SYMBIOSIS STABILITY, PATHOGENS AND REEF-BUILDING CORALS' HEALTH: INSIGHTS ON THE ECOLOGY OF THE HUMAN BODY

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ABSTRACT

In search of insights for general rules about the host-symbiont-pathogen interaction, a review on the ecology of the interaction between hermatypic corals (Cnidaria: Scleractinia) and their symbiotic zooxanthellae (photosynthetic dinoflagellates, *Symbiodinium*) is done. In the last three decades a global decline on coral reef barriers has been observed and this has been attributed to, among other causes, two processes that directly interferes in the coral-zooxanthellae interaction: 'coral bleaching' and epidemics. Bleaching events are characterized by a sudden loss of zooxanthellae, commonly leading to mass mortality on coral colonies. Although it is not possible to establish causal relations, the intensities of epidemics and bleaching events are correlated, indicating that the symbiosis is a protective factor on coral's health. Some of the insights for human epidemiology are: the recurrent evolution of pathogens and the interference of symbionts on the host-pathogen interaction, either by direct competition exclusion or by an indirect effect on host's energy budget.
Keywords: Human microbiota; Scleractinia; *Symbiodinium;* symbiont; pathogen.

RESUMO

ESTABILIDADE DE SIMBIOSES, PATÓGENOS E SAÚDE DE CORAIS HERMATÍPICOS: PERSPECTIVAS PARA A ECOLOGIA DO CORPO HUMANO. Recentemente, a importância de diversos micro-organismos na fisiologia humana foi revelada, porém, pouco se sabe sobre a importância epidemiológica dessas interações. Nesse artigo, é feita uma revisão sobre a ecologia da interação entre corais hermatípicos (Cnidaria: Scleractinia) e zooxantelas (dinoflagelados fotossintetizantes, gênero Symbiodinium) com foco em perspectivas que possam ser aplicadas à dinâmica de transmissão de patógenos em humanos. Nos últimos 30 anos, observa-se um declíno global na abrangência dos recifes de corais e, entre outras causas, estão a intensificação de dois processos que interferem na relação coral-zooxantela: 'coral bleaching' e epidemias. Eventos de 'coral bleaching' são caracterizados pelo clareamento súbito dos corais, devido ao demembramento da interação entre coras e zooxantelas, podendo levar a mortalidade em massa de colônias de corais. Apesar de ainda não ser possível estabelecer relações de causalidade, existe uma correlação entre a intensificação de surtos epidêmicos e eventos de 'bleaching', indicando que a simbiose com zooxantelas é um fator protetor à saúde dos corais. Entre as perspectivas a serem avaliadas na epidemiologia humana estão a evolução recorrente de patógenos e a interferência de simbiontes na relação patógeno-hospedeiro.
Palavras-chave: Microbiota humana; Scleractinia; *Symbiodinium;* simbionte; patógeno.

RESUMEN

ESTABILIDAD DE SIMBIOSIS, PATOGENOS Y SALUD DE CORALES HERMATÍPICOS: PERSPECTIVAS PARA LA ECOLOGIA DEL CUERPO HUMANO. Recientemente se ha demostrado

la importancia de diversos micro-organismos en la fisiología humana, sin embargo, poco se sabe sobre la importancia epidemiológica de estas interacciones. En este articulo, se realizó una revisión sobre la ecología de la interacción entre los corales hermatípicos (Cnidaria: Scleractinia) y las zooxantelas (dinoflagelados fotosintetizadores, género Symbiodinium) haciendo foco en perspectivas que puedan ser aplicadas a la dinámica de transmisión de patógenos en humanos. En los últimos 30 años, se observó una declinación global en el área de cobertura de los arrecifes de coral y entre otras causas, se registra la intensificación de dos procesos que interfieren en la relación coral- zooxantela: "coral bleaching" y epidemias. Los eventos de "coral bleaching" se caracterizan por un aclaramiento súbito de los corales, debido al desmembramiento de la interacción entre corales y zooxantelas, pudiendo provocar la mortalidad en masa de las colonias de corales. A pesar de que aún no es posible establecer relaciones de causalidad, existe una correlación entre la intensificación de los eventos epidémicos y los eventos de "bleaching", indicando que la simbiosis con las zooxantelas es un factor protector de la salud de los corales. Entre las perspectivas a ser evaluadas en la epidemiología humana está la evolución recurrente de patógenos y la interferencia de simbiontes en la relación patógeno-hospedador.
Palabras clave: Microbiota humana; Scleractinia; *Symbiodinium;,* simbionte; patógeno.

