SAND2018-6279C

Viral infections

General knowledge

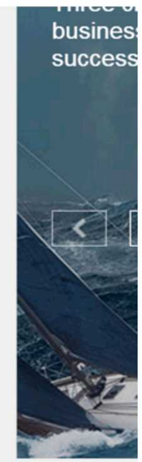
Progress towards a broad antiviral treatment

Apr 30th 2016 | From the print edition

IN THE medical armoury vaccines are a wonderful piece of ammunition. But they are like bullets that can hit one target only. Different vaccines are needed to prevent specific viral infections. If a person is already ill, vaccines won't help. Various antiviral drugs might, shortening the time people are ill or preventing serious complications. The trouble is viruses are a moving target because they can evolve rapidly. Researchers have tinkered with some antiviral treatments that might work against a wide spectrum of diseases, but all have had shortcomings. Now one group thinks they have found a method that might protect cells in the body from a viral invasion.

The new research, led by James Hedrick of the IBM Almaden Research Center in California, Naoki Yamamoto of the National University of Singapore and Yi Yan Yang of the Institute of Bioengineering and Nanotechnology, also in Singapore, stems from an old tactic that has been problematic in the past.

Lots of experiments have demonstrated that the theory is sound. Unfortunately, many of the materials used to interfere with the electrical charges have also been toxic to the cells they are supposed to protect. Dr Hedrick and his colleagues speculated that it might be possible to work around this problem with polyethylenimine. Previous work has shown



… All viruses depend upon similar electrical charges at their surfaces to connect to the cells that they are trying to infect. If the charges on viruses and cells could somehow be meddled with, it should make things harder for the virus to infect the host…

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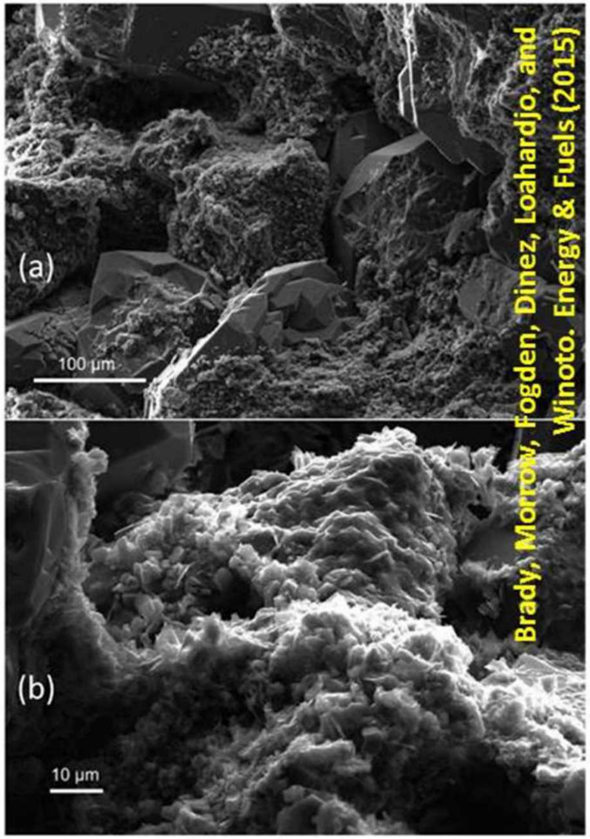
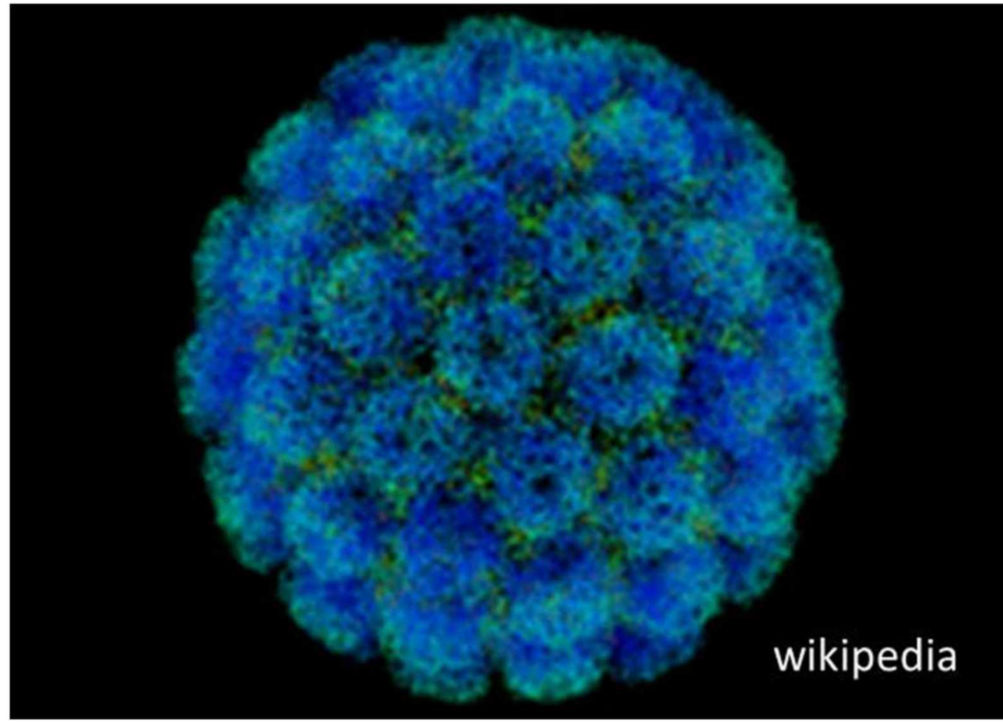
More Oil, Better Drugs

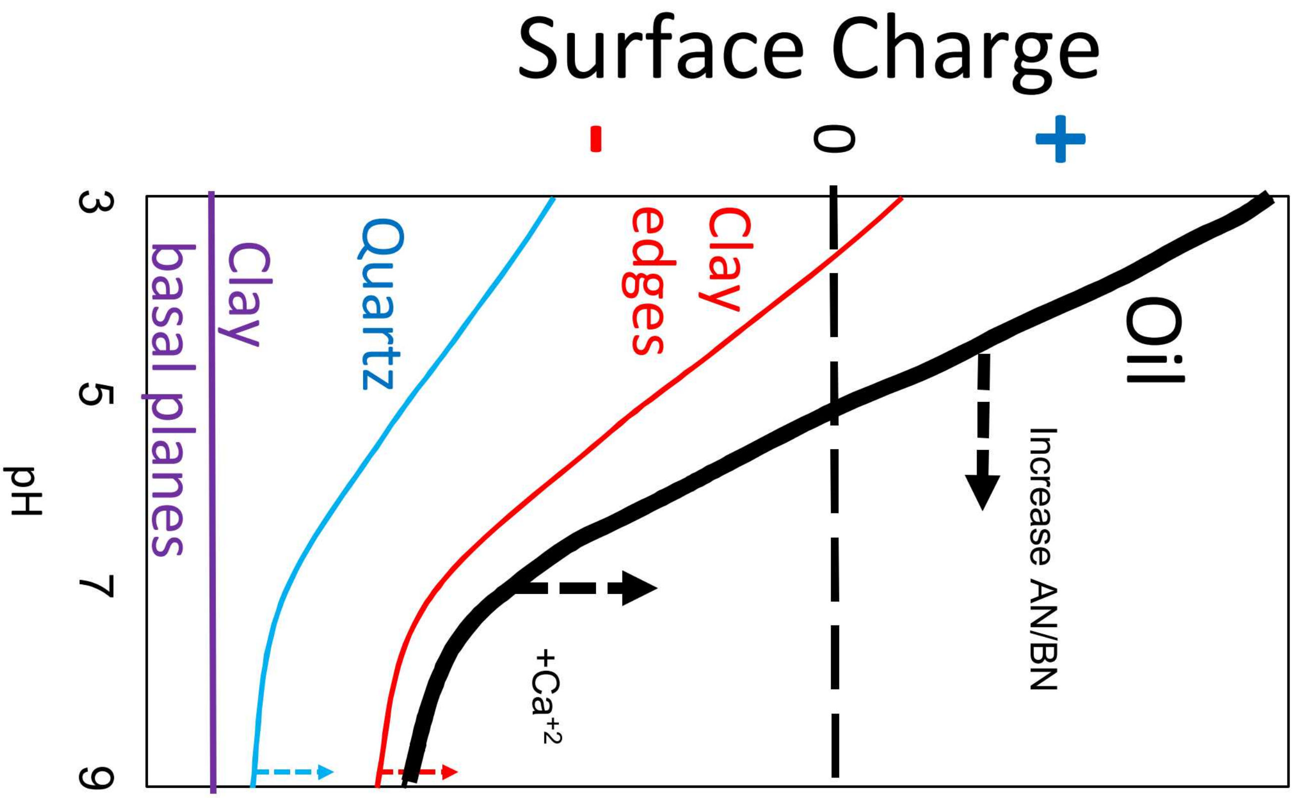
Pat Brady
Senior Scientist,
Sandia National Laboratories

