Laser Therapy Dosage -The Reciprocity Rule in Photobiology (BLR) vs the Arndt-Schultz Rule
By Paul Schwen

The Bunsen-Roscoe Law (BRL) of Reciprocity
http://www.photobiology.com/reviews/bunsen/index.htm

The Bunsen-Roscoe Law of Reciprocity states that specific biological effects are directly proportional to the total energy dose irrespective of the administered regime.

In Photomedicine, dosage is primarily the product of intensity and the duration of exposure; thus, the time required to deliver a certain dose is influenced by the intensity of the source and whether the exposure is continuous or fractionated (pulsed). This law is named after R. Bunsen and H. E. Roscoe, who, by their work in the 19th century opened a new field of research entitled Photochemistry. For photochemical reactions, it can be assumed that this law is valid only, at least within a certain dose range which must be individually defined for each reaction. However, responses of cells and tissues to electromagnetic radiation usually involve a sequence of interacting biological reactions, making a linear dose-time relationship less likely. Additionally, photosensitizing molecules might induce different cellular and molecular responses than does radiation alone.

A survey of the available literature on dose-time relationships in photobiology strengthen the view that the Bunsen-Roscoe law seems to be restricted to narrow limits for most photobiological reactions. With this knowledge it is surprising that the available information on the influence of radiation intensity is limited, and that in most experimental and clinical studies variations in radiation intensity are not included in the experimental setup (or simpler: are not studied). In photomedicine where endpoints such as therapeutic efficacy, carcinogenesis, immunosuppression and photoaging are of major importance, validity and failure of the BRL are either completely unknown, suppressed, or subject to speculation based on in-vitro-only studies, with the endpoint usually already predetermined.

In photomedicine, investigations into the molecular events underlying the differential effects of varying doses and intensities are necessary for a comprehensive understanding of the way living tissues respond to NIR radiation; in this regard to date, most investigations are limited to *low-level energy* and *in-vitro environments* because of a stubborn adherence to the stated Arndt-Schultz Rule.

Basic Laws of Photochemistry

The Grotthuss–Draper Law
http://www.newworldencyclopedia.org/entry/Photochemistry
"Only radiation absorbed in a system can produce a chemical change."
The Grotthuss–Draper Law (also called the Principle of Photochemical Activation) states that only that light which is absorbed by a system can bring about a photochemical change. This law provides a basis for fluorescence and phosphorescence; the law was first proposed in 1817 by Theodor Grotthuss and in 1842, independently, by John William Draper.

Stark–Einstein Law
http://ccb.rutgers.edu/sites/default/files/coursefiles/courses_sp10/512/Handout_I_Photochemistry_I.pdf
"Number of activated molecules = number of quanta of radiation absorbed."
The Stark–Einstein law is named after German-born physicists Johannes Stark and Albert Einstein, who independently formulated the law between 1908 and 1913, and is also known as the Photochemical Equivalence Law. It says that every photon that is absorbed will cause a (primary) chemical or physical

reaction; the photon = one unit of radiation; therefore, this is a single unit of EM radiation that is equal to Planck's constant (h) times the frequency of light. This quantity is symbolized by γ, hv, or ħω.

The Beer-Lambert Law

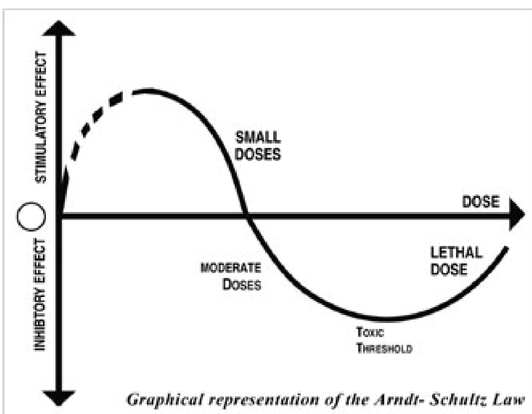
http://www.pci.tu-bs.de/aggericke/PC4/Kap_I/beerslaw.htm

The Beer-Lambert Law (or Beer's law) is the linear relationship between absorbance and concentration of an absorbing species. The general Beer-Lambert law is usually written as: A = a(lambda) * b * c where A is the measured absorbance, a(lambda) is a wavelength-dependent absorptivity coefficient, b is the path length, and c is the analyte concentration. When working in concentration units of molarity, the Beer-Lambert law is written as: A = epsilon * b * c, where epsilon is the wavelength-dependent molar absorptivity coefficient with units of M -1 cm -1.