INTRODUCTION

SYMBIOSIS AND A NEW PERSPECTIVE ON HUMAN BIOLOGY

Throughout the 20th century, biologists investigated the importance of symbiosis on the biology of animals and plants. However, it was only on the later half of the century that enough evidence was gathered and the endosymbiotic theory for the origin of eukaryotes cellular organelles became widely accepted among biologists (Sagan 1967, Douglas *et al*. 1982, Kutschera & Niklas 2005). The fact that symbiosis was a central issue on eukaryote (and consequentially human) evolution has promoted a revolution on definition of individuals and on evolutionary theory itself (Margulis & Sagan 2002).

More recently, several studies have highlighted the importance of human-bacteria associations for human physiology (Ley *et al*. 2006, Gao *et al*. 2007, Dethlefsen *et al*. 2007) and it has been estimated that 90% of human body weight is, in fact, of bacterial cells (Turnbaugh *et al*. 2007). These new findings have put symbiosis on the spotlight once again: now it is relevant not only to human evolutionary history, but also to our physiology and ecology in present days. Bacterial-associated traits are being described and the effects of these new findings on human physiology and epidemiology are yet to be understood (Dethlefsen *et al*. 2007).

The Human Microbiome Project (HMP) is a worldwide effort for sampling and cataloging human associated micro-organisms (microbiota) which relies mainly on metagenomics for assessing the diversity and functional traits of the microbiota (Turnbaugh *et al*. 2007). The identification of a wide diversity of bacteria and other micro-organisms in the human body claims for a novel interpretation of human bodies as ecological communities. The main ecological issues considered by the HMP initiative article were related to the species composition of the microbiota: the stability and resilience of the microbiota on several body sites, the similarity degree between different families and among family members and whether there is a common species core for all persons despite cultural and regional differences (Turnbaugh *et al*. 2007).

Anyway, this novel interpretation is "new only in terms of the system to which it applies" (Turnbaugh *et al*. 2007, p. 804). Symbiotic systems are widespread in ecology, ranging from marine invertebrates to terrestrial plants (Begon *et al*. 2006), and the study of these can bring valuable contributions for understanding the human microbiota, highlighting the essential characteristics of such systems (Dethlefsen *et al*. 2007). In this sense, this article is a review on the ecology of the coral-zooxanthellae symbiosis in coral reefs, with focus on the insights it can bring to the host-symbiont-pathogen system. It also describes a theoretical model for multi-partner interactions,

which may be useful for the coral-zooxanthellae and other host-simbiont systems.

SYMBIOSIS ON CORAL REEFS

Coral reefs are found all over the tropical seas, typically on shallow, warm and oligotrophic waters and are formed by cnidarians of the order *Scleractinia,* sessile cnidarians which harbors photosynthetic endosymbionts. Those are commonly known as zooxanthellae, most often dinoflagellates of the genus *Symbiodinium*. Corals and its associated zooxanthellae are important contributors to the production of organic matter on coral reef ecosystems, established in nutrient-poor and sun-lighted waters (Muller-Parker & D'Elia 1997).

The coral-zooxanthellae association is mutualistic: corals benefits from excess of photosynthetic organic compounds while zooxanthellae will benefit from corals metabolic inorganic residues, protection from grazers and a more stable environment in the photic zone (Stat *et al*. 2006). Coral also benefits from a hard substrate to establish, consolidated by a higher calcification rate: the reef-building ability of scleractinian corals is intimately related to the symbiosis (Muller-Parker & D'Elia 1997). There is also good geological and phylogenetic support for the positive effect of the interaction: both Scleractinia and *Symbiodinium* spread and diversification occurred on the same period, about 50 million years ago (Kiessling & Baron-Szabo 2004, Pochon *et al*. 2006, Stat *et al*. 2006).

ENDOSYMBIONT TRANSMISSION MODE

Endosymbionts may be transmitted from parents to offspring, vertical transmission mode, or acquired from the environment, horizontal transmission. These different routes have huge implications on symbiosis, including the stability of the interaction (Sachs *et al*. 2004).