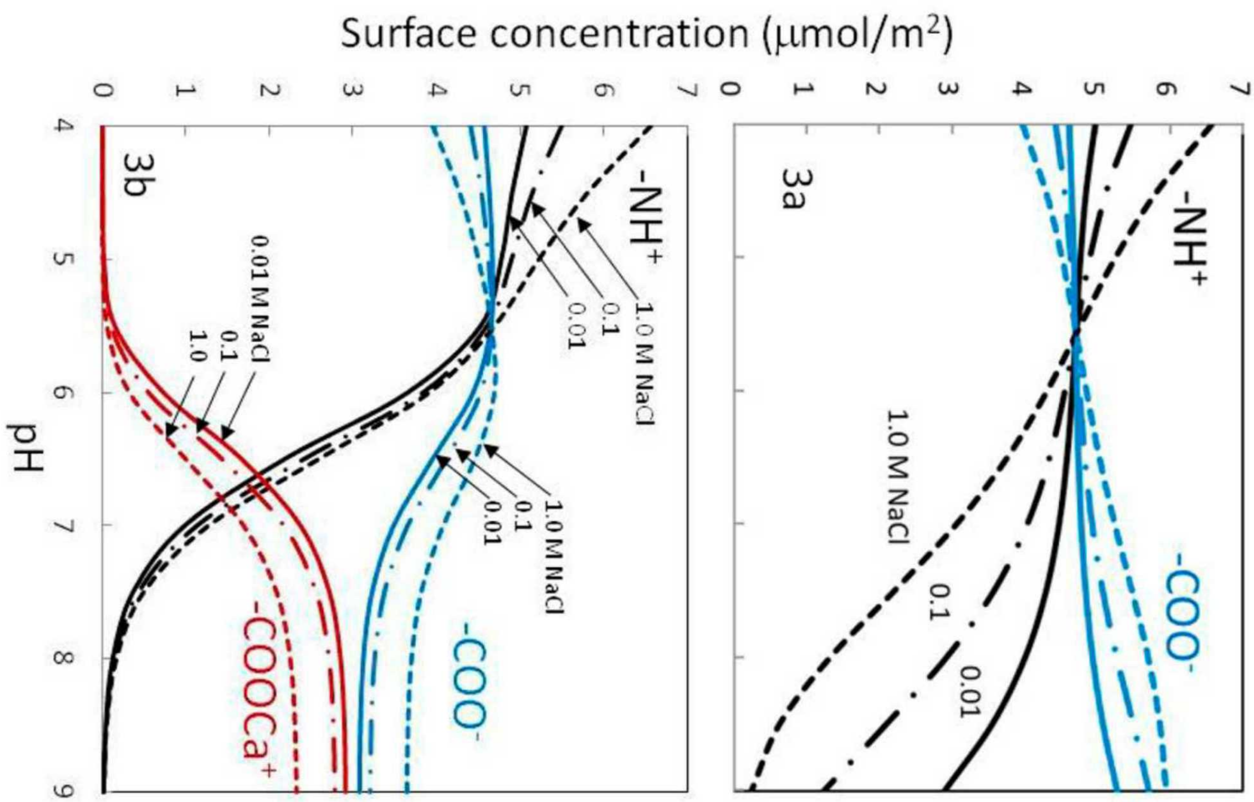




Oil|Virus -NH^+ --- ^-O- Rock|Cell

13th International Symposium on Reservoir Wettability and its Effects on Oil Recovery
May 8-9, 2018, at The University of Texas at Austin





Brady, P. V., Morrow, N. R., Fogden, A., Deniz, V., & Loahardjo, N. and Winoto (2015). Electrostatics and the low salinity effect in sandstone reservoirs. *Energy & Fuels*, *29*(2), 666-677.

Oil

$-NH + H^+ \leftrightarrow -NH_2^+$

$-COOH \leftrightarrow -COO^- + H^+$

$-COOH + Ca^{+2} \leftrightarrow -COOCa^+ + H^+$

Kaolinite Edges

$>Al-O-H_2^+ \leftrightarrow >Al-O-H + H^+$

$>Al-O-H \leftrightarrow >Al-O^- + H^+$

Illite, Smectite Basal Planes

$Na + H^+ \leftrightarrow >H + Na^+$

$>Na + -NH^+ \leftrightarrow >-NH + Na^+$

$>Na + -COOCa^+ \leftrightarrow >-COOCa + Na^+$

$2>Na + Ca^{+2} \leftrightarrow >Ca + 2Na^+$

Calcite

$>CaOH + H^+ \leftrightarrow >CaOH_2^+$

$>CaOH + HCO_3^- \leftrightarrow >CaCO_3^- + H_2O$

$>CaOH_2^+ + SO_4^{-2} \leftrightarrow >CaSO_4^- + H_2O$

$>CO_3H \leftrightarrow >CO_3^- + H^+$

$>CO_3H + Ca^{+2} \leftrightarrow >CO_3Ca^+ + H^+$

$>CO_3H + Mg^{+2} \leftrightarrow >CO_3Mg^+ + H^+$

RESERVOIR: who measured it and why

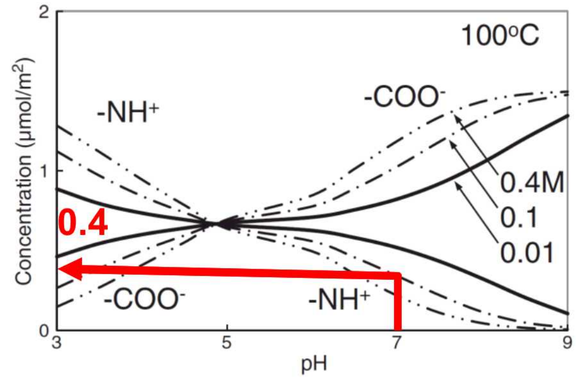
SANDSTONES: geologists, to predict kaolinite reactivity during diagenesis.

SHALES/TIGHT FORMATIONS: Soil scientists, to understand salt movement.

LIMESTONES: geologists, marine chemists, to predict dissolution/growth rates.

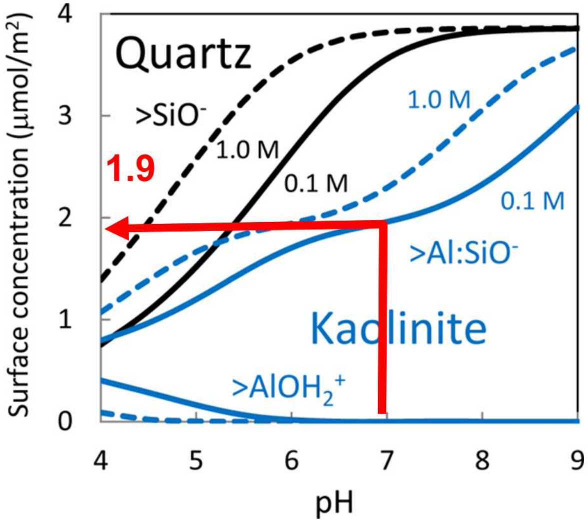
How to Model Oil-Rock Adhesion?

