Refuge Plots

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One mistake that is easy for a Biological Engineer to make is to aim for perfection in his or her designs. This includes perfect elimination of unwanted organisms. However, management and control, not total elimination, is the key to a successful biological strategy. Biocontrol can be achieved through the application of one or more living natural enemies, parasites or predators, or through the recruitment of natural tendencies, none of which are absolutely effective. Working in harmony with nature beats working against nature in the long run.

Biological scientists have made many impressive discoveries, and these can often be used as mechanisms to solve some puzzle needing fixing. Advances made in knowledge about genetics, behaviors, or toxins have been foundational for new methods and strategies to control pests, reduce disease, or increase yields. However, these seminal advancements have usually come one at a time, after much toil and travail, and unfortunately, they are then used one at a time to solve some problem of importance.

Redundancy is the hallmark of biological response. Whether the problem is pestilence, disease, predators, or environmental challenges, living things react to these affronts with multiple responses. The immune system is a great example of this, depending on not just one, but a whole host of means to thwart challengers to health and survival. It needs to be thus, because the biological threats themselves are constantly changing and attempting to nullify or avoid immune responses. The result is a dynamic, a biological parry and thrust, that rewards the strong and sacrifices the weak. Control of the target over the challenger is never totally achieved, but the target survives as long as it can, and that, in itself, is biological victory.

We as biological engineers have all too often depended upon unidimensional magic bullets to solve our problems. These remedies have included incorporation of individual genes, dependence on pesticides with one action mechanism, and saturation with toxins differentially poisonous to pathogens over hosts. The results are genetically modified crops, antibiotics *du jour*, anticancer drugs, and overuse of antiseptics. It's not that these solutions are bad, because they aren't, but they do not take into account that single mechanisms have not proven to be long-term solutions to problems. Pests can overcome single gene protections, microbes develop means to overcome antibiotics, cancers can survive drugs, and no antiseptic is guaranteed to kill all unwanted organisms. What one gets when one depends on a single magic bullet is a temporary victory at best.

Rather than try for a complete and total knockout of the enemy, a better solution may be, and usually is, one that establishes a dominance of the favored over the unfavored individuals. Thus, the ideal pesticide is not one that eliminates all individuals of a problem pest, it's the one that shifts the balance back in favor of natural enemies. The ideal antibiotic is not the one that cures the disease 100% of the time; it's the one that weakens disease organisms but does not select for antibiotic immunity. The ideal chemotoxic anti-cancer drug is not the one that kills all rapidly-growing cells; it's the one that favors effective immune system response.

There have been many modern incidences of invasive pests, and one strategy for dealing with them is to discover natural enemies that can bring invasive pests back into natural balance. We know that in order for these natural enemies to continue to be effective a small population of pests must be maintained. The result is not elimination of the pests, but a balance that can be tolerated.

Bt (*Bacillus thurengiensis*) corn is a genetically-modified grain that is poisonous to *Lepidoptera* larvae, such as corn earworm. This pest used to be very destructive to corn yields, but, since Bt corn has been grown, corn yields have increased greatly, with the additional benefit that chemical pesticides are no longer needed to control corn earworm. Bt corn is so good that farmers want to plant nothing else. Yet, 100% of a corn crop that is Bt corn would ultimately lead to corn earworm insects resistant to the protection of the Bt gene; Bt corn would no longer be effective.

Farmers are required to plant 5-15% of their corn crops to non-Bt corn. These are called *refuge plots*. Refuge plots reduce the reproductive pressure for all corn earworm insects to develop Bt resistance. With refuge plots, any Bt resistant insects have ample opportunity to mate with nonresistant insects, thus diluting resistance genomes and reducing the possibility that resistance will be passed on to the next insect generation.

The concept of refuge plots should be known by all Biological Engineers and be a candidate for application to many other situations. Not all household locations need to be spotlessly clean and not all hands need to be disinfected. Not all defective genes need to be eliminated, and not all microbial infections need to be treated with the most powerful antibiotics. Imagine, if you will, that MRSA (*methicillin-resistant Staphalococcus aureus*) would not have existed if antibiotics had not been so generally used. Some Staph patients could have fought the infection without the use of powerful antibiotics, perhaps with the help of some probiotics, and acted as refuge plots for nonresistant staph bacteria. *Staphalococcus aureus* bacteria are omnipresent on human skin, but kept from becoming a problem because of resource competition from other bacteria also on the skin. These other bacteria are the natural enemies of Staph that we could have exploited as part of our refuge plot strategy.

Agricultural fungicides are very important to protect fruit, grain, and vegetable crops from infections that could destroy them. The most effective fungicides are those with single modes of action. These are also the fungicides that promote disease resistance. Fungicide manufacturers are beginning to package these very effective single-mode pesticides with broad spectrum pesticides. Any disease that could develop resistance to the single-mode fungicide is killed by the broad spectrum fungicide. The second fungicide acts as the refuge plot for the first fungicide.

Biological Engineers should appreciate the value of natural mechanisms and work with them rather than trying to conquer nature. Total control of the entire biological system is not, nor ever will be, a possibility for a biological engineering solution. Balance, not perfection, is the key to successful designs.