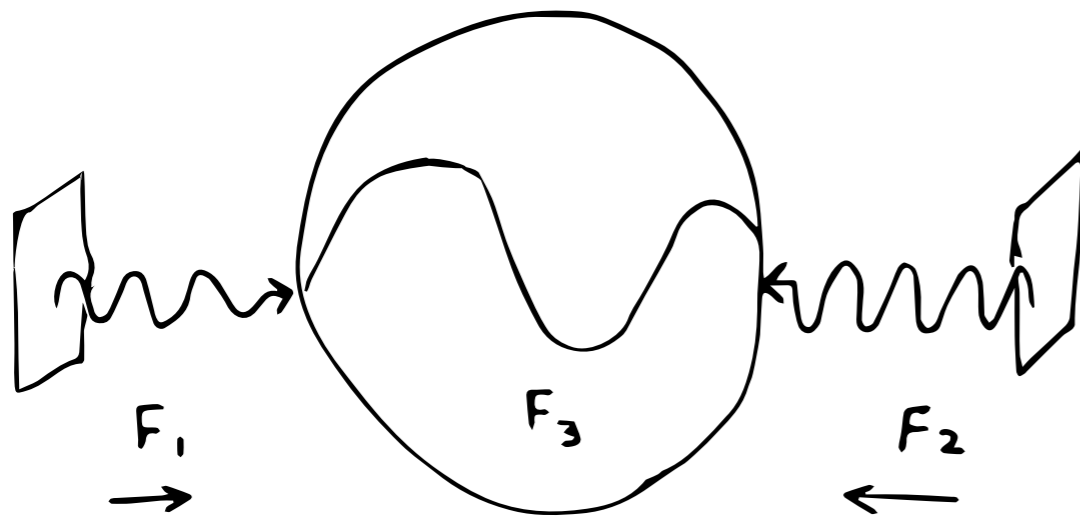


# Novel heterodyned RF concepts for cancer medicine and anti-viral applications

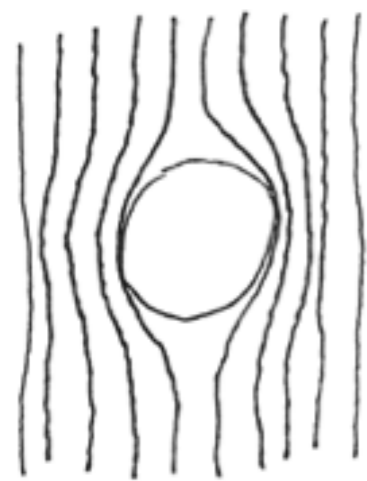
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Presented to the Australian Centre for Electromagnetic Bioeffects Research (ACEBR)  
Science and Wireless 2015 Public Forum at RMIT, Melbourne

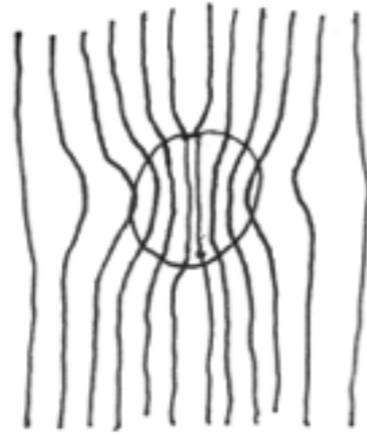


## **HRIFE TECHNOLOGY : COMBINING RADIO WAVES**

Usually, it is not possible for the human body to absorb electromagnetic (EM) fields below around 300 kHz. The proposed HRIFE technology can superimpose two parent radio frequency (RF) waves at frequencies  $F_1$  and  $F_2$  to generate a third lower frequency  $F_3$ , given by  $F_3 = (F_2 - F_1) / 2$  (RF heterodyning). HRIFE stands for Heterodyned Radiofrequency Induction Field Emitter devices. One possible medical application is to inject internal alternating electric fields at frequencies below about 34 kHz that can induce ionic eddy currents (Warburg limit).