If the symbiont transmission relies entirely on host's reproduction, i. e. the zooxanthellae is transmitted only vertically, then a 'Partner Fidelity Feedback' must operate in that system: the more cooperative the symbiont is, the higher will be host's fitness and, consequently, the higher will be symbiont's own fitness (Sachs *et al*. 2004). Under this

transmission mode, natural selection shall optimize both host and symbiont cooperative traits and a high degree of specialization must be observed. This will result on a high concordance on host's and symbiont's phylogenies, each symbiont phylogenetic group shall be associated to a phylogenetic group in hosts (Cook & Rasplus 2003). In contrast, if symbionts are exclusively acquired from the environment during host life-cycle, then zooxanthellae community composition in coral's establishment site will be determinant for the resulting interaction (Stat *et al*. 2006) and both hosts and symbionts shall be, to some extent, generalists (Sachs *et al*. 2004). The free-living stage in symbiont's life-cycle shall prevent extreme genome reductions and evolutionary transitions from mutualistic to commensal or pathogenic habits (appearance of 'cheaters') are more common (Moran & Wernegreen 2000, Sachs & Simms 2006). In this framework, known in the literature as 'Partner Choice', switching partners is an important strategy that enables an individual to avoid non-cooperative partners and select the most beneficial ones (Noë & Hammerstein 1995, Sachs *et al*. 2004, Edwards *et al*. 2010).

Those frameworks are not mutually exclusive (Sachs *et al*. 2004), but while 'Partner Fidelity' favors specialization and efficiency, 'Partner Choice' favors generalism and robustness, leading to a well known trade-off in ecology (Angilletta *et al*. 2003). Which model will be favored in nature depends on factors such as abundance of hosts and symbionts, each partner's dependence on the interaction and environmental stability (Noë & Hammerstein 1995, Begon *et al*. 2006).

Although the term symbiosis originally means any intimate association between organisms of different species, it will be used as a synonym for mutualism in this article (Willkinson 2001). Intimate interactions that are not mutually beneficial will be explicitly distinguished.

CORAL REPRODUCTION AND ZOOXANTHELLAE ACQUISITION

During Scleractinia life-cycle, zooxanthellae may be transmitted from parents to offspring or acquired from the environment, depending on corals' reproduction mode (Baird *et al*. 2009). Most

sexual reproduction in Scleractinia is done via egg spawning, when eggs and sperms are released in the water column and zooxanthellae is (usually) acquired from the environment, but some species may brood the planulae, when zooxanthellae is transmitted vertically (Baird *et al*. 2009). Although there are examples of correlation between zooxanthellae transmission mode and specificity of the coral-zooxanthellae interaction (Thornhill *et al*. 2006), this is not an obvious trend, and the ratio of specialist and generalist zooxanthellae may be equivalent in spawning and brooding corals (Van Oppen 2004, Stat *et al*. 2006). This indicates that even in brooding corals, the acquisition of zooxanthellae from the environment may be ecologically and evolutionarily relevant.

Scleractinian corals may also reproduce asexually (vertical transmission) and the frequency of sexual versus asexual reproduction differs among species and is rarely known (Muller-Parker & D'Elia 1997, Baird *et al*. 2009). With such diverse reproduction modes, the Scleractinia-*Symbiodinium* transmission dynamics will be influenced by varying degrees of both vertical and horizontal transmission, depending on the coral species considered (Stat *et al*. 2006).

As zooxanthellae is not transmitted exclusively from parents to offspring, theory predicts that evolutionary transitions from mutualistic to commensal or parasitic habits might be common (Sachs & Simms 2006) and at least a mild pathogeneicity in zooxanthellae is selected when horizontal transmission is forced in the *Cassiopeia-Symbiodinium* system, a jellyfish-zooxanthellae interaction with exclusive vertical transmission in nature (Sachs & Wilcox 2006). This means recurrent evolution pathogenic zooxanthellae may occur and corals ability to expel non-beneficial zooxanthellae strains is essential for the maintenance of the interaction. Otherwise, the system will be vulnerable to invasion by cheaters (Edwards *et al*. 2010).

CORAL – ZOOXANTHELLAE INTERACTION COMMUNITY STRUCTURE

The coral's Scleractinia order is a highly diverse group comprising more than 1000 species divided in 220 genera or 24 families (Cairns 1999). In addition, the *Symbiodinium* genus, initially thought as a single species, is now recognized as a diverse group, comprising free-living lineages (or clades, subgenera level) and lineages able to colonize a myriad of other organisms, such as foraminiferans, sponges, cnidarians and molluscs (Carlos *et al*. 1999, Hirose *et al*. 2008, Pochon *et al*. 2006). Scleractinian corals themselves also harbors diverse other symbiotic micro-organisms which may influence coral health and the stability of the coral-zooxanthellae association (Knowlton 2003, Ainsworth *et al*. 2009). Nevertheless, in this article the focus is on the coral-zooxanthellae interaction.