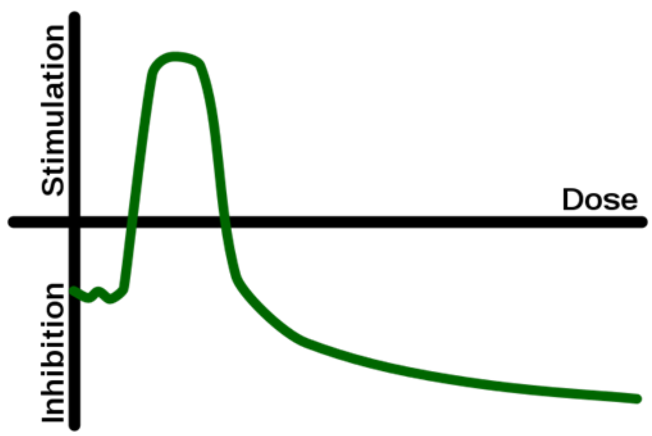
The Ubiquitous Arndt-Schultz Rule in Photomedicine

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2790317/

It is important to understand the orders of magnitude involved when it comes to therapeutic applications of photonic radiation. Far too often in photomedicine, generalized doses are conceived without a relative scale of comparative tissue interactions other than those initially achieved in-vitro; with energy often less than 5-10mW, dosages exist at or near the bottom of the U-shaped *Dose Response Curve,* illustrated by the oft-quoted Arndt-Schultz Rule (see below).



Graphical representation of the Arndt- Schultz Law



The Arndt-Schultz Rule, although enshrined as a ruling principle by LLLT proponents, was not derived for photomedicine and *no longer applies* even in pharmacology, for which it was originally derived. The Arndt–Schulz Rule or Schulz' Law is a claimed law concerning the effects of pharmaca, or poisons in various concentrations; it states that:

For every substance, small doses stimulate, moderate doses inhibit, large doses kill; in other words, highly diluted pharmaca or poisons enhance life processes, while strong concentrations may inhibit these processes or even terminate them.

The rule was named after Hugo Paul Friedrich Schulz and Rudolf Arndt, who originally formulated it in 1888; however, exceptions to the rule are so numerous that it cannot be considered a general law in pharmacology and *has no application in photomedicine*. For example, many paralyzing substances have no exciting effect in weak doses, and what constitutes a weak, medium or strong stimulus is highly individual, as pointed out by Arndt himself.

The Arndt-Schultz Rule is no longer cited in modern pharmacology texts, having been supplanted by the theory of hormesis; in addition, application of the Arndt-Schulz Rule in photomedicine never made sense.