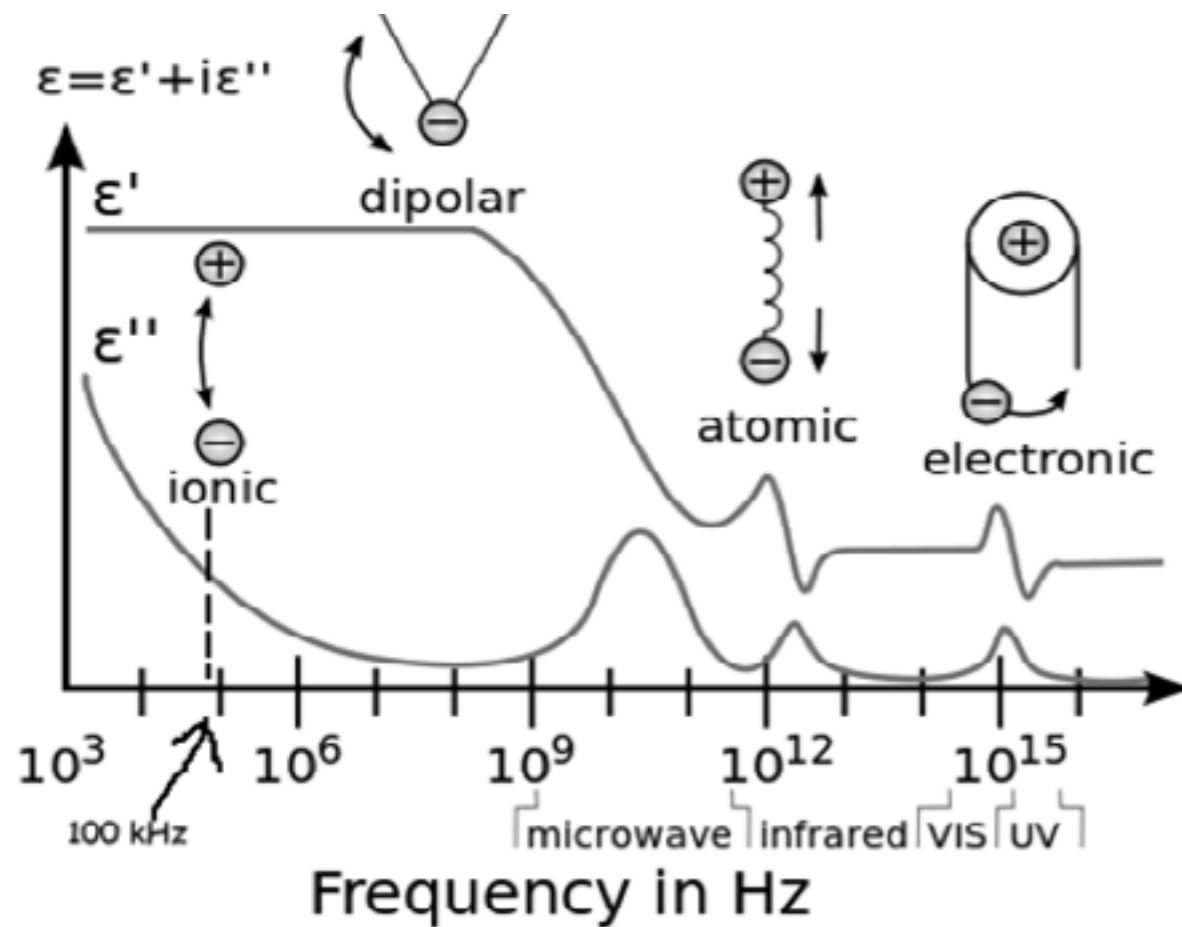


10 kHz



1.0 MHz

Perturbation of electric field lines by a lossy dielectric object during EM exposure. RF radiation is absorbed by animal bodies but Low Frequency (LF) electric fields do not penetrate.



Bode plot or Nyquist plot. Contributions by real and imaginary components of permeability that determine impedance are shown. Real (ionic) currents tend to dominate at frequencies below 100 kHz, but real currents are insignificant in the RF range.

The Warburg limit of ionic current induction is approx 34 kHz. Above around 100 kHz, imaginary current (also including the so-called displacement current) begin to dominate. Ionic currents tend to cancel out internal E-fields. Also, back-electromotive force from cationic current is opposed and cancelled by that from the anionic current. Later in this presentation we look at whether H<sup>+</sup> ion currents can exist.



## FASCINATING FACTS FROM HISTORY

A blip at around 60 GHz in the Bode plot allowed Russian researchers in the 1970's to exploit real current phenomena to kill bacteria within narrow frequency windows. (Shashlov et al). 60 GHz cannot be achieved in HRIFE applications, but it may be possible to kill virus within the LF or lower RF ranges by exploiting putative resonances in virus icosahedral macrostructures.



## LOW POWER LIGHT FOR VIRUS KILLING

American researchers used low average power femtosecond pulsed laser light to inactivate Tobacco mosaic Virus by energetically disrupting the molecular packing (Tsen et al).

## WHY ADD ENERGY SPIKES ?

The amount of energy in HRIFE applications may be enough to begin to induce motion or mechanical strain in some macromolecules or in virus walls, but additional energy from some other device may be required to actually break them when they are vibrating. The most powerful type of energy is Ultrasonic shock waves. The idea is to synchronise the timing of shock wave repetition to the match F3 HRIFE output (or a subharmonic). Other candidate technologies might be electric field spikes, or electric discharges or radar-like very intense very short-pulsed microwaves (thermoelastic shock waves).



