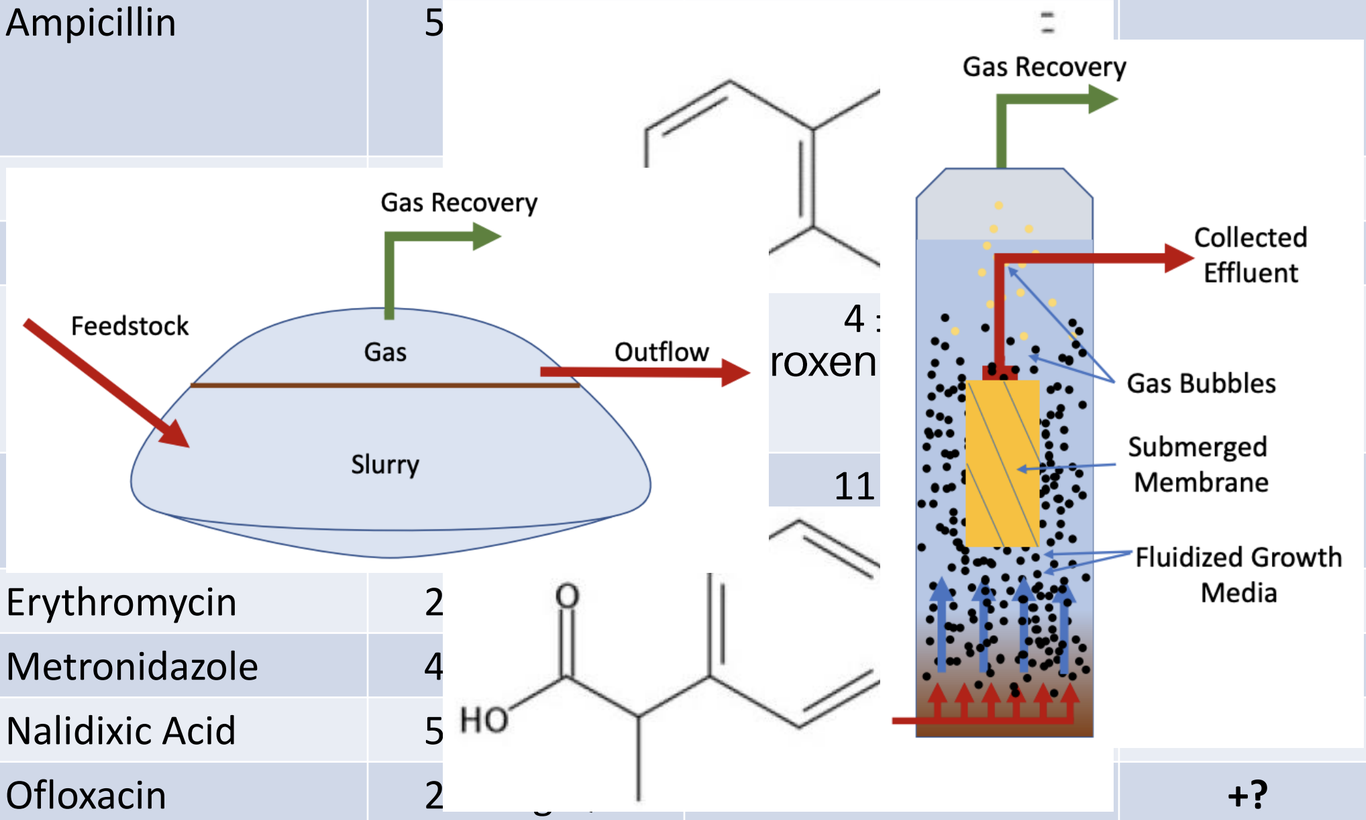
Biodegradation

- Primary removal mechanism
- Slower growing microbes

Sorption

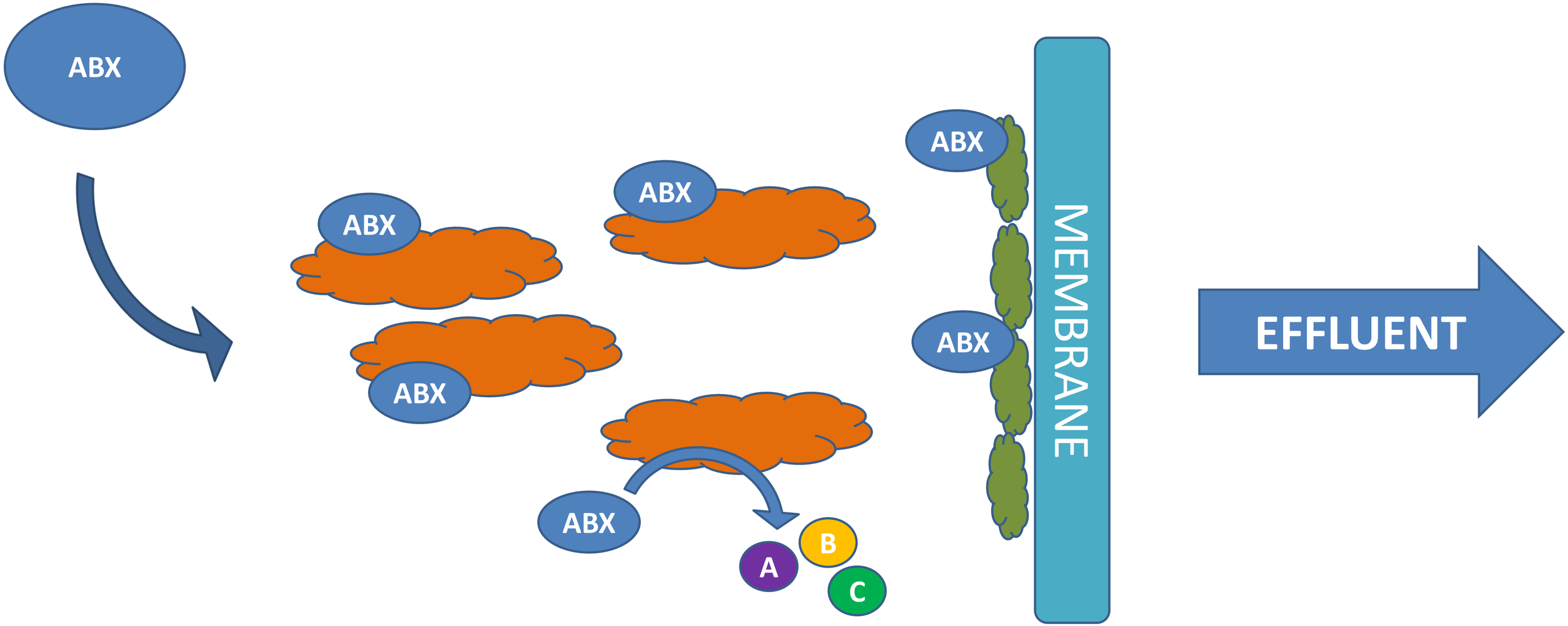
- Biologically based sorptive capacity
- Supplemental capacity, e.g. GAC, PAC

Drug	Dose	Fecal Concentration (mg/kg)	Active Drug
Ampicillin	5		
Erythromycin	2		
Metronidazole	4		
Nalidixic Acid	5		
Ofloxacin	2		+?
Vancomycin			+



Adapted from Steinbakk 1992

Drugs: Toxicities/Inhibition



Drugs and Anaerobic Bioreactors

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Drugs: Relevant Entities

Antibiotics:

- Beta-lactams
- Quinolones
- Tetracyclines
- Macrolides
- Sulfonamides

↓↓

- Antibiotic resistance genes

Analgesics:

- NSAID's (ibuprofen, "xxxx-olac", etc.)
- Acetaminophen

Cardiovascular:

- Beta-blockers
- Anti-hypertensives (ACE-inhibitors, Ca-channel blockers, diuretics)
- Statins

Metabolic:

- Statins
- Metformin

Drugs: Studied

Antimicrobials:

- Beta-lactams +
- Quinolones +
- Tetracyclines +
- Macrolides +
- Sulfonamides +
- Antivirals (acyclovir, lamivudine) +
- Antifungals +/-
- Antibiotic resistance genes +

Miscellaneous:

- NSAID's (ibuprofen, "xxxx-olac", etc.) +
- Acetaminophen +
- Corticosteroids +

Cardiovascular:

- Beta-blockers +
- Anti-hypertensives (ACE-inhibitors, Ca-channel blockers, diuretics)
- Statins +

Metabolic:

