Optimal Cell Size for Resource Uptake in Fluids: A New Facet of Resource Competition

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ABSTRACT: Planktonic microorganisms are affected by various size-dependent processes both from the bottom up and from the top down. We developed a simple resource-consumer model to explore how size-dependent resource uptake and resource loss influence the growth of, and competition between, planktonic microorganisms. We considered three steps of resource uptake: diffusive transport of resource molecules, uptake by membrane transporters, and cellular enzymatic catalysis, and we investigated optimal cell size when one, two, or three of those steps limit resource uptake. Optimal cell size depends negatively on the size of resource molecules when resource uptake is limited by diffusive transport and membrane uptake. When competing for two resources of different molecular sizes, two different-sized consumers can coexist if the inputs of resources and sizes of consumers are correctly chosen. The model suggests that mixtures of various-sized resources can promote coexistence and size diversity of microorganisms even if the availability of one element, such as carbon, nitrogen, or phosphorus, limits the whole community. Model predictions include that bacteria grown on maltose or polysaccharides should be smaller compared with those grown on glucose under carbon limitation. Our results suggest that size of resource molecules can be an important factor in microbial resource competition in aquatic environments.

Keywords: optimal cell size, resource molecule size, molecular diffusion, resource competition, microbial diversity, allometric exponent.

One of the most fascinating features of aquatic ecology is the tremendous size diversity of single-celled organisms. Bacteria range in size from the ultramicrobacteria found in oligotrophic oceans (<0.2 μm; Velimirov 2001) to giants such as the sulfur bacterium *Thiomargarita namibiensis* found in sediments of the continental shelf off Namibia (up to 750 μm; Schulz et al. 1999; Schulz and Jørgensen 2001). Phytoplankton also show a considerable size range in diameter, from 0.6 μm (*Prochlorococcus* spp.; Chisholm 1992) to >1,000 μm (*Ethmodiscus* spp.; Villareal 1992; Villareal et al. 1999). Those microorganisms, either heterotrophs or autotrophs, rely on dissolved nutrients, which are delivered by molecular diffusion and taken up by membrane transporters at cell surface (Berg and Purcell 1977; Logan and Dettmer 1990; Karp-Boss et al. 1996).

Existing theory suggests that smaller cells should be more efficient at resource uptake primarily due to the greater surface-volume ratio (Bratbak and Thingstad 1985) and the diffusion limitation of resource transport (Thingstad et al. 2005). Without top-down controls (Jiang et al. 2005; Thingstad et al. 2005) or fluctuations in resource supply (Grover 1991; Stolte and Riegman 1996), it is thought that cell size should evolve to be as small as physiological constraints allow (Koch 1996; Raven 1998).

However, some experimental results contradict this theory, showing that larger cells can be superior resource competitors under a constant resource supply. It has been suggested that larger bacterial cells grow faster than smaller cells during the course of batch-culture incubation of natural samples, and larger cells often show higher resource uptake rates (Button and Robertson 2000; Nishimura et al. 2005).

Whether smaller or larger cell sizes are advantageous in resource competition theoretically depends on the size dependence of growth and loss (Laws 1975). If growth rate is proportional to $(\text{cell size})^a$ and an increasing function of resource and loss rate is proportional to $(\text{cell size})^b$, larger cells outcompete smaller when the exponent of growth (a) is greater than that of loss (b) by reducing resource to the lower level at steady state.

Resource uptake in fluids is a multistep process where each step depends on cell size in a different way. Step 1 is the diffusive transport of resource molecules from the medium to the cell surface, step 2 is resource uptake by

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membrane transporters, and step 3 is enzymatic catalysis within a cell. For a spherical cell, the diffusive transport is proportional to cell radius ($\propto r$; Berg and Purcell 1977). When both membrane uptake per unit surface area and cellular catalysis per unit volume are constant, these rates per cell are proportional to cell surface area ($\propto r^2$) and volume ($\propto r^3$), respectively. Because growth rate is resource uptake divided by the amount needed to make a new cell (Thingstad et al. 2005), the dependence of growth rate on cell size is potentially affected by which of these three steps limits the uptake.

In most theoretical models, growth rate is simply formulated as a linear or a Monod function of a resource concentration in the medium. Pasciak and Gavis (1974, 1975) introduced a concept of colimitation by diffusive transport and membrane uptake of resource molecules. Synthetic steps such as enzymatic catalysis within a cell may also limit resource uptake. Colimitation by membrane uptake and enzymatic catalysis within a cell was formulated by Droop (1974) and applied in various models (e.g., Thingstad 1987; Grover 1991, 2003; Klausmeier et al. 2004). Although diffusive transport, membrane uptake, and cellular catalysis probably limit resource uptake simultaneously in aquatic environments, no model other than that of Baird and Emsley (1999) has considered all these processes simultaneously.