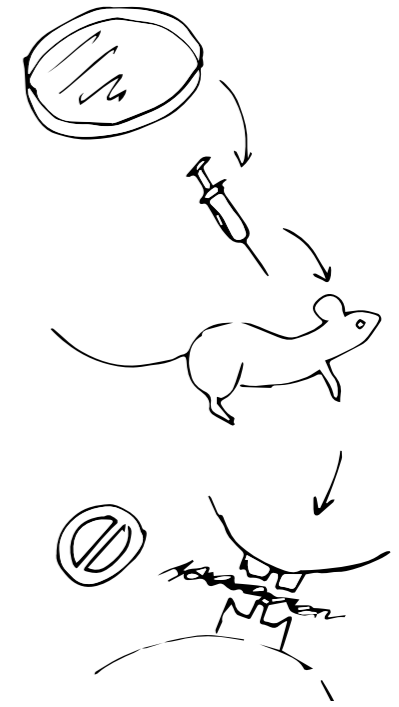
## SHOCKING FACTS ABOUT SHOCK WAVES

Certain ultrasound devices can inject sound waves into tissue. (Extracorporeal Shock Wave Therapy or ESWT). Energy is transformed into tiny bubbles (cavitations) which form at solid-liquid interfaces. They undergo implosions to release large amounts of energy focused on cell surfaces. ESWT could be useful in an "anti-fouling" modality for cancer ("slime busting").

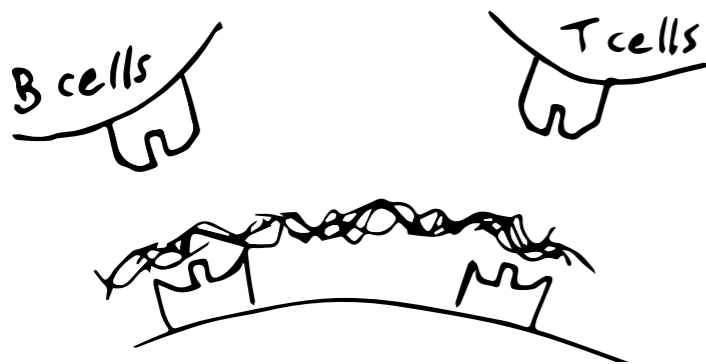


Polysaccharides are electronegative branched filamentous macromolecules that can experience induced forces by low frequency internal E-fields from HRIFE. Induced pendulum-like motion is opposed by drag from surrounding water molecules. Mechanical strains arise due to uneven distribution of the opposing forces. If synchronised energy spikes are also applied, covalent bond breakage is predicted particularly at branching points. HRIFE beat frequencies below 4 Hz might help reduce the water drag effect and enhance bond breakage.

### CAN HRIFE SUPPLEMENT IMMUNOTHERAPY ?



Mice injected with T-cells cloned in the lab that recognise a specific tumor antigen are injected back into the mouse (autologous T-cell therapy). Autologous therapy usually fails, possibly due to antigen masking and / or immunosuppression.



Antigen masking by polysaccharide deposits. Immune recognition of cancer cells can fail when slimy deposits block the access of immune receptors.

One proposed use for HRIFE combined with shock waves or other types of energy spikes is as an anti-fouling modality to unblock the immune cells' access to tumor antigens. This may also improve the outcomes for autologous T-cell therapy

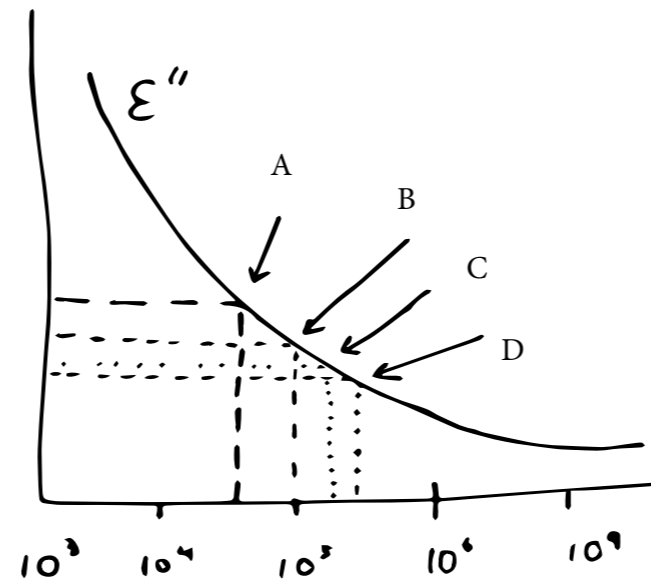


## WHY USE 300 KHZ IN CANCER THERAPY ?

100 kHz to 300 kHz was shown to inhibit tumor growth and cause mitotic arrest and spindle alignment in a mouse cancer model in vivo and in vitro while not affecting normal cells. The proposed mechanisms were a) that natural morphogenic fields became aligned and b) these frequencies were optimal to generate dielectrophoresis forces that prevented polymerisation of the growing filaments. However, it may be that a mechanism of proton current could also be usefully exploited at 300 kHz.

The principle of the Warburg frequency threshold for ionic current induction could be extended to model a frequency threshold for a proton motive force. If we roughly model the Warburg threshold as applying to a set of ions with a mean molecular weight of 20 ( $m_w = 20$ ) as 34 kHz, then we might assign an upper threshold for  $H^+$  ( $m_w = 1$ ) above 600 kHz. Any "proton current" at 300 kHz would be unopposed by any cationic current, and thus might cause a back-electromotive force, with an inductive force on free electrons. An increase in the probability of hydrophobic attack events and / or of Reactive Oxygen Species production (ROS) might occur. The dynamics of proton-exchange ion channels might be affected. Other targets in cancer medicine might be the Krebs cycle or the cholesterol metabolism.