- Statins +
- Metformin +

	Removal efficiency (%)		
	AFBR	AFMBR	Overall
Sulfonamide antibiotics			
Sulfadiazine	39.7	89.5	93.7
Sulfamethoxazole	35.5	83.0	89.1
Sulfathiazole	–	–	–
Sulfamethazine	–	–	–
Macrolides antibiotics			
Erythromycin-H_2O	58.7	66.7	86.3
Clarithromycin	56.9	74.6	89.0
Josamycin	–	–	–
Roxithromycin	–	–	–
Tylosin	–	–	–
Quinolone antibiotics			
Nalidixic acid	80.7	100	100
Flumequine	0	100	100
Pipemidic acid	94.5	100	100
Norfloxacin	–	–	–
Ciprofloxacin	89.4	100	100
Ofloxacin	94.4	95.3	100
Cephalosporins antibiotics			
Cephalexin	69.6	86.3	95.8
Cephradine	52.7	86.4	93.6
Other antibiotics			
Trimethoprim	87.42	100	100

2-Stage AFBR, AFMBR, Dutta 2014

Antibiotic types	Treatment strategies	Antibiotic/ARGs removal (%)	References
Sulfamethoxazole	AnMBR	67.8 ± 13.9	Xiao et al.

AnOMBR-MD.

PhACs	C_{DS} (ng L^{-1})	C_{dist} (ng L^{-1})	R_{AnOMBR} (%)	$R_{AnOMBR-MD}$ (%)
17α-Ethynilestradiol	9008.55 ± 2922	<83.61	90.54 ± 7.4	>97.88
Betamethasone	124.39 ± 136	96.28 ± 86	94.41 ± 0.47	98.22 ± 3.20
Fenofibrate	< 02.83	<1.09	>99.79	>99.94
Fluconazole	3561.84 ± 909	90.13 ± 10	92.67 ± 4.55	98.29 ± 0.20
Ketoprofen	3070.40 ± 639	<0.81	97.57 ± 2.10	>99.97
Loratadine	<20.08	<0.71	>99.44	>99.98
Prednisone	<59.55	74.33 ± 41	>97.02	97.41 ± 1.40

AnOMBR-MD, Arcanjo 2021

Sulfamethoxazole Trimethoprim	AnMBR	Nearly complete removal	Hapb et al. (2016)
Sulfadiazine	Two-stage AFMBR	93.7	Dutta et al. (2014))
Sulfamethoxazole		89.1	
Erythromycin-H2O		86.3	
Clarithromycin		89	
Quinolone antibiotics		100	
Cephalexin		95.8	
Cephradine		93.6	
Trimethoprim		100	
Benzothiazole	AFMBR	82.3 ± 3.7% (HRT = 12 h); 85.7 ± 2.6% (HRT = 18 h); 97.6 ± 0.5% (HRT = 24 h)	Li et al. (2018)

Cheng, 2018

Compound	Elimination from the aqueous phase (%)			
AnOMBR-MD.				
PhACs	C_{DS} (ng L^{-1})	C_{dist} (ng L^{-1})	R_{AnOMBR} (%)	$R_{AnOMBR-MD}$ (%)
17α-Ethynilestradiol	9008.55 ± 2922	<83.61	90.54 ± 7.4	>97.88
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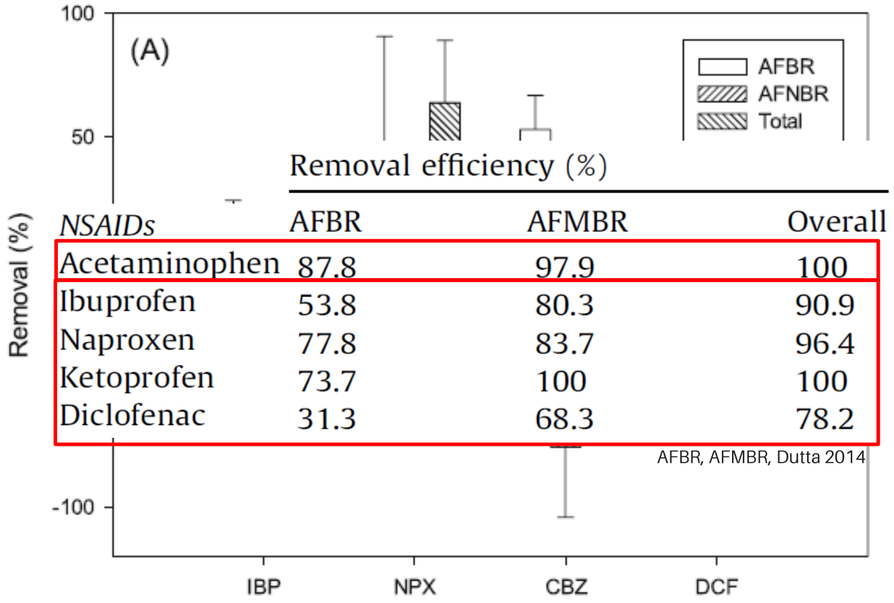
Prednisone	<59.55	74.33 ± 41	>97.02	97.41 ± 1.40
Indomethacin	n.e.		41.4 ± 20.6	39.7 ± 26.2
Anti-histamines				
Ranitidine	24.7 ± 44.9		44.2 ± 29.6	29.5 ± 47.9
Loratidine	15.0 ± 43.9		n.e.	33.5 ± 52.2
Famotidine	60.1 ± 22.3		64.6 ± 24.5	47.4 ± 63.0