- Disjoining pressure
- Zeta potentials
- **Bond product sum**

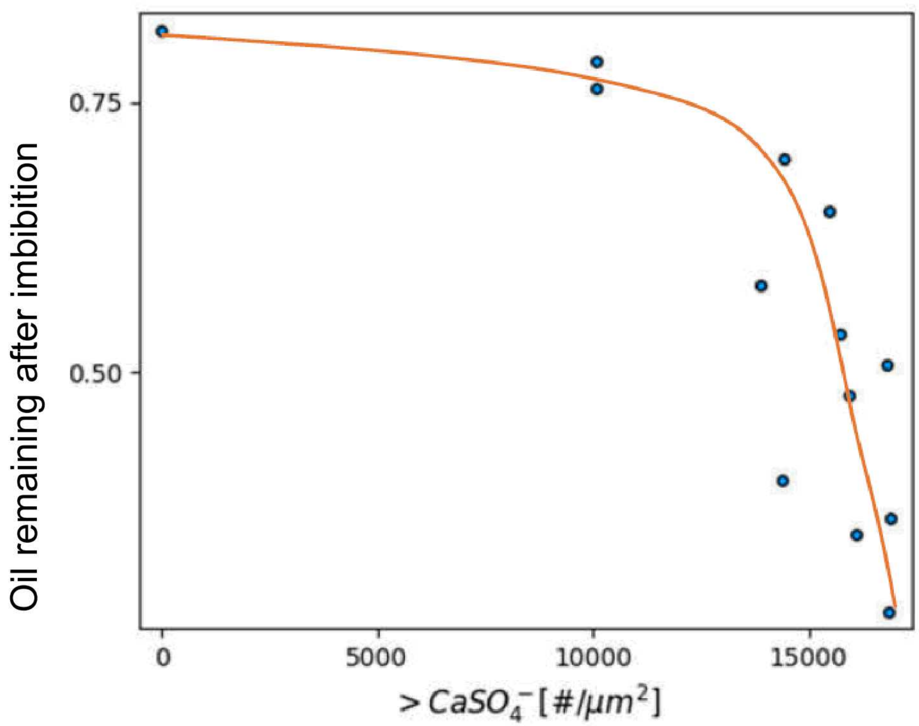


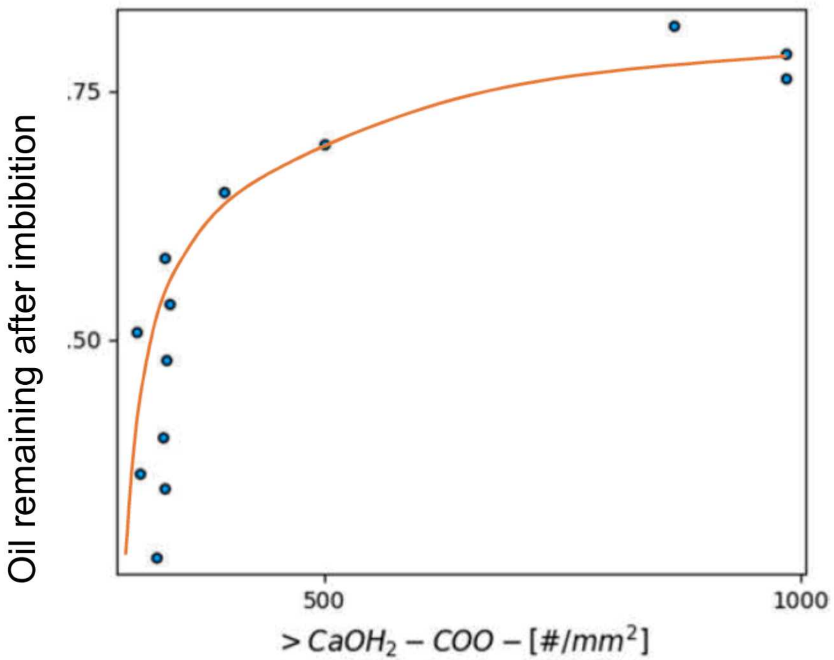
Example: Oil-NH^+ to Kaolinite >AlO^-, pH 7, 0.1M NaCl, 100°C.

Bond product = [-NH^+][>AlO^-] = 0.4*1.9 = 0.76 $(\mu mol/M^2)^2$



Bond Products and imbibition





From: Eftekhari, A. A., H. Baghooee, M. la Cour Christensen, K. Thomsen, H. M. Nick, and E. Stenby. "Uncertainties in the Mechanistic Models of the Modified Brine Water-flooding of Chalk." In *IOR 2017-19th European Symposium on Improved Oil Recovery*. 2017.

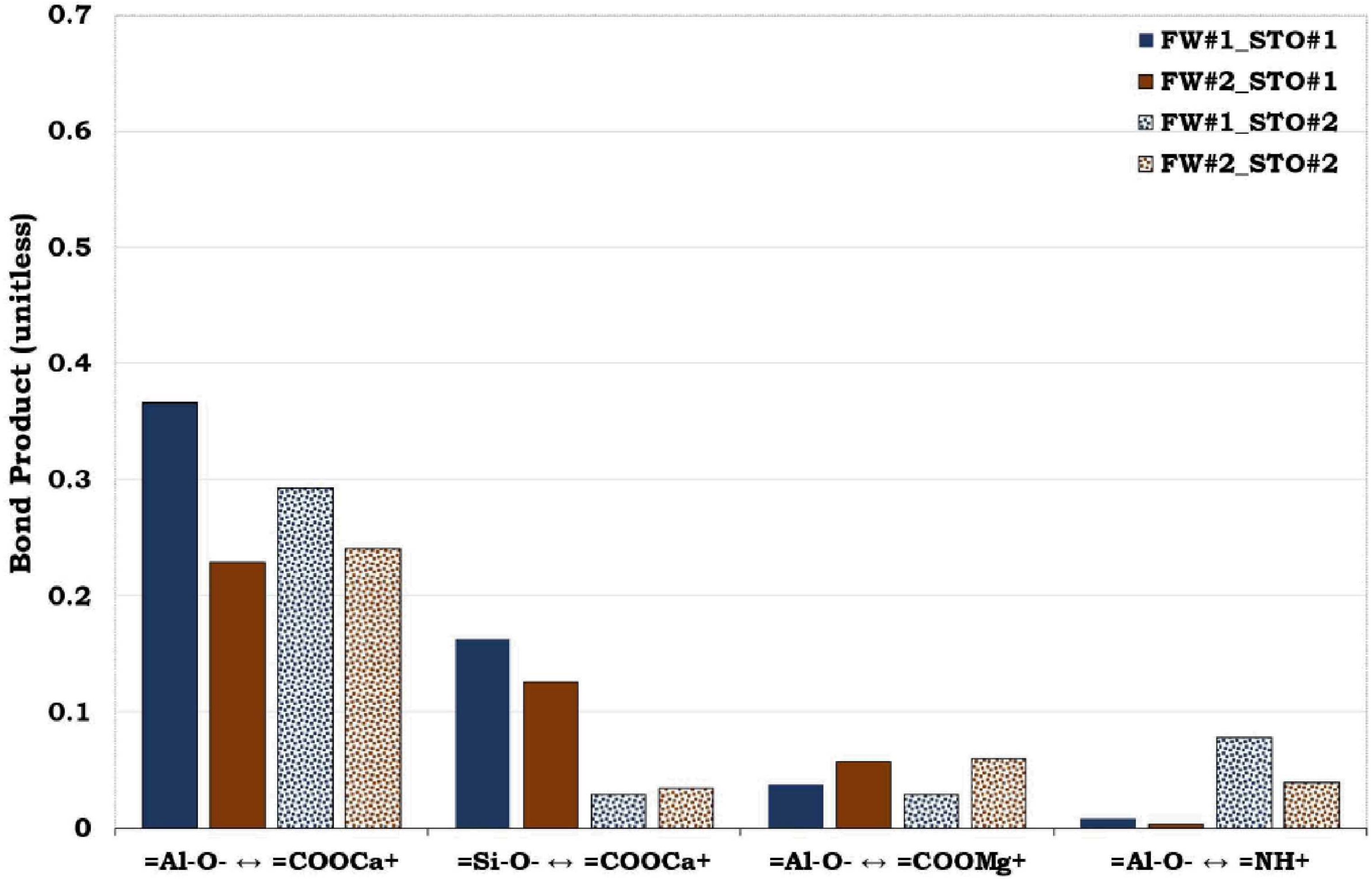
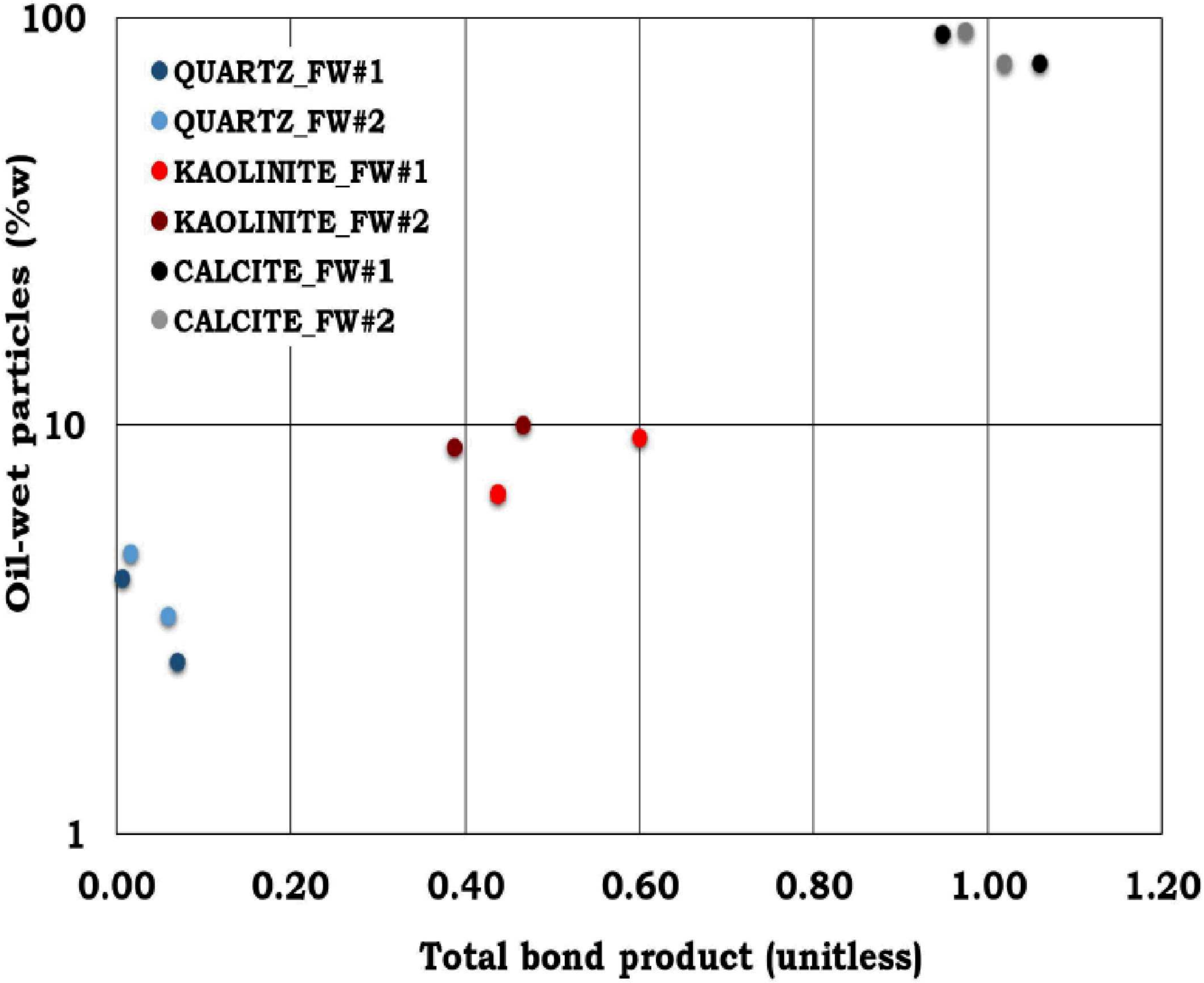