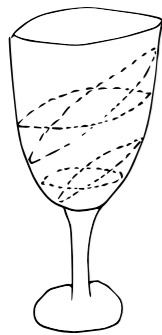
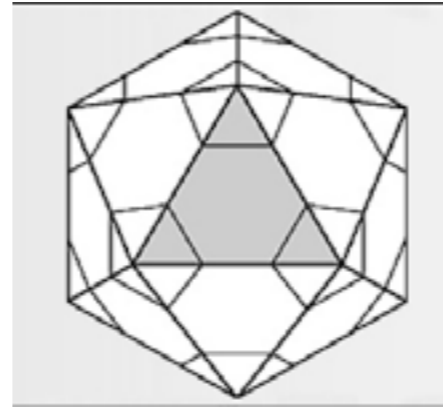
300 kHz is at the far lower limit of the RF spectrum. It does not capacitatively couple very efficiently to the human body due to sub-optimal field perturbation, and its SAR or heating power is poor. It is proposed to select higher RF carrier frequencies between 2 MHz and 100 MHz in a heterodyning protocol such as HRIFE. A triple or quad carrier protocol could generate additional ELF beat frequencies if required. Even if the primary therapeutic goal is for anti-fouling therapy, involvement of 300 kHz may be synergistic.



Extrapolating from the Nyquist plot, we can define frequency regions for a) the Warburg limit of ionic current induction at 34 kHz, b) the upper threshold for low mass ions like Lithium near 100 kHz, c) the proposed optimal frequency for proton current induction around 300 kHz and d) the roughly estimated upper threshold of proton current induction above 600 MHz.

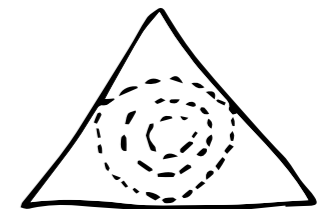
## CAN HRIFE SHATTER VIRUS WALLS ?

Many virus species have regular spherical icosahedral geometry composed of adjacent isosceles triangles. (See <http://vipfdb.scripps.edu>). We can model each triangle as being stiffer on the outside edge than in the center. This drumskin-like phenomenon could support tympanous vibrational resonance. The pentagonal profiles might also support resonance. Whole-sphere resonances could also occur. It should be possible to use HRIFE exposure to entrain virus capsid walls into vibrational resonance. Addition of synchronised high-energy spikes from shock waves or other sources might be able to cause structural damage when applied to a vibrating system.



A wineglass stroked by a finger along the rim can go into singing resonance. Many frequencies from the applied acoustic white noise can couple into this resonant system because many path lengths are available.

In a simple vibrational mode, a triangular plane of a virus wall may also be able to couple energy from a wide window of frequencies. HRIFE applications probably contain white noise that is modulated at the F3 frequency. Where F3 matches the native resonance, energy coupling might be further enhanced. Even though white noise from background Brownian motion is much larger than the noise from sine modulated ionic current, when we consider amplitude fluctuation at F3, the large offset is irrelevant. Similarly, any thermoelastic effect of the F3 beat frequency modulation of heat absorption of the RF carriers could transform into sinusoidal pressure fluctuation, and again the existence of a large “average SAR offset” also has no impact on the acoustic transformation.