Until now, at least 8 lineages (named A - H) of *Symbiodinium* have been described (Pochon *et al*. 2006). Lineages A, B, C and D form regular associations with corals, with *Symbiodinium* C being the most common one, interacting with a wide range of coral species and occupying central ecological areas (LaJeunesse 2002, Knowlton *et al*. 2003, LaJeunesse *et al*. 2004). Lineage B is also a common one while lineages A and D although are also found on tropical seas, are dominant in marginal ecological places, as high latitude locations, deep or extremely shallow waters and regions with a higher influence of coastal areas (Toller *et al*. 2001a, 2001b, LaJeunesse *et al*. 2004, Stat *et al*. 2006). Zooxanthellae classified as belonging to clade E in Toller *et al*. (2001a, 2001b) are in fact members of clade D (Baker 2003).

The initial view of an 'one coral – one zooxanthellae' specific relation ('Partner Fidelity') has been surpassed as it was demonstrated that a single coral species may interact with several zooxanthellae clades (Rowan & Knowlton 1995). Moreover, a single colony may host different zooxanthellar types, depending on micro-climatic variables as depth, temperature and solar irradiance (Rowan & Knowlton 1995, Rowan *et al*. 1997, Van Oppen *et al*. 2001). *Symbiodinium* species are not necessarily specialists either, a single species may interact with several coral species (LaJeunesse *et al*. 2004, Stat *et al*. 2006) and zooxanthellae community structure in a coral colony may change seasonally and during coral's ontogeny. In pacific corals of the genus *Acropora,* zooxanthellae recruitment after sexual reproduction started with *Symbiodinium* D, further replaced by *Symbiodinium* C (Little *et al*. 2004). The interaction seems to be highly dynamical: multiple zooxanthellae strains may colonize a given coral species and corals can control population in its tissues, expelling the excess

of zooxanthellae (Muller-Parker & D'Elia 1997) or damaged cells (Douglas 2003).

DISEASES AND STRESS-RELATED SYMPTOMS IN CORAL REEFS

In the last 30 years, a global decline in coral reefs has been observed around the world (Hughes *et al*. 2003). Among others threats, epidemics and mass bleaching events were found to be increasing in frequency and severity (Brown 1997, Cervino *et al*. 2001, Porter *et al*. 2001, Toller *et al*. 2001b, Jones *et al*. 2004, Sutherland *et al*. 2004), possibly because of anthropogenic impacts and global climate changes, in special rise in seawater temperature and solar irradiance (Brown 1997, Douglas 2003, Hughes *et al*. 2003, Sutherland *et al*. 2004, Bruno *et al*. 2007). Those threats are related to the coral-zooxanthellae association and some reports of them are presented below.

CORAL BLEACHING

Coral bleaching is a symptom characterized by an abrupt zooxanthellae loss (or loss of its pigments), leaving coral's calcareous skeleton visible. Bleaching is often associated to alterations on environmental conditions in the vicinity of the coral colony, as a higher turbidity, solar irradiance and, most often, seawater temperature rise (Douglas 2003). The ultimate factors triggering bleaching events are not well understood, but those are probably associated to reduction on zooxanthellae photosynthetic activity (photo-inhibition) and expulsion of zooxanthellae cells by corals (Douglas 2003, Muller-Parker & D'Elia 1997). Most efforts has been concentrated on understanding physiological changes on zooxanthellae that may promote disruption of the symbiosis, but those are probably accompanied by changes in coral's physiology as tissue thinning and lower production of heat-shock (protective) proteins (Baird *et al*. 2008).