Figure 3—The bond product of the dominant electrostatic pair linkage in kaolinite

From: Erzuah, S., I. Fjelde, and A. V. Omekeh. "Wettability Estimation by Surface Complexation Simulations." In *79th EAGE Conference and Exhibition 2017-SPE EUROPEC*. 2017.



From: Erzuah, S., I. Fjelde, and A. V. Omekeh. "Wettability Estimation by Surface Complexation Simulations." In *79th EAGE Conference and Exhibition 2017-SPE EUROPEC*. 2017.

Bond Products and Core floods

From: Qiao, Changhe, Li Li, Russell T. Johns, and Jinchao Xu. "A mechanistic model for wettability alteration by chemically tuned waterflooding in carbonate reservoirs." *SPE Journal* 20, no. 04 (2015): 767-783.

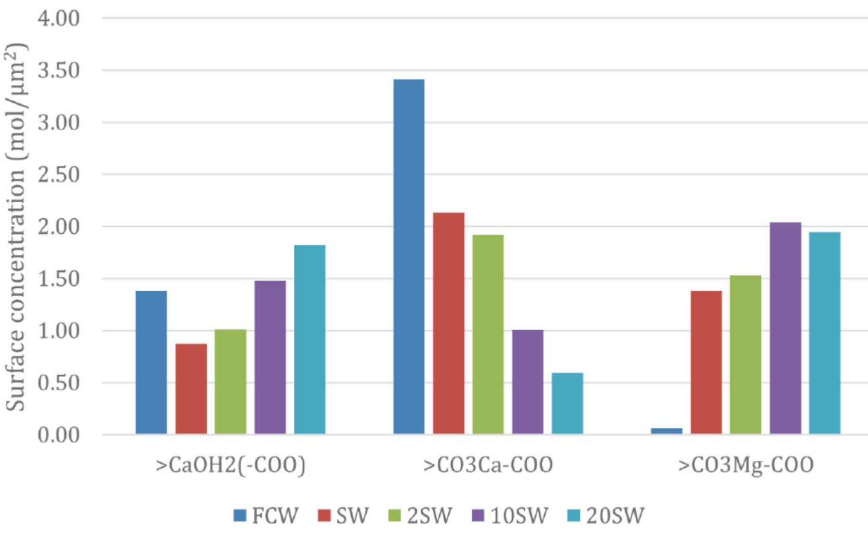
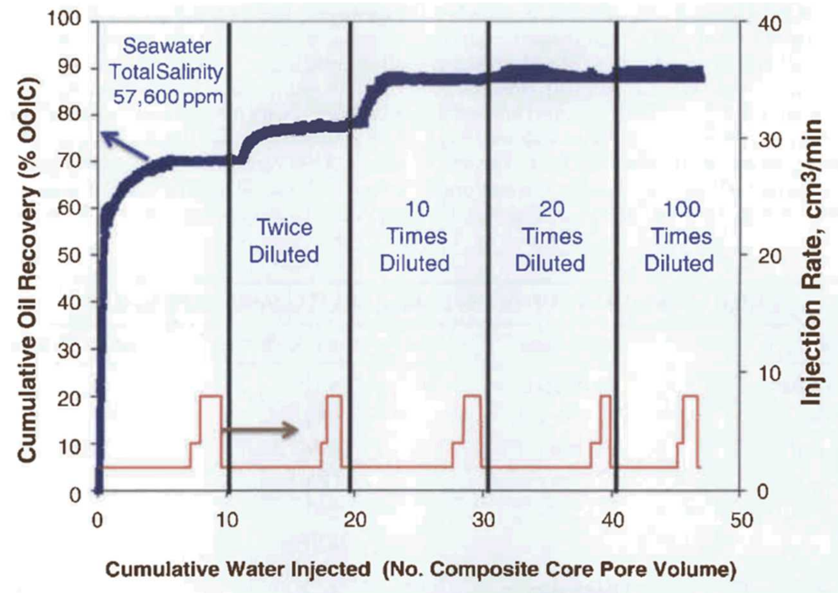
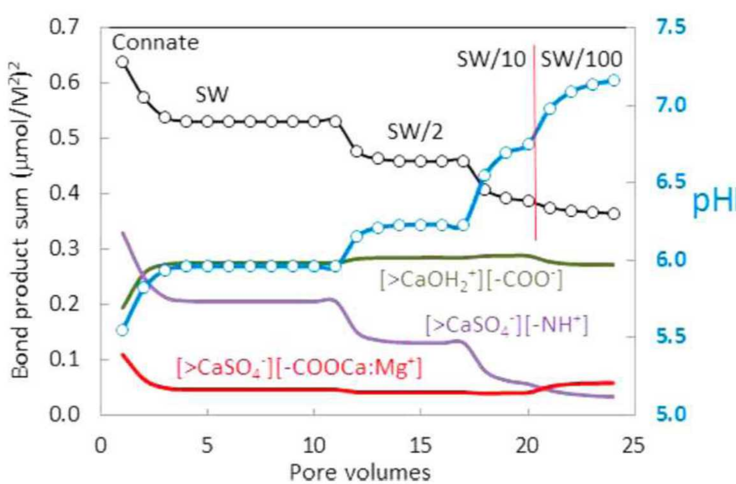


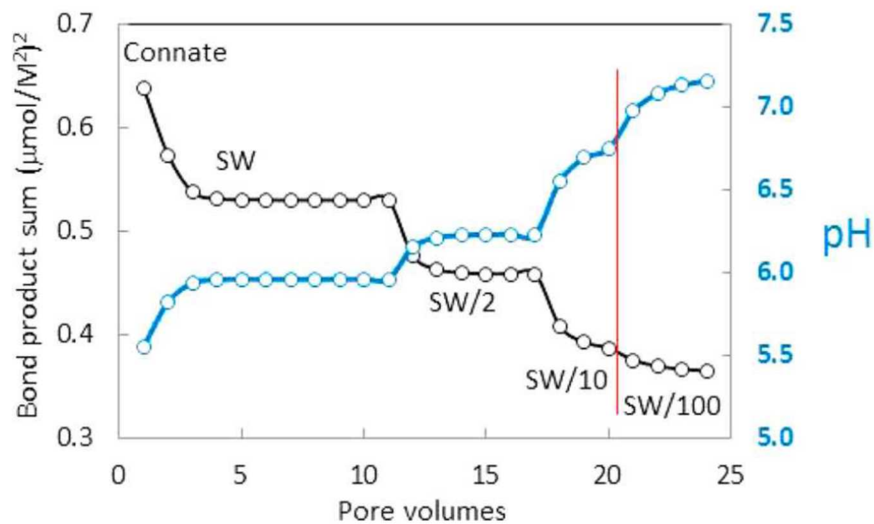
Figure 2—Calculated adsorbed carboxylic acid for brine in Yousef et al. (2010).