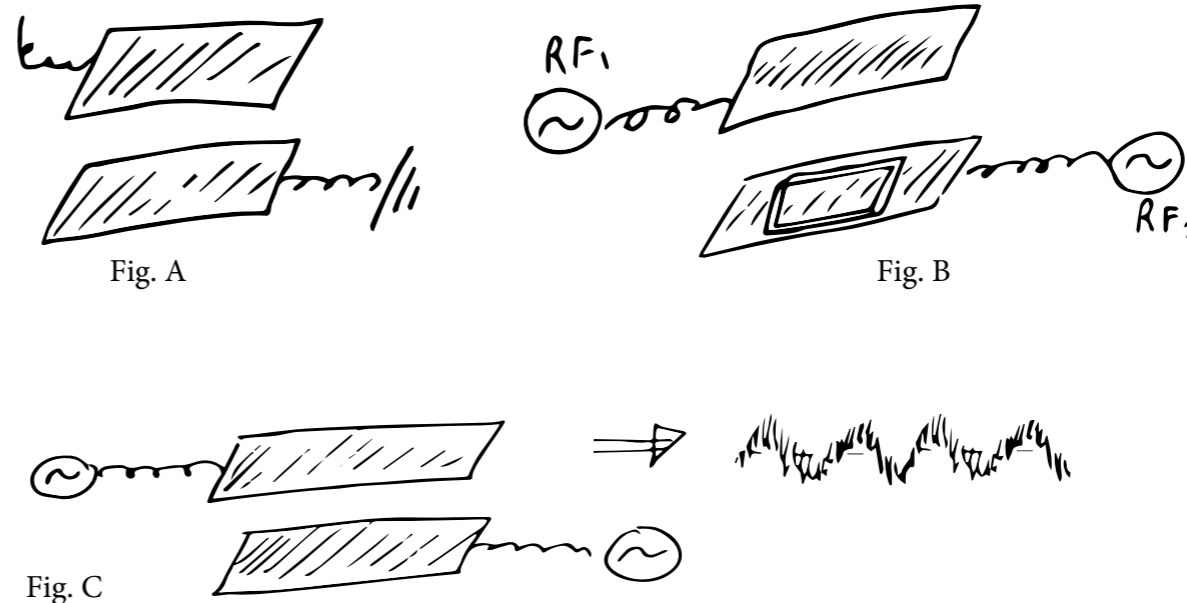


## HOW TO DETECT VIRUS RESONANT FREQUENCIES ?

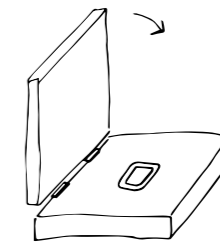
The slow way to discover virus resonant frequencies is to scan many windows of HRIFE F3 frequencies and then later assay changes in the replication rate by measuring the virus DNA content by real time PCR assay. It may also be possible to develop nanochambers for spectroscopy methods including monitoring SWR (Standing Wave Ratio), or Low Frequency Impedance spectroscopy using a reference current synchronised to F3. It may also be possible to adapt high resolution optical imaging systems such as SIAM, or possibly to adapt the new Low Frequency Impedance Spectroscopy imaging systems to detect physical vibration during a HRIFE scan.

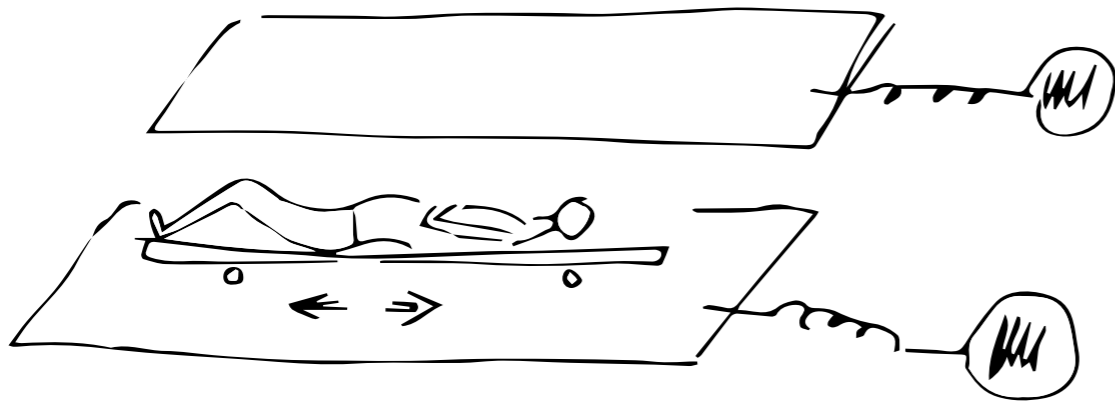
A primitive optical interferometric method is to image a discrete virus particle smaller than the Abbe limit of approx 0.3 micron to produce interference rings (Arie discs) and then perform frequency scans while monitoring by eye or by a real-time digital algorithm. Fuzzing of the band boundaries indicates vibration. A prototype exposure system developed at Griffith Uni School of Physics in 1996 can expose microscope cover slips to RF electric fields (see next panel).

Indium Tin Oxide coated glass slides are conductive but they remain optically transparent. They can be used for RF and HRIFE exposures for in situ microscopy. Schemes shown are: a) earthed bottom plate with superimposed HRIFE signals to top plate, b) RF1 and RF2 to separate plates (gasket shown) and c) RF carrier to top plate with IF or LF signal to bottom plate, to generate offset modulation of RF carrier.

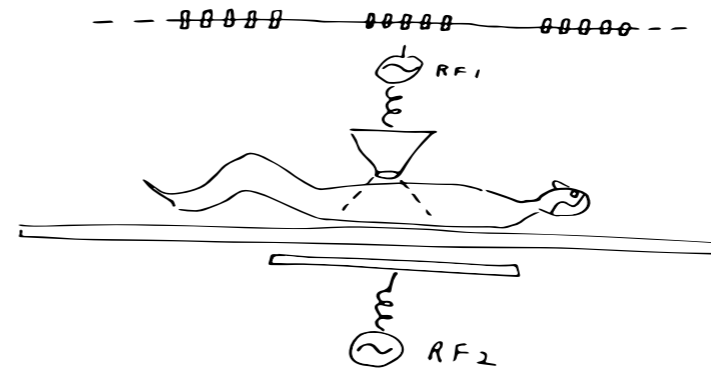


A fold-down chamber with a small gap of less than 1 mm can be adapted from the Nanodrop design. Here a containing gasket is shown which can house a virus suspension or a coverslip with cultured infected cells.