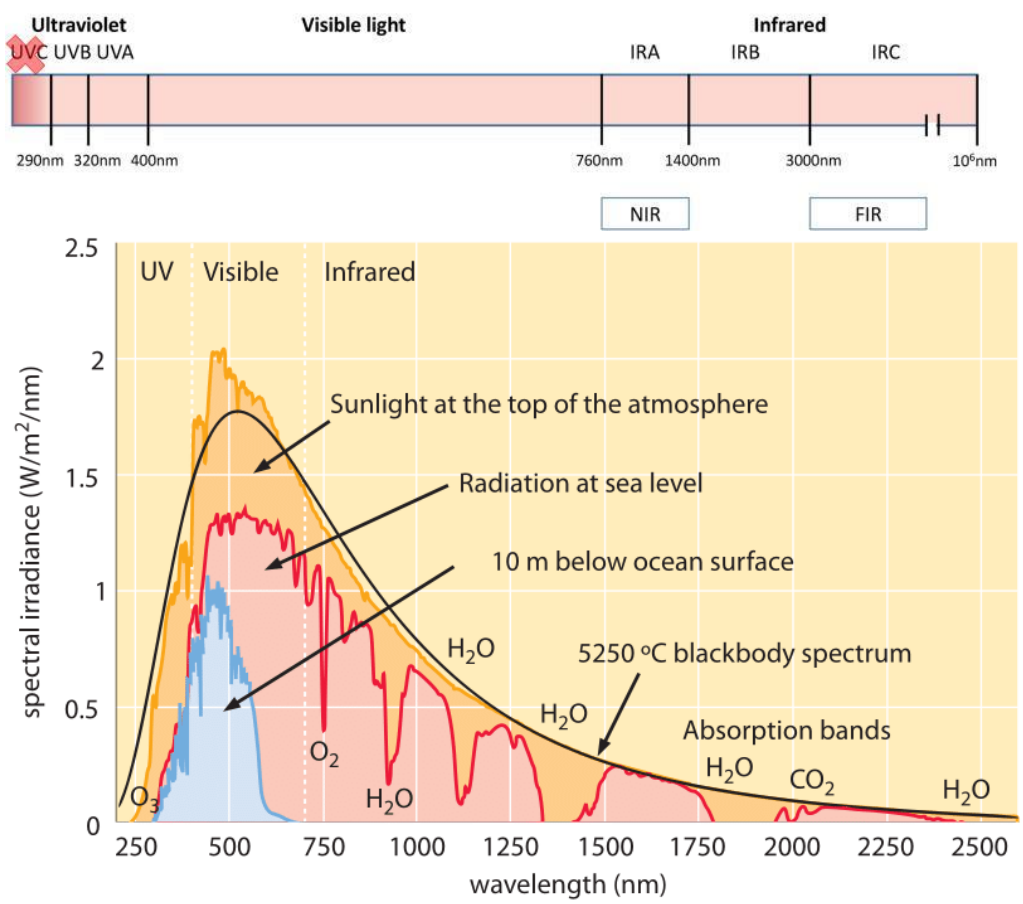
Solar Irradiation

At the upper reaches of our atmosphere, the energy density of solar radiation is approximately 1,368 W/m2 (watts per square meter). At the Earth's surface, the energy density is reduced to approximately 1,000 W/m2 for a surface perpendicular to the Sun's rays at sea level on a sunny day.

The spectrum of solar radiation reaching the Earth ranges from 290nm to more than 1,000,000nm and is divided as follows: 6.8% UV, 38.9% visible, and 54.3% near infrared radiation (NIR). Infrared constitutes the waveband longer than 760nm and up to 1mm and accounts for approximately 40% of the solar radiation reaching the ground at sea level.

Infrared energy has been divided into three bands: IR-A (760–1400 nm), IR-B (1400–3000 nm), and IR-C (3000 nm – 1 mm) (see below). IR radiation can penetrate the epidermis, dermis, and subcutaneous tissue to differing extents depending on the specific wavelength; exposure to IR is perceived as heat.