AnOMBR-MD, Arcanjo 2021

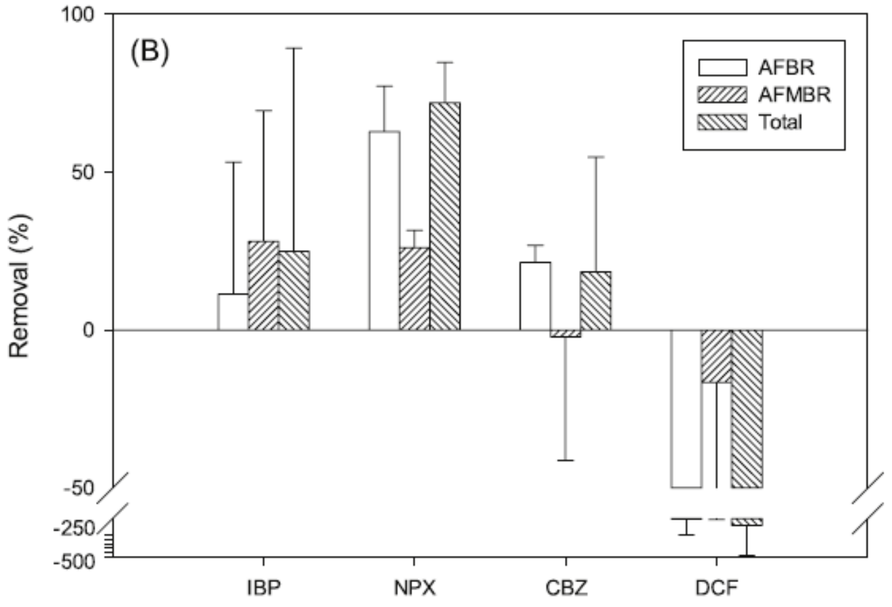
Radjenović, 2008



Removal efficiency (%)

NSAIDs	AFBR	AFMBR	Overall
Acetaminophen	87.8	97.9	100
Ibuprofen	53.8	80.3	90.9
Naproxen	77.8	83.7	96.4
Ketoprofen	73.7	100	100
Diclofenac	31.3	68.3	78.2

AFBR, AFMBR, Dutta 2014



AFBR, AFMBR, Chen, 2019

Drugs: “Antihistamines”

- Relevant drugs:
  - Loratadine (H1 blocker)
  - Ranitidine, Famotidine (H2 blockers)

- Variable removal by method, ie. CAS vs HF/FS MBR
- High removal rates possible

Compound	Elimination from the aqueous phase (%)		
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Anti-histamines				
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Famotidine	60.1 ± 22.3		64.6 ± 24.5	47.4 ± 63.0

AnOMBR-MD, Arcanjo 2020

Radjenović, 2008

Drugs: Cardiovascular

- Cardiovascular:
  - Beta-blockers
  - Cholesterol altering
  - Anti-hypertensives (ACE-inhibitors, Ca-channel blockers, diuretics)