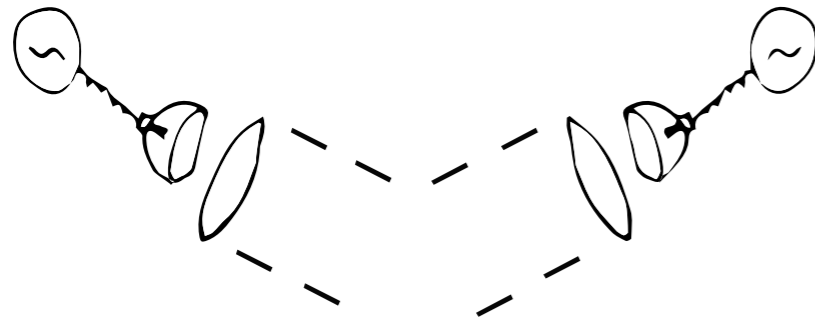




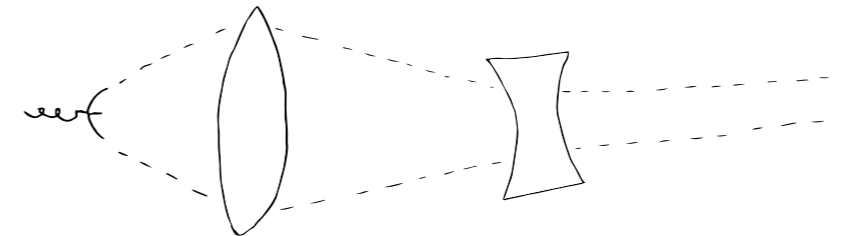
Capacitive coupling



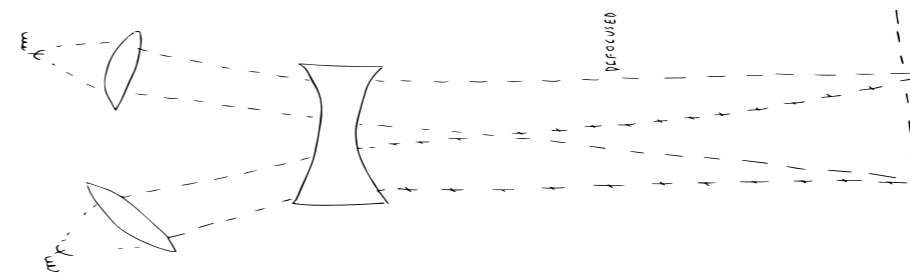
Variant based on the Oncotherm configuration



Angled configurations may be desirable because opposed-wave configurations might result in technical issues from F2 signal going up the F1 coax line (signal cross-reflection). Although apparent wavelength of F3 will vary with the angle, frequency of F3 does not vary.