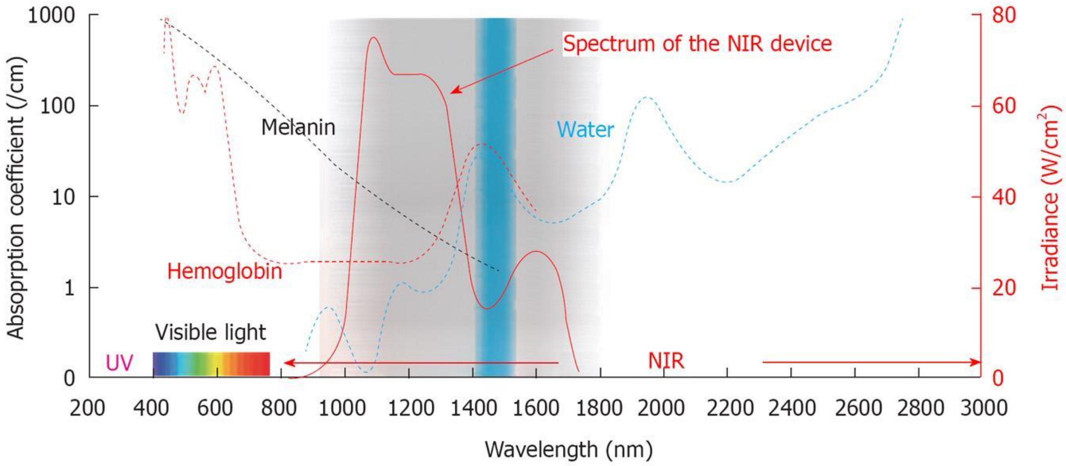
Solar spectrum



The strength of electromagnetic radiation depends on the energy of the individual particles or waves as well as the number of particles or waves present.

Electromagnetic radiation that has insufficient energy to completely remove electrons from atoms and molecules is referred to as non-ionizing radiation. Examples of this kind of radiation are visible light, ***infrared (NIR and FIR)***, and radio waves. Ionizing radiation has enough energy to remove tightly bound electrons from atoms, thus creating charged ions, and includes X-rays and gamma rays.

Ultraviolet (UV) radiation is intermediate between these two broad ranges; short-wavelength UV has enough energy to break chemical bonds and carry out photochemical reactions. Although the consequences of sun exposure on the skin have been extensively studied over the years, the impact of IR radiation has received far less attention than its UV counterpart, which is well known to cause skin cancer, photoaging, and immune suppression. Moreover, the solar IR-A (also called NIR) irradiance level is critical to trigger beneficial effects in the skin beyond which it becomes deleterious. Most studies reporting the detrimental effects of IR-A (upregulation of matrix metalloproteinase 1 or MMP-1) used artificial light sources far above the solar IR-A irradiance threshold.



Solar Irradiance Threshold of Therapeutic Energy

Solar irradiance is equal to the amount of energy (J, or Joules) delivered via sunlight to an area of the skin measured in CM^2; the solar irradiance threshold varies according to variable *Tissue Factors* listed below:

Wavelength	**Irradiance/Power Density**	**Hourly Dosage**
280nm – 400nm (UV)	6.4mW/CM^2	23J/CM^2 per hour
400nm – 700nm (visible)	46mW/CM^2	160J/CM^2 per hour
700nm – 3000nm (NIR, FIR)	48mW/CM^2	170J/CM^2 per hour

The wavelengths used in therapeutic photomedicine are in the visible and infrared range, typically:

635nm +/- 20nm	6.4mW/CM^2	21J/CM^2 per hour
810nm +/-20nm	4.3mW/CM^2	16J/CM^2 per hour
980nm +/- 20nm	2.7mW/CM^2	10J/CM^2 per hour

Therapeutic Window

(700nm – 1100nm)	33mW/CM^2	120J/CM^2 per hour

In other words, in one hour of sunlight, an exposed back would receive approximately 800,000J of therapeutic energy – orders of magnitude more than the minimal doses suggested by proponents of the Arndt-Schultz Rule. In addition, the same proponents neglect to consider basic rules of photomedicine – that tissue response is governed by the following *Targeted Tissue Factors:*