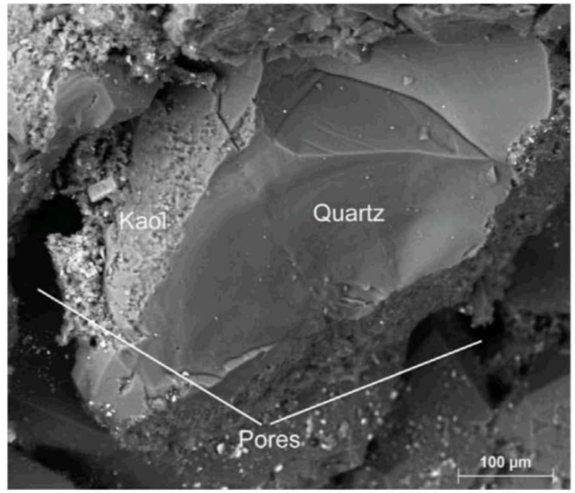
Yousef et al. 2010, SPE Journal

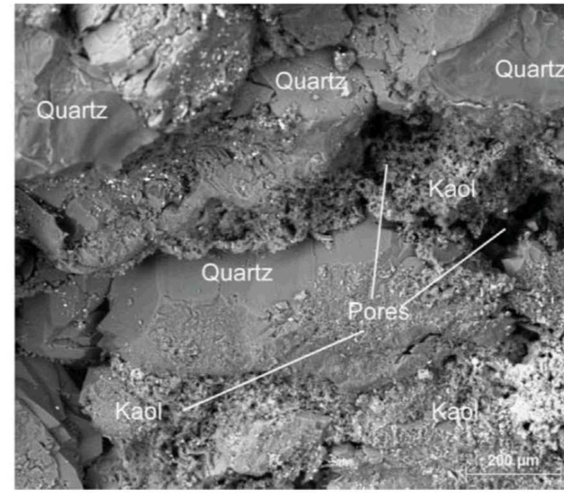
Brady, Patrick V., and Geoffrey Thyne. "Functional wettability in carbonate reservoirs." *Energy & Fuels* 30, no. 11 (2016): 9217-9225.



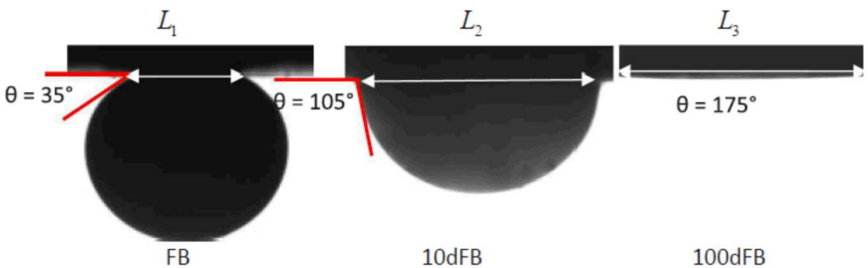


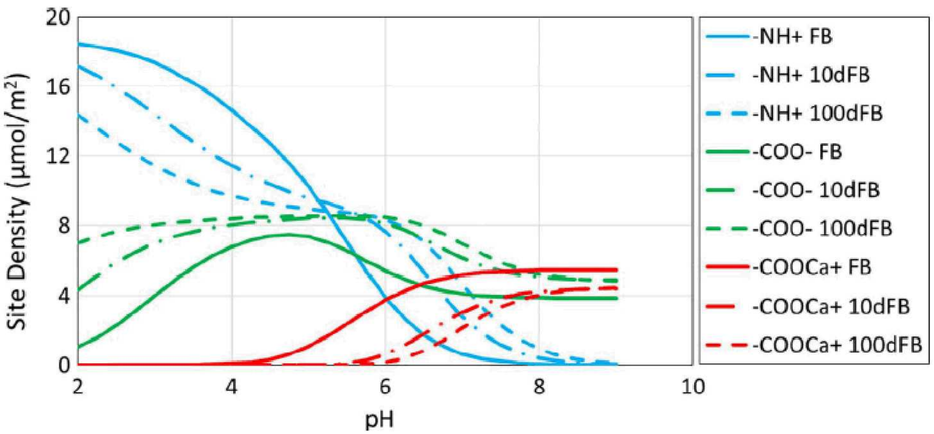
Fines migration,
Temperature,
CO_2 flooding



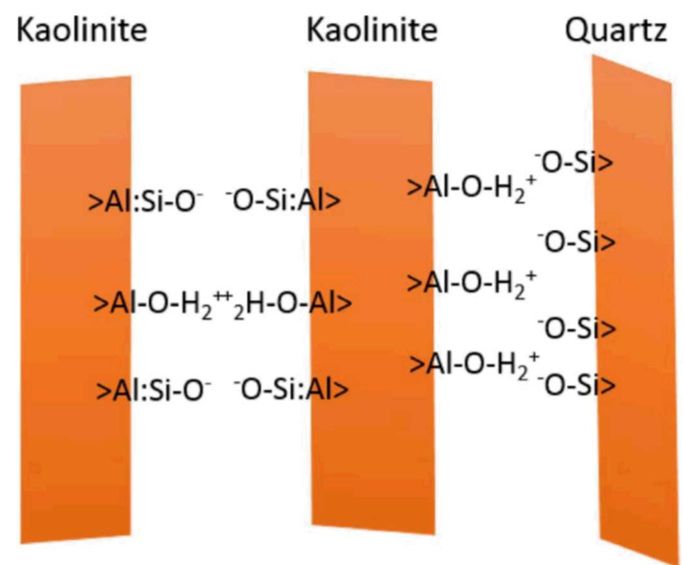


Xie, Quan, et al. "Fines migration during CO_2 injection: Experimental results interpreted using surface forces." *International Journal of Greenhouse Gas Control* 65 (2017): 32-39.



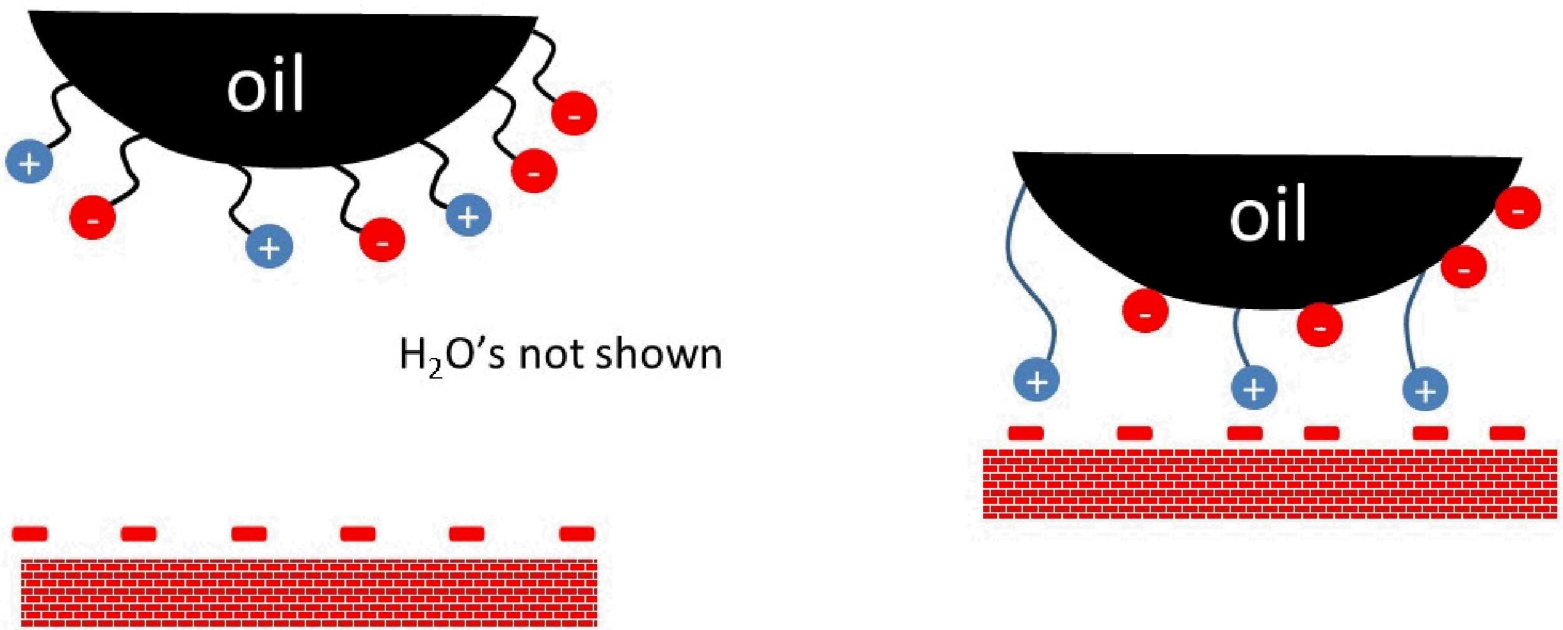


Chen, Y., Xie, Q., Sari, A., et al. (2018). Oil/water/rock wettability: Influencing factors and implications for low salinity water flooding in carbonate reservoirs. *Fuel, 215,* 171-177.