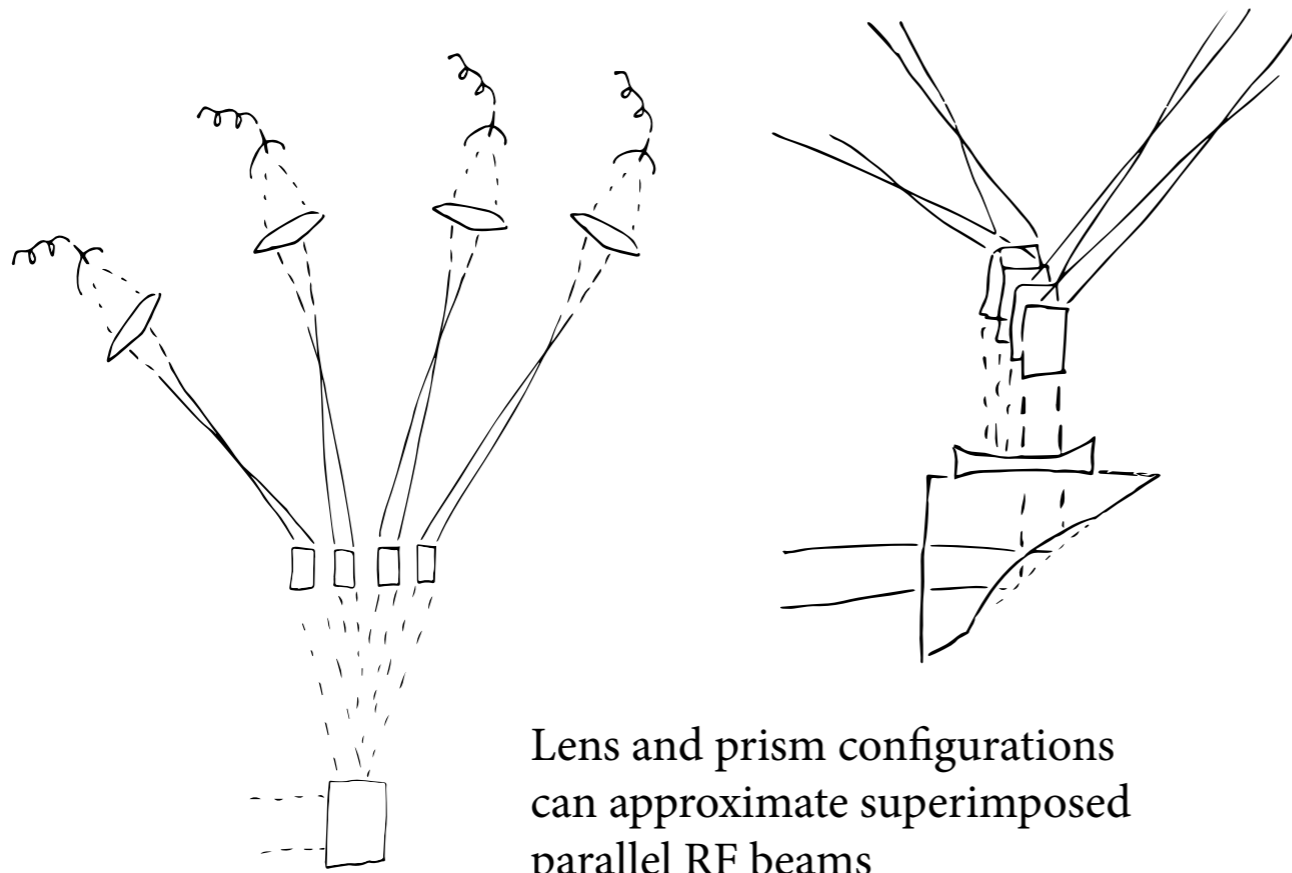


A collimating lens can create parallel RF beam

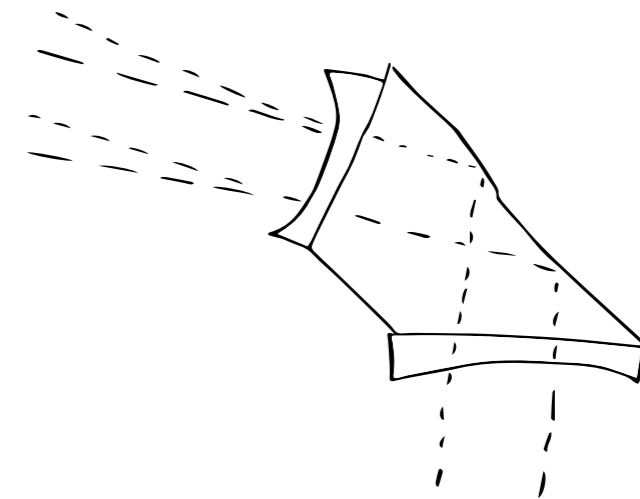


Dual or quad simple defocused





Lens and prism configurations can approximate superimposed parallel RF beams



Using a TIR prism and lenses to create a parallel RF beam

### IMMUNE STIMULATION RX ?

There is some evidence that acute RF exposure can stimulate transient immune hyperactivity, possibly after a cytokine cascade. ESWT shock waves are also thought to enhance healing responses and capillary blood supply. These effects might be synergistic.

## **ELECTROMAGNETIC COUPLING**

HRIFE is predicted to allow electromagnetic coupling of F3 to biological macro-assemblies and / or macromolecules that possess net electric dipole. These could include macromolecules such as electronegative polysaccharides that can mask tumor antigens.

Virus tend to associate with lipid cell membranes. The phospholipid molecules could impart net electric dipole moment to the virus macrostructure. Any “electric charge geometry” of virus walls may allow HRIFE to couple energy into excitation of virus resonance with a goal of vibrating the virus capsid wall.

## **ACOUSTIC TRANSFORMATION**

Some effects of internal electric fields at Low Frequencies (LF) could be to transform the energy state of the parent RF waves into acoustic modes via various putative mechanisms including :

- a) modulated kinetic energy from ion collisions
- b) a thermoeleastic pressure oscillation at very low amplitude
- c) where a sharp rise-time pulse gating scheme is applied, tiny sonic clicks are generated by the thermoelastic effect.

The amplitude of thermoelastic effects is directly related to RF parent SAR or power. Acoustic energy could be useful in anti-fouling applications and to possibly to couple energy into a resonant virus wall or capsid macroassembly. Acoustic impacts could be synergistic or helpful when combined with IF or LF electromagnetic coupled energy. Both types of energy are predicted in HRIFE applications, and they both manifest at the F3 frequency.