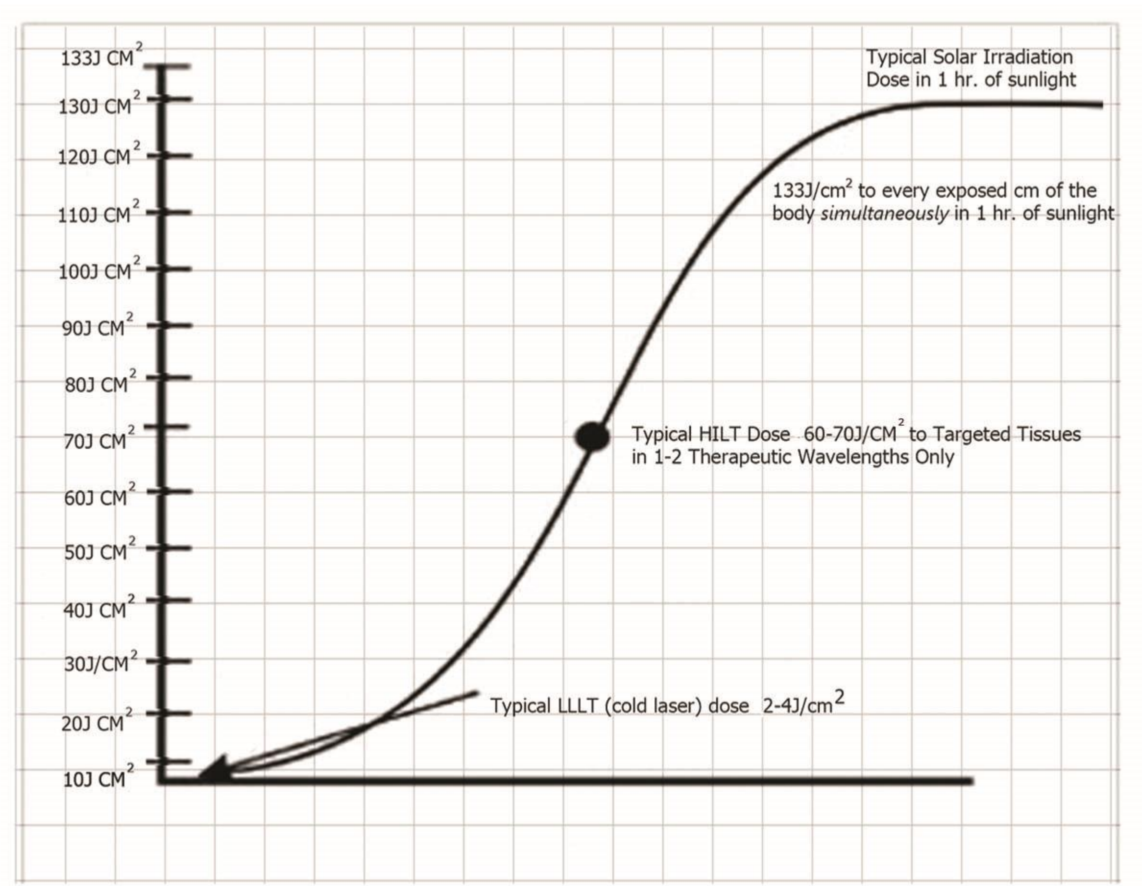
1. Tissue Mass: adiposity index or body mass index
2. Tissue Hydration: (fluid content) min. 54.8% to max. 78.1%
3. Tissue Structure: density/permeability of tissue structure

4. Tissue Proximity: (depth of tissue (shallow vs. deep)
5. Tissue Pigmentation: six levels, from white to black, according to Fitzpatrick Scale
6. Tissue Age: entropy, atrophy index
7. Tissue Stress: biobehavioral factors, allostasis vs. allostatic overload (acute vs. episodic or chronic stress and its effects on the human body)

Based on the above, it is logical to assume that effective treatment of mouth ulcers will require a much lower dosage than effective treatment of disc herniations or osteoarthritis of the knee joint, and effective dose ranges can be much higher than those suggested by proponents of the Arndt-Schultz Rule.

The BLR Dose Curve in Photomedicine

Based on solar irradiance threshold data, a more logical representation of the therapeutic dose curve in photomedicine would look like this:



<u>Conclusion</u>

Systematic clinical research into carefully designed studies will result in optimized higher-energy phototherapeutic regimens and dosages, with an improved therapeutic index, i.e. a maximized therapeutic benefit with minimized adverse reactions vs. the current LLLT standard, which represents minimal therapeutic benefit with minimal adverse reactions.