Oil Surface Chemistry Peculiarities

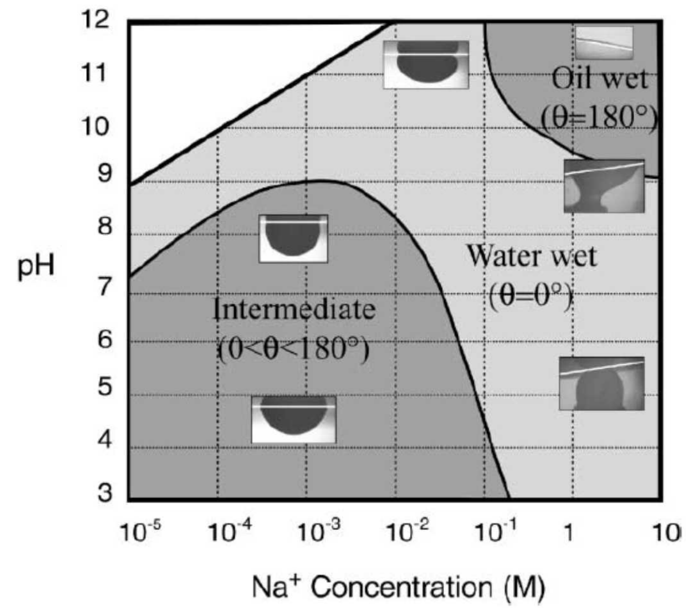
1. Smudged pK_a's,
2. Self-association of acids and bases,
3. Other surface groups.
4. "Hairiness"?



After Somasundaran et al., 1993

Hairy DLVO

Drummond and Israelachvilli (2004) “It is important to emphasize that the results obtained with this crude oil cannot be explained in terms of the DLVO theory alone, and it is necessary to invoke polymer-like steric and bridging interactions, to quantitatively describe the measured force profiles”



Drummond, Carlos, and Jacob Israelachvili. "Fundamental studies of crude oil–surface water interactions and its relationship to reservoir wettability." *Journal of Petroleum Science and Engineering* 45, no. 1 (2004): 61-81.

From Somasundaran et al. 1998, Role of reconformation of hairs in anomalous deposition of zwitterionic latex particles. Colloids and Surfaces.

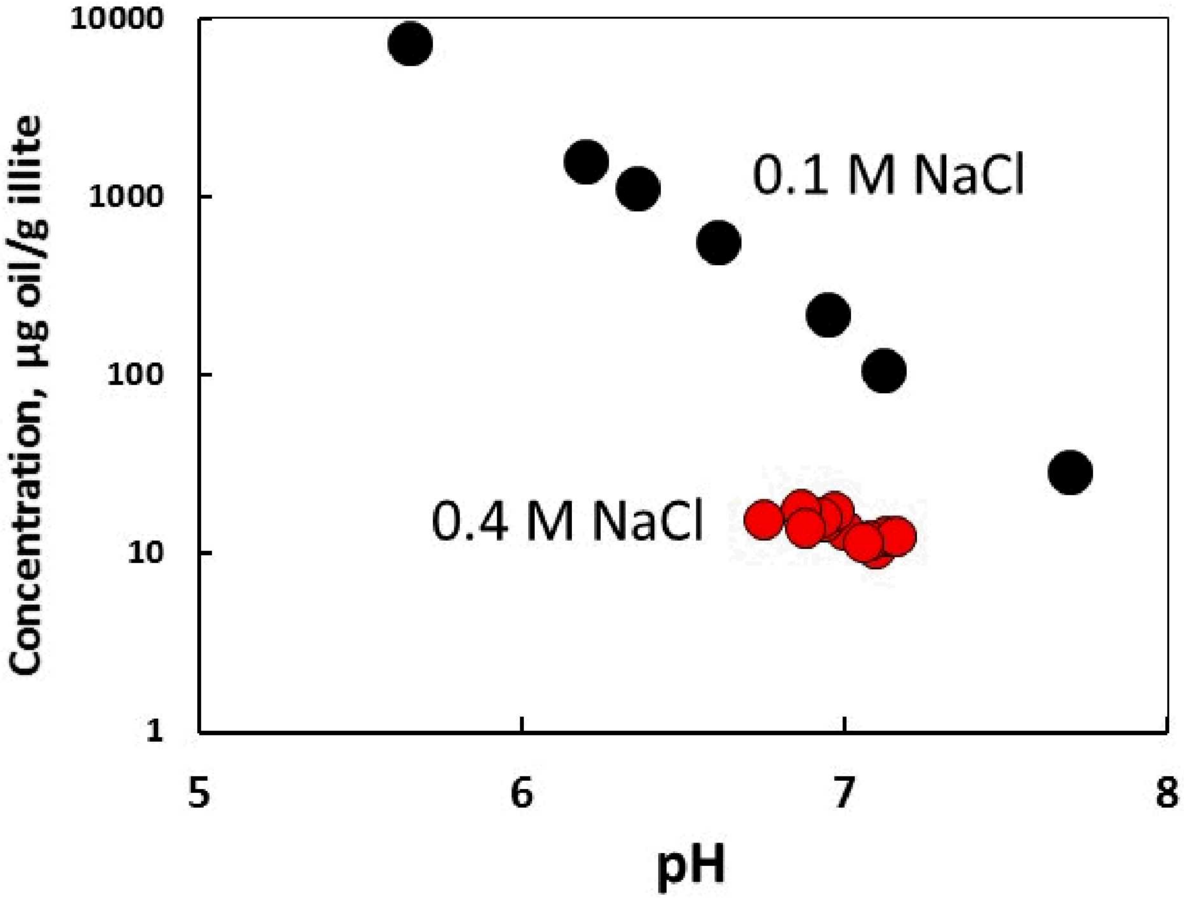
5. Unconventional deposition of zwitterionic latex particles

It is proposed that the deposition of the zwitterionic latex particles to be due to the rearrangement of the mixed charge groups present in the latex surface in such a manner that the positive charge sites are extended towards the glass surface and the negative ones retracted away from it. Thus even though the overall average zeta potential is negative, the hairy charges are proposed to reconfigure when the two surfaces begin to feel each other.

Zeta Potentials tell only part of the story

Oil Adsorption on Illite

Source: C.R. Bryan, Sandia Labs

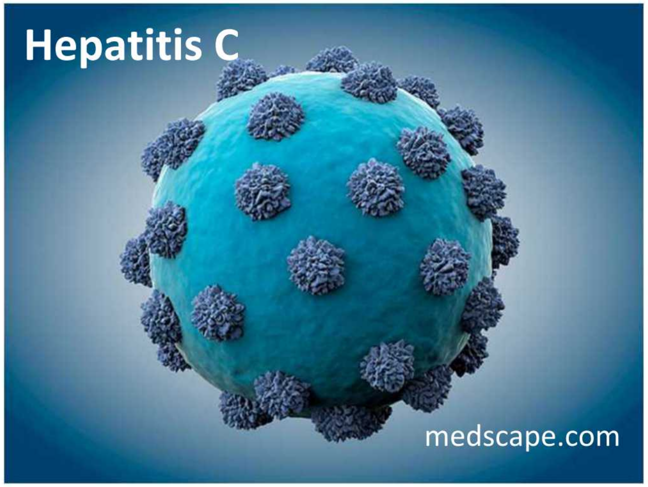


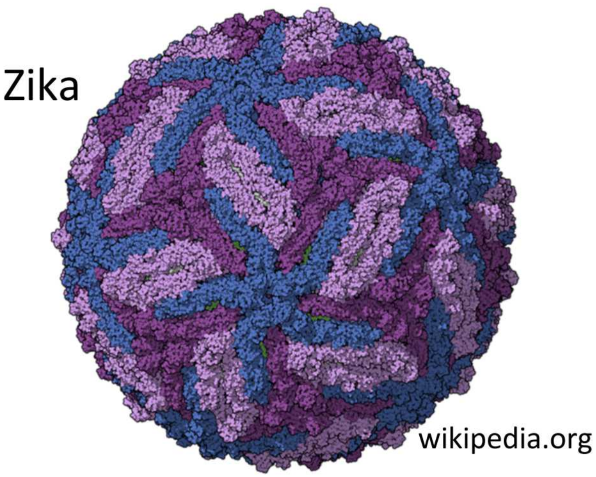
Both Oil and Illite have negative zeta potentials, but there is still sorption.