As most Scleractinian species forms obligate symbiosis with *Symbiodinium*, mass coral mortality is commonly observed after bleaching events (Douglas 2003, Jones 2008). Bleaching magnitude (and hence coral mass mortality) vary from species to species (Baird & Marshal 2002) and, in a review of

bleaching reports, Stimson *et al*. (2002) establishes a ranking of the magnitude of bleaching induced mortality for corals from the Caribbean and the Pacific. However, as described below, *Symbiodinium* lineages also differ in bleaching susceptibility and the exact bleaching threshold is an emergent property of the coral-zooxanthellae interaction (Day *et al*. 2008). Adding plasticity to the phenomena, Brown *et al*. (2000) report a case where differential bleaching cannot be attributed neither to coral nor to zooxanthellae species: a colony of *Goniastrea aspera* hosting a single *Symbiodinium* lineage, experienced different bleaching rates in its east and west surfaces. The explanation was that irradiance resistance acclimatization should have been achieved by differences in coral tissue composition, stimulated by long-term exposure to higher solar irradiance on the west surface of the colony (Baird *et al*. 2008).

In the Caribbean, coral species *Montastraea annularis* and *M. faveolata* host *Symbiodinium* A, B and C, with most colonies hosting lineage C in intermediate depths (4-7 meters). After a bleaching event *Symbiodinium* C abundance decreased substantially, even disappearing in some colonies, whilst abundance of *Symbiodinium* A and B has increased (Rowan *et al*. 1997). Other example is the field transplant experiment of Baker (2001), where colonies of 9 different coral species were moved from deep to shallow waters and vice-versa. In downward transplanted (from shallow to deep waters), colonies presented lower bleaching effects, no shifts in *Symbiodinium* composition was evident and a higher mortality was observed after 12 months. Whereas in upward transplant, higher bleaching effects and low mortality occurred. A shift from *Symbiodinium* C dominated colonies in deep waters to *Symbiodinium* A and D in shallow waters was observed, but it's not clear if these changes were achieved by acquisition of new zooxanthellae from the shallow environment or by changes in dominance in colonies hosting multiple zooxanthellae lineages. A similar result was found in a transplant experiment in Australia: a shift from *Symbiodinium* C to *Symbiodinium* D dominated communities occurred after moving colonies from a cooler to a warmer seawater site. (Berkelmans & van Oppen 2006).

Symbiodinium C appears to be the zooxanthellae least resistant to thermal stress and lineages A and D

are often found in more resistant associations (Rowan *et al*. 1997, Baker 2001, Toller *et al*. 2001a, 2001b, Rowan 2004, Berkelmans & van Oppen 2006). A laboratory experiment support this findings: while there were no differences at 28ºC, *Pocillopora* corals harboring *Symbiodinium* D had higher photosynthesis rate than those harboring *Symbiodinium* C at the warmer temperature of 32ºC (Rowan 2004). This differences in bleaching susceptibility in zooxanthellae led to the formulation of an 'Adaptive Bleaching Hypothesis', stating that bleaching is an event that enables corals to shift symbionts, expelling non-resistant zooxanthellae and being colonized by more resistant strains (Buddemayer & Fautin 1993). This hypothesis is supported by the observed shifts in symbiont communities in post-bleaching corals (Baker 2001, Baker *et al*. 2004, Berkelmans & van Oppen 2006). However, such events are usually followed by death of coral colonies (Stimsom *et al*. 2002, Douglas 2003), higher incidence of diseases (Jones 2008) and there are cases of no shifts in zooxanthellae community composition after bleaching (Thornhill *et al*. 2006). If zooxanthellae is acquired from the environment, then the outcome of a bleaching event will be determined by *Symbiodinium* local community structure, which cannot be predicted by corals. Thereby, bleaching should be viewed as a stress symptom, an extreme event of the complex symbiotic regulatory mechanism of the coral-zooxanthellae association (Baker 2003).

EPIDEMICS

Disease diagnostic in corals are often confusing because of difficulties in culturing the associated pathogens and much of the so-called diseases or syndromes may in fact be caused by the same pathogen or even be a stress symptom (Richardson 1998). Despite this confounding factors, some causative agents have been identified (Kushmaro *et al*. 1997, Sutherland *et al*. 2004, Sussman *et al*. 2008) and disease in corals have been increasing in incidence, species affected and severity in the last years (Porter *et al*. 2001, Sutherland *et al*. 2004). Disease peaks often occurs in late summer after bleaching events, when coral tissues are thinnest and zooxanthellae densities lowest, indicating that the disruption of the coral-zooxanthellae symbiosis

may facilitate infections and/or enhance pathogen virulence (Fitt *et al*. 2001). Actually, it's known that temperature rise itself may promote higher infection rates and morbidity and both factors shall, probably, act in synergy (Jones *et al*. 2004).