	Elimination from the aqueous phase (%)		
ß-blockers	CAS	FS MBR	HF MBR
Atenolol	61.2 ± 18.6	76.7 ± 12.6	69.5 ± 12.5
Sotalol	21.4 ± 31.5	53.1 ± 24.1	30.4 ± 25.3
Metoprolol	24.7 ± 44.9	44.2 ± 29.6	29.5 ± 47.9
Propranolol	58.8 ± 24.5	77.6 ± 12.2	65.5 ± 22.4
Hypoglycaemic agents			
Glibenclamide	46.1 ± 40.8	95.6 ± 4.4	82.2 ± 28.6
Lipid regulator and cholesterol lowering statin drugs			
Gemfibrozil	n.e.	42.2 ± 36.7	32.5 ± 49.3
Bezafibrate	80.8 ± 20.9	90.3 ± 10.1	88.2 ± 15.3
Pravastatin	59.4 ± 16.2	86.1 ± 9.1	83.1 ± 12.5
Diuretics			
Hydrochlorothiazide	n.e.	n.e.	n.e.

Radjenović, 2008

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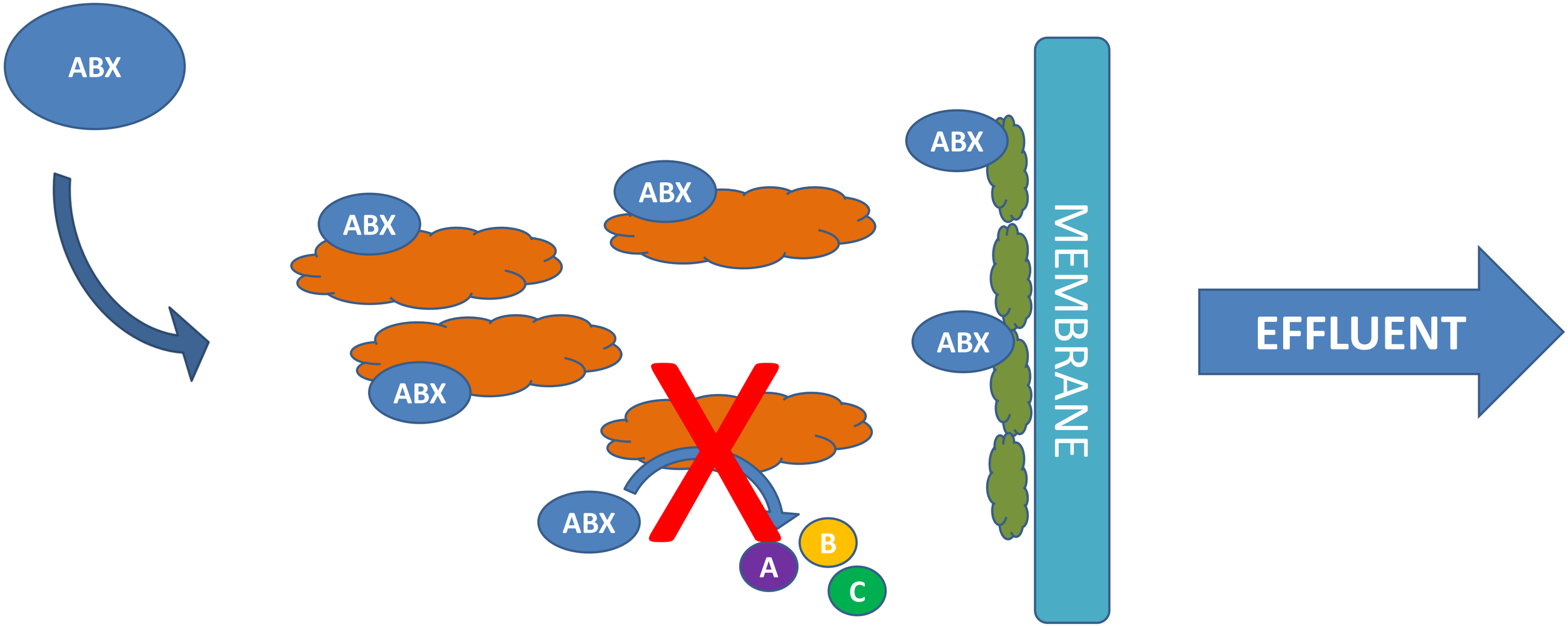
Drugs: Toxicities/Inhibition



Drugs: ARG's

- Location, location, location:
  - Variable depending on "where" in reactor
  - Variable by resistance gene
- Antibiotics specific effects
- Concentration specific effects