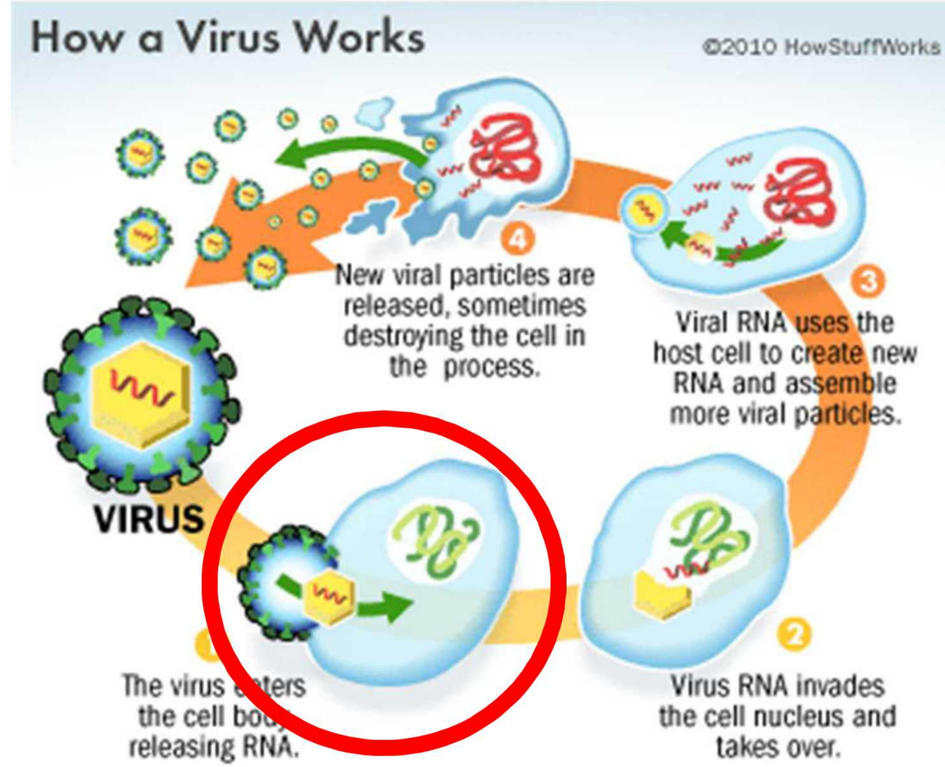
Decreased ionic strength thickens the double layer, but <u>increases</u> oil sorption.

Oil from West Pearl Queen Field, Hobbs, New Mexico

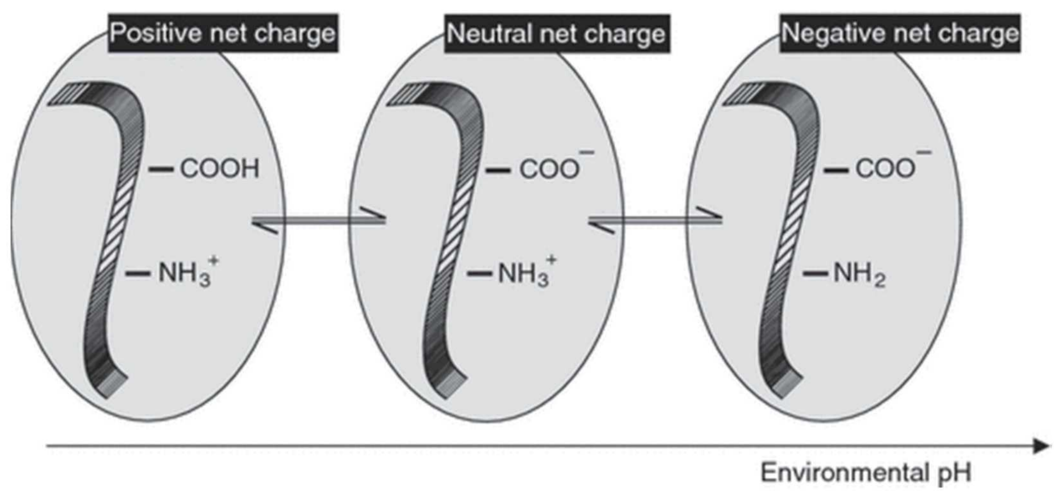
TBN/TAN ~ 1.3



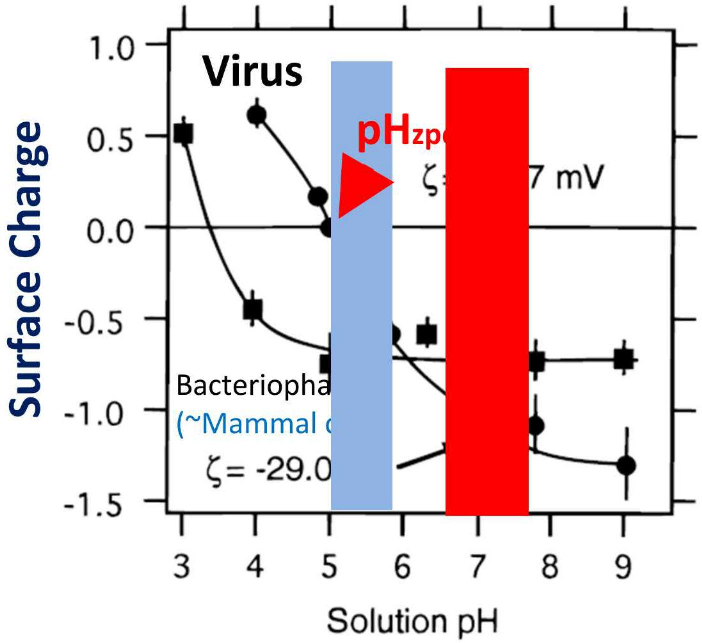




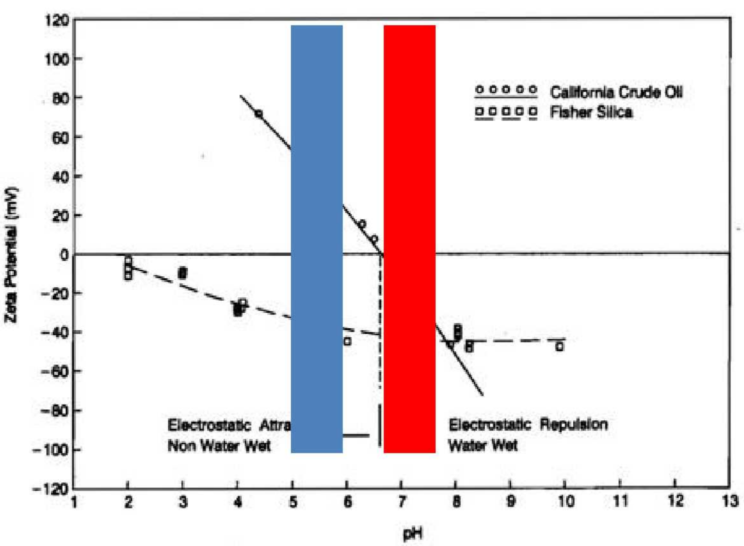
Michen & Graule (2010) J. Applied Microbiology



Endosomal pH 5-6.5 Physiological fluid pH 7.4



From Redman et al., 1997 ES&T



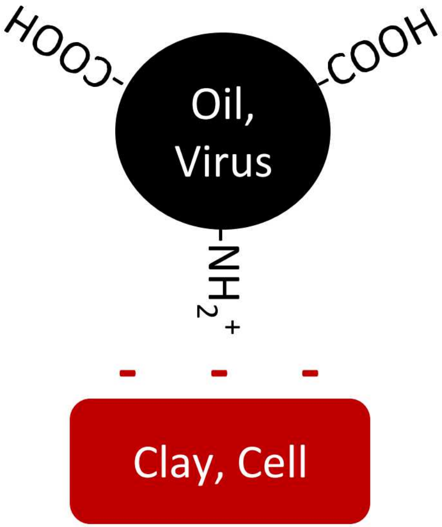
from Dubey and Doe (1993) *Base number and wetting properties of crude oil.* SPE Reservoir Engineering, 8 (195-200).