For 'White syndrome', considered the most prevalent disease condition in the Great Barrier Reef in Australia (Roff *et al*. 2006), it was demonstrated that the highest disease incidence, observed in the summer of 2002, was positively correlated to a rise in seawater temperature (Bruno *et al*. 2008). Authors also found that disease incidence was affected by coral cover density (surrogate for the abundance of susceptible individuals), a known epidemiological criteria (May & Anderson 1991). Recently, bacteria of the *Vibrio* genus were identified as the causative agents of 'White Syndrome' and cultured in laboratory (Sussman *et al*. 2008). In this study, infection was followed by bleaching in two of the three scleractinian species inoculated with pathogens (bleaching occurred 9 hours after inoculation in *Acropora hyacinthu*s and after 12 hours in *Pachyseris speciosa*).

A case of disease outbreak and mass bleaching occurring simultaneously is presented in Jones *et al*. (2004). Populations of *Montipora aequituberculata* in Australia were monitored over a 16 month period monitoring and both bleaching and disease (characterized by coral tissue lesions) incidence started at the summer, when seawater temperature exceeded 30ºC. In this case, without manipulative experiments, it was not possible to determine if this disease promotes bleaching or if it is a secondary opportunistic infection. Independently, whether the disruption of the coral-zooxanthellae symbiosis enhance pathogen virulence or favor opportunistic infections, the highest mortality rates in scleractnian corals are often observed in events of bleaching associated with epidemics (Jones 2008).

Even in non-bleached corals, disease incidence and severity might be related to the zooxanthellae strain preferentially hosted. Toller *et al*. (2001b) observed that *Montastrea* corals associated to *Symbiodinium* A had higher incidence of yellow blotch disease. Stat *et al*. (2008) also reports higher incidence of diseases and abnormalities in corals with *Symbiodinium* A. In this case, acroporid corals harboring *Symbiodinium* A were more affected than

those harboring *Symbiodinium* C. Authors have found that *Symbiodinium* A released less carbon than lineage C when cultured either in fresh seawater or in the presence of a synthetic host factor. Based on these findings they proposed that *Symbiodinium* A would not be able to provide the host the necessary organic compounds, considering it a 'cheater' strain, a zooxanthellae with parasitic habits. It's not clear if abnormalities found in coral tissues were caused by the zooxanthellae or by opportunistic infections, but harboring a sub-optimal zooxanthellae lineage can make the coral more susceptible to diseases (Baker 2001).

BIOLOGICAL MARKETS – A THEORETICAL FRAMEWORK

'Biological Market' is a game-theoretical approach, derived from economy models to represent nutrients trade between different species. Partners of the interaction are divided in two trader classes, *i. e.*, entities "that can choose a trading strategy independently" (Noë & Hammerstein 1995, p. 336). As it allows the inclusion of multiple partners, it helps understanding the dynamics of partner switching and the persistence of cheaters among cooperative partners in each trader class (Noë & Hammerstein 1995), making it particularly interesting for modeling

'Partner Choice' situations. It has been applied to the legume-rhizobia interaction, as there is evidence for partner switching in this system: legumes can punish non nitrogen-fixing rhizobia and favour the most effective ones (Simms & Taylor 2002).