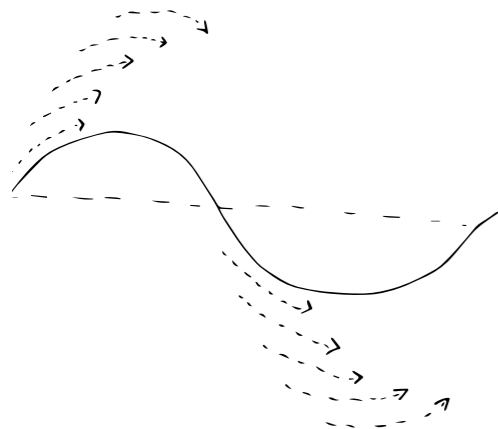
## **TRIPLE RF COMBINATION**

Heterodyning multiple RF parent waves can generate two or more F3 waves in the LF or IF ranges. When these secondary products interfere with each other, it is possible to generate another frequency in the Extremely Low Frequency range (ELF). Triple constructive interference allows three parallel beam devices to achieve instantaneous E-field intensity values at the triple antinodes that are relatively high. When a gating scheme with 10% duty cycle is applied to a system using three RF beams each at a nominal SAR of 100 W/kg, average heating would be reduced from 300 W/kg to only 30 W/kg, suitable for mild or tolerable hyperthermic effect. Where desired, hyperthermic exposure can be limited to the abdomen or even smaller regions by using focusing RF lenses. A quad configuration is also possible.

## PULSE GATING

HRIFE signals can be rapidly switched on and off as a square wave pulse gating with fast rise-time, with 20% duty cycle in synch with F3 (biphasic). This may be useful to reduce average bulk heating. An additional or second slower switched gating can also be added to help eliminate cellular acclimatisation to the stimulus (50% duty cycle or less). Again, pulse repetition rates are synchronised to be a sub-harmonic of F3.

In theory a 5-pulse train gating scheme with a relaxation period may allow some leeway for frequency mismatch tolerance between a native resonance and the applied frequency. In the diagram, a train of five consecutive HRIFE pulses are applied (biphasic) and the applied F3 is +/- 5% mismatched to the native resonance, but destructive interference is avoided. Hit-or-miss protocols with 10 scan windows per decade are permitted in virus research.



The diagram shows a 5-pulse train (dashed lines) with a 5% mismatch of frequency to the native resonance (solid line). Each consecutive pulse is illustrated as 18 degrees advanced. Because the pulses are applied with much shorter duration than the native resonance, destructive interference is avoided.

## WHAT IS THE BEST PARENT RF SAR ???

Usually there is some power loss or attenuation of RF as it penetrates deeper inside flesh. The actual SAR or heating power of the parent RF waves are irrelevant to the amplitude or strength of internal F3 E-fields, except for the influence of parent RF attenuation on F3 attenuation. However parent SAR would be important to optimise if we want to exploit some of the putative thermoelastic acoustic transformation phenomena. 100 MHz exposure gives a much higher SAR than 2 MHz exposure.

Attenuation or power loss in a human becomes increasingly significant above 100 MHz - 500 MHz. Elephant diathermy (or RF heating therapy) requires below 20 MHz and mouse diathermy can be over 1,000 MHz. Carrier selection is a trade-off between the benefit of lower heating using lower frequency where electromagnetic coupling is the primary goal, versus higher frequency where some of the acoustic effects are more pronounced. Where ISM bands are used, choices are more limited.

# ISM HETERODYNING FOR CANCER RX

## DUAL- HEAD ISM HETERODYNING SCHEME

$$27.12 \text{ MHz (+ 300 kHz)} = 27.42 \text{ MHz}$$

$$27.12 \text{ MHz (- 300 kHz)} = 26.82 \text{ MHz}$$

Heterodyning gives 300 kHz

## TRI- HEAD ISM HETERODYNING SCHEME

$$27.42 \text{ MHz} \quad 27.422 \text{ MHz} \quad 26.82 \text{ MHz}$$

Heterodyning gives 300 kHz and 302 kHz

Secondary heterodyning gives 1.0 kHz

## “HETERODYNAMIC THEORY” : PHYSICS OF THERMOELASTIC ACOUSTIC TRANSFORMATION IN HRIFE APPLICATIONS

In ungated HRIFE exposure, we can write the inductive force of an internal E-field at frequency F3 as  $B \sin \omega t$  where  $\omega$  is the F3 frequency.

Because heating power (manifesting as heat deposition  $dQ/dt$ ) is proportional to  $E^{1/2}$ , then  $dQ/dt = A^{1/2} \cdot \sin \omega t$ , where A is proportional to the E-field intensity (amplitude).

To express heat deposition in a homogeneous lossy dielectric, if we include functions for tissue impedance Z, and ignoring depth attenuation, we can write  $dQ/dt = f(Z) \cdot A^{1/2} \cdot \sin \omega t$

For ungated HRIFE, the second differential (acceleration of heat deposition) is written as  $d^2Q/dt^2 = -f(Z) \cdot A^{1/2} \cdot \cos \omega t$  which we postulate as a force that drives “thermoelastic pressure oscillations” (see also Lin et al, 2007)

Here, in biological systems, there may (or may not) be a field focusing effect at the boundary of aqueous and hydrophobic impedances, or perhaps adjacent to small pores, which we could write as a function  $g(P)$ , thus we can approximate  $dQ/dt = g(P) \cdot A^{1/2} \cdot \sin \omega t$  where Z is the aqueous impedance.

In an acoustic wave propagated outwards from the plane of impedance discontinuity (or perhaps near pores) into the aqueous media, the second differential could be written as  $d^2Q/dt^2 = -g(P) \cdot f(Z) \cdot A^{1/2} \cdot \cos \omega t$

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