How to make a broad spectrum anti-viral

1. Shift the endosomal pH from 5 to 7.4 so that virus $-NH_2^+$ groups don't dock to cell $-COO^-$ groups,
2. Do the pH jump with a cationic polymer containing lots of NH_2^+ groups (base buffer capacity).
3. Oops! some of the polymeric NH_2^+ groups will trigger binding to virus $-COO^-$ groups at the higher pH, so.
4. Add more polymeric NH_2^+ groups to make the virus cationic too, so the cell and virus will have the same charge and be repelled from each other.

From Ichiyama et al. (2016)* Cooperative orthogonal macromolecular assemblies with broad spectrum antiviral activity, high selectivity, and resistance mitigation. *Macromolecules.

Better drugs; More oil.



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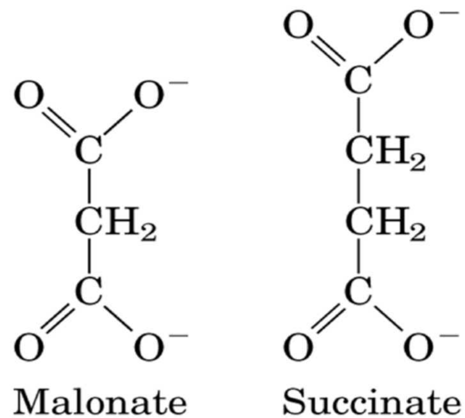

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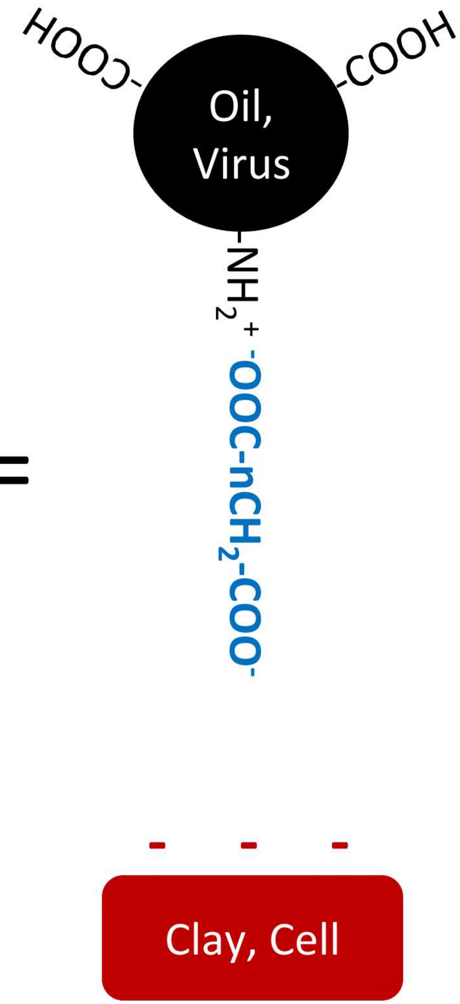


Potential obstacles

More Oil

Solubility w.r.t Ca/Mg

N-Carboxylate binding strength

Better Drugs

Speciation in blood plasma,

Solubility

Linking with proteins,

Toxicity

BACKUP SLIDES

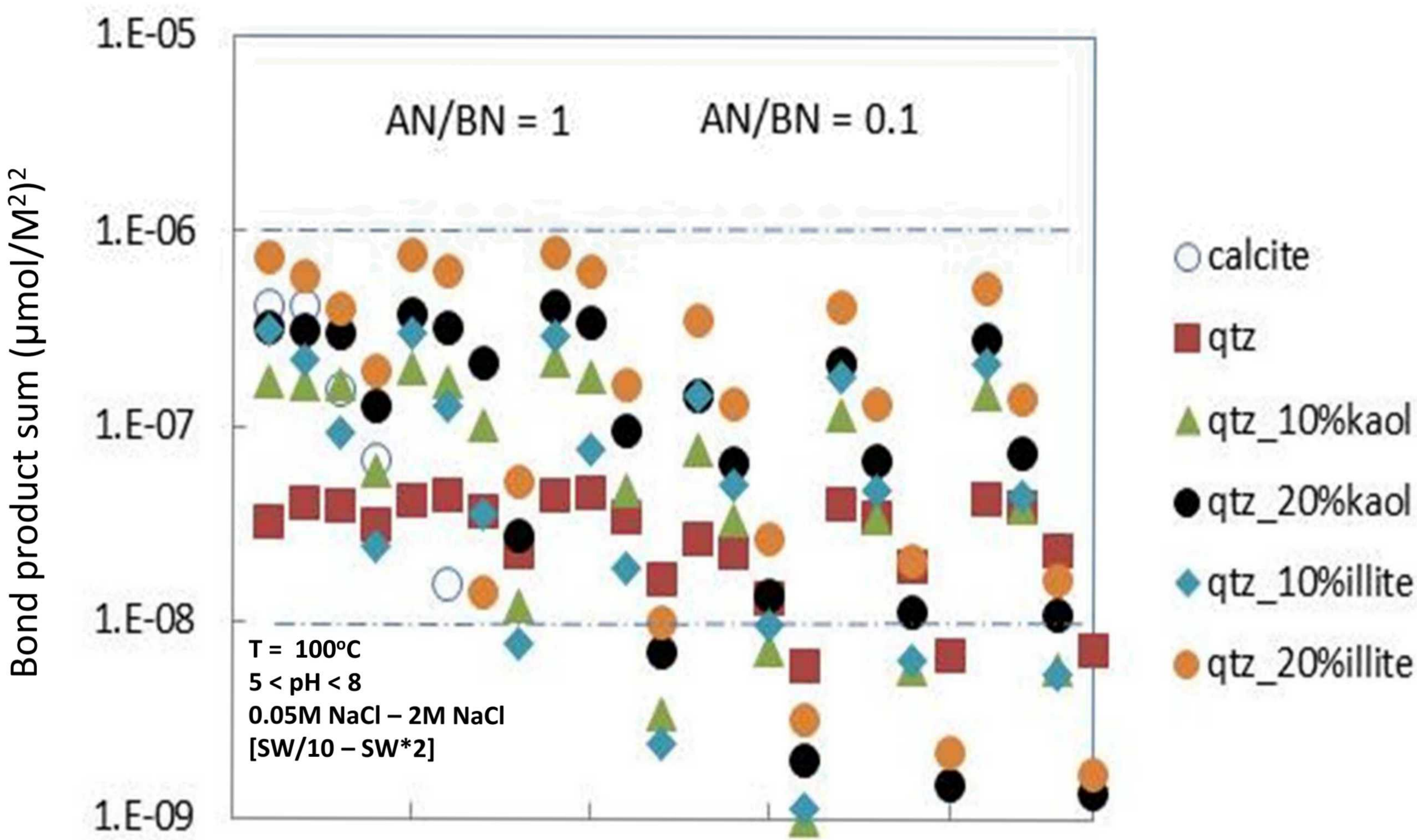
FIND STACK OF VIRUS PAPERS/UPDATE

Oil
Blocking agents
Quan's stuff?
What did you talk about last time? Shales too? Potholes
Highlight austads bunch

Drugs
Insert stuff from virus patent
Everett shock article – WHAT TO COVER
Solubilities (scale formation in our veins)
Virus zpcs
Urgh machine learning?
Scm of hair + shampoo +coditioners? https://blog.anton-paar.com/how-the-surface-charge-of-the-hair-affects-its-care/
Babaks code?

More oil, better drugs
Pat Brady, Sandia National Laboratories
The chemical reactions controlling adhesion of oil to reservoirs and viruses to our cells are very similar. These reactions can be quantified by acid-base surface chemistry calculations and might, in theory, be forward-engineered to produce more oil and/or better anti-viral drugs. Of particular importance are nitrogen bases at the oil or virus surface which are electrostatically attracted to mineral inorganic broken bonds (oil in a sandstone) or surface carboxylate group (virus on a cell). Introducing a chemical agent to block, or reverse, adhesion of N base-bearing oil to a reservoir could enhance oil recovery. A chemical that blocked adhesion of N base-bearing viruses to cells might be an effective broad spectrum anti-viral medicine. Designing such chemical agents is most easily done

Initial Wettability and Primary Recovery



Oil Adhesion to the World's Reservoirs