Figure 1 is an illustration of a Biological Maket model for a hypothetical Scleractinia-*Symbiodinium* interaction. The photosynthetic activity of each zooxanthellae lineage troughout an environmental gradient is represented by the curves drawn and is taken as an estimate of the amount of carbon released to corals. These can be seen as the relative benefit a coral will receive when it associates with each *Symbiodinium* lineage, but the curve will probably be unique for each coral-zooxanthellae association. In this model it's assumed that *Symbiodinium* A and D are more resistant to extreme environmental conditions (ex. seawater temperature) than *Symbiodinium* C and that in moderate environmental conditions *Symbiodinium* C has higher competitive ability, due to carbon fixation potential. Because of that, lineage C shall be preferred and occupy most coral colonies in central ecological places, while in extreme environmental conditions *Symbiodinium* A or D would be preferred and displace lineage C (Toller *et al*. 2001a, 2001b). C_L and C_U represents lower and upper bleaching tresholds for *Symbiodinum* C and, equivalently, the same holds for *Symbiodinum* A and D.
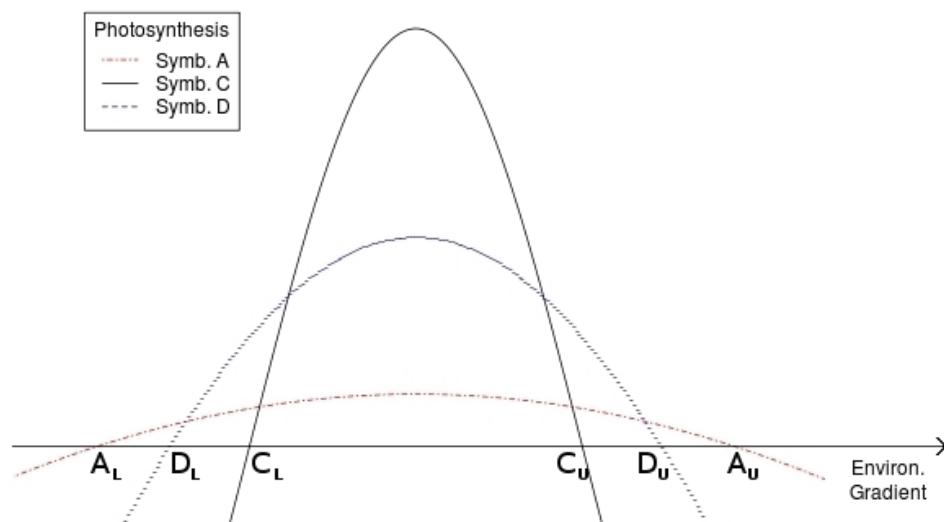

Figure 1. Hypothetical photosynthetic activities of three Symbiodinium strains A, C and D. Curves may be seen as the relative amount of carbon released to corals in a specific environmental condition. The x-axis intercepts represents the lower and upper bleaching tresholds for each zooxanthellae strain. Differences in phtosynthetic activities are based on the results of Toller et al. (2001a, 2001b), Rowan (2004), Berkelmans & van Oppen (2006) and Stat et al. (2008).

This framework helps understanding the preferential loss of *Symbiodinium* C and shift to lineage A observed in the bleaching of *M. annularis* and *M. faveolata* (Rowan *et al*. 1997): temperatures in that ocasion must have been between C_U and A_U. An analogous rationale can be applied to the transplanted colonies described in Berkelmans & van Oppen (2006), where there was a shift from *Symbiodinium* C to *Symbiodinium* D dominated colonies. In the experiment of Baker (2001), *Symbiodinium* A, C and D were present and temperatures in the interval between C_u and A_u (and D_u) would explain the bleaching of *Symbiodinium* C and acquisition of lineages A and D (or proliferation, if *Symbiodinium* A were already in corals tissue) observed in upward transplants. This analysis seems to support the 'Adaptative Bleaching Hypothesis' (Buddemeier & Fauntin 1993), but community composition may restringe the adaptability promoted by zooxanthellae shifting. As an example, in the Pacific, *Pocillopora* species are known to occur with both *Symbiodinium* C and D (Rowan 2004). If seawater temperature rise above D_u, then no interacion would be sustained and coral would die if thermal stress is too prolongued.

In 'Partner Choice' situations, the cost of rejecting a potential partner is higher if few alternative partners are available (Sachs *et al*. 2004). This could explain the persistence of *Symbiodinium* A interactions, a lineage associated with health disorders (Toller *et al*. 2001b, Stat *et al*. 2008). In warmer or higher irradiance habitats where *Symbiodinum* C cannot survive, corals would have to choose the 'lesser of two evils': expelling *Symbiodinum* A and a prolongued time with no zooxanthellae would result in an even lower energy budget leading to coral's death.

'Biological Market' is a framework for modelling cases where parasites and mutualists uses the same host physiological pathway and parasites can be seen as cheaters of the endosymbiont trader class (Noë & Hammerstein 1995). In other cases, pathogens and endosymbionts might use different host physiological pathways and such a direct competition approach won't be supported (Moran & Wernegreen 2000). In these cases, the effect of symbionts on disease outcome will be indirect and the 'biological market' shall be combined with compartment epidemiological models, as the SIR (May & Anderson 1991). As an example, an alternative explanation for the higher abnormalities found in the *Acropora-Symbiodinium*

A interaction is the action of opportunistic infections (Jones *et al*. 2006). The lower carbon release of *Symbiodinium* A relative to *Symbiodinium* C would lead to a lower resistance to infections and/or a higher disease severity in *Acropora* corals bearing *Symbiodinium* A. Under this scenario, the effect of *Symbiodinium* A on coral health will only be fully understood within the epidemiology context.

INSIGHTS FOR HUMAN HEALTH AND EPIDEMIOLOGY

Human microbiota is not passed through the germline, but can be preferentially transmitted from parents to offspring by pathways as breast-feeding, skin contact and the birth moment (Ley *et al*. 2007). In this sense the human-microbiota resembles the coral-zooxanthellae association: its transmission is a combination of parent-offspring and environmental pathways in varying degrees, depending on the specific body site and environmental conditions. Evidences of partner switching are necessary in order to apply the 'Biological Market' approach to the human-microbiota system, but the relative stable composition of intestinal microflora in each individual and interpersonal differences (Ley *et al*. 2007) suggests it may occur.

Some harsh differences in these systems must be considered; 1 - Scleractinia is a diverse order and *Homo sapiens* a single species; 2 - corals have only two differentiated tissues and zooxanthellae is located on gastrodermis (Muller-Parker & D'Elia 1997) while microbiota is associated to diverse human body sites as intestine, skin, mouth and vagina (Turnbaugh *et al*. 2007). Although much of the variation observed in the Scleractinia-*Symbiodinium* interaction may be restrained by phylogenetic homogeneity in humans, threats for human health might be triggered by factors altering the human-microbiota interaction dynamics and some general lines can be drawn from the coral-zooxanthellae interaction, keeping in mind the taxonomical and histological differences of these systems.

RECURRENT EVOLUTION OF NEW PATHOGENS

As is the case for the *Cassiopeia-Symbiodinium* interaction (Sachs & Wilcox 2006), systems of horizontally-transmitted symbionts are more

vulnerable to the appearance of cheaters and the recurrent evolution of new pathogens is a concrete possibility for certain human-microorganisms associations. Skin allergies are good candidates for such examples, as the rate of horizontal versus vertical transmission on superficial skin is possibly the highest of the human body. The low interpersonal similarity on forearm bacterial biota supports this possibility (Gao *et al*. 2007).

GEOGRAPHICAL VARIATIONS ON MICROBIOTA COMPOSITION

One of the questions pursued by the Human Microbiome Project is whether there is a microbiota "core", a common assembly of microorganisms inhabiting a significant fraction of human population (Turnbaugh *et al*. 2007). The focus has been on the microbial core and its application on medical treatments, but the peripheral microorganisms might be informative too. In the *Coral-Zooxanthellae* association it was observed that sub-optimal *Symbiodinium* lineages are found preferentially on marginal ecological habitats (Stat *et al*. 2006) and those lineages are associated to higher disease incidence (Stat *et al*. 2008). Would the same occur with human populations? Homeothermy may provide a more stable environment to human microbiota, but this is achieved with a higher energy cost which can make the interaction prone to stress symptoms and the disruption of the symbiosis.

DISRUPTION OF THE SYMBIOSIS AND SUSCEPTIBILITY TO DISEASES

In analogy to what has been observed in post-bleaching events in corals (Jones *et al*. 2006), humans may become more susceptible to infections after perturbations on symbiont's community. The effect of a sub-optimal endosymbiont lineage on human health may be undesirable (Stat *et al*. 2008) and the worsening on disease condition due to disruptions on symbiosis after an initial infection is also a possibility. Beldomenico & Begon (2009) suggest co-infections would influence disease transmission trough impoverishment of host health and, consequently, higher susceptibility and/or pathogen load. In this context it's clear that host condition shall also be influenced by mutualistic endosymbionts: an optimal symbiotic relationship may prevent infections or diminish pathogen load, improving host condition.

Whether an efficient symbiont will prevent diseases and stress symptoms by direct competition and displacement of harmful (or less beneficial) strains (Noë & Hammerstein 1995, Stat *et al*. 2008) or by an indirect effect on health caused by an extra input in individual's energy budget is not clear and will probably depend on the specific pathogen and endosymbionts being considered. Anyway, as researchers are mapping out the diversity of human microbiota, examples of multi-partner interactions on disease dynamics become more evident (Verhelst *et al*. 2004, Ley *et al*. 2006) and theoretical models are necessary to integrate this advances. Despite its inherent difficulties, the inclusion of other pathogens and symbionts on the pathogen-host game is clearly a step forward for a better understanding of disease transmission dynamics.

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