Theoretical studies have shown that, at equilibrium, the number of coexisting species is limited by the number of resources (Phillips 1973; Armstrong and McGehee 1980). Different forms of an element have been considered as substitutable resources (e.g., N_2, NO_2^-, NO_3^-, NO_4^+ as inorganic nitrogen; Tilman 1982, p. 35); however, coexistence on substitutable resources is impossible without trade-offs in uptake of different resources in a homogeneous environment (Vincent et al. 1996). Therefore, limiting resources in aquatic environments are traditionally considered to be a handful of essential elements. One way to explain the coexistence of planktonic microorganisms in the apparently homogeneous environments (the paradox of the plankton; Hutchinson 1961) is to expand the concept of resources. For example, Huisman and Weissing (1994) emphasized the importance of light as a resource for phytoplankton, and Stomp et al. (2004) showed that light is not an indivisible resource but that different wavelengths of light can be thought of as different resources that may promote phytoplankton diversity. Nevertheless, it seems difficult to attribute the tremendous degree of microbial diversity to the known diversity of resources that microbes require (Hutchinson 1961; Torsvik et al. 2002).

In this study, we consider resource-consumer dynamics where resource uptake is colimited by three steps in series: diffusive transport, membrane uptake, and cellular catalysis, and we generalize the concept of optimal cell size in resource competition. We show that the optimal cell size decreases with size of resource molecule when resource uptake is limited by diffusive transport and membrane uptake. In turn, this size dependence enables coexistence of microorganisms on multiple-sized resources.

Model

Resource Uptake in Fluids

We consider spherical cells that take up resource molecules in an aqueous medium. For simplicity, we assume that cells do not change their size during the cell cycle. We first consider the case that a single type of resource molecule (e.g., glucose, nitrate, phosphate) supplies a limiting element (carbon, nitrogen, or phosphorus); the case of multiple types of resources is considered later. Here the resource uptake is dissected into three steps. Resource molecules are (1) transported by diffusion to the cell surface (diffusive transport), (2) taken up by membrane transporters (membrane uptake), and (3) synthesized by enzymatic catalysis within cells (cellular catalysis). We formulate the general case where resource uptake is limited by all three steps, and then consider special cases of limitation by one or two of the three steps.

Let M (nmol element mL^{-1}) be the resource concentration in the medium and m (nmol element mL^{-1}) be the concentration at the cell surface (note that the units are in element concentrations, not molecule concentrations). The diffusive transport of resource (nmol element day^{-1} $cell^{-1}$) to the surface of a spherical cell of radius r (μm) is expressed by (Berg and Purcell 1977; Jumars et al. 1993; Karp-Boss et al. 1996)

$$4\pi r S_h D(M - m), \tag{1}$$

where S_h is the Sherwood number, defined as the ratio of mass transfer in total to that in the absence of fluid motion; D (m^2 day^{-1}) denotes the molecular diffusion coefficient of resource that inversely correlates with the molecular radius according to the Stokes-Einstein equation. Membrane uptake per unit surface area is assumed to be independent of cell radius and to be a function of m and relative cell quota, $q = (Q - Q_{min})/(Q_{max} - Q_{min})$, where Q (nmol element $cell^{-1}$) is the cell quota, and Q_{max} and Q_{min}, respectively, are the maximum and minimum cell quotas. Cellular catalysis per unit volume is assumed to be independent of cell radius and to be expressed by a function of q.

At steady state, the three steps are balanced, and a steady flux of resource to a cell (J, nmol element day^{-1} $cell^{-1}$) is

$$J_{\mathrm{DVC}} = 4\pi r S_{\mathrm{h}} D(M - m) = 4\pi r^2 f(m, q) = \frac{4}{3}\pi r^3 g(q), \quad (2)$$

where the subscripts D, V, and C denote the simultaneous limitation by diffusive transport, membrane uptake, and cellular catalysis, respectively. The functions $f(m, q)$ and $g(q)$ are the membrane uptake rate per unit surface area (nmol element $\mu\mathrm{m}^{-2}$ day^{-1}) and cellular catalysis rate per unit volume (nmol element $\mu\mathrm{m}^{-3}$), respectively. In our model, $f(m, q)$ is expressed by a Monod function with negative feedback from the internal resource pool (Thingstad 1987):

$$f(m, q) = (1 - q)\frac{\nu m}{m + K}, \quad (3)$$

and $g(q)$ is expressed by a linear function $g(q) = \alpha q$ for $0 \le q \le 1$.

If S_{h} or D is sufficiently large, then $(M - m)$ goes to 0. In an extreme case, $M = m$, and limitation by diffusive transport can be neglected. If membrane uptake (or cellular catalysis) is sufficiently fast compared to other steps, $m = 0$ (or $q = 0$) in an extreme case, and limitation by membrane uptake can be neglected. When one or two steps limit resource uptake, equation (2) is modified to represent diffusive transport limitation:

$$J_{\mathrm{D}} = 4\pi r S_{\mathrm{h}} D M, \quad (4)$$

membrane uptake limitation:

$$J_{\mathrm{V}} = 4\pi r^2 f(M, 0), \quad (5)$$

cellular catalysis limitation:

$$J_{\mathrm{C}} = \frac{4}{3}\pi r^3 g(q), \quad (6)$$

diffusive transport and membrane uptake limitation:

$$J_{\mathrm{DV}} = 4\pi r S_{\mathrm{h}} D(M - m) = 4\pi r^2 f(m, 0), \quad (7)$$

diffusive transport and cellular catalysis limitation:

$$J_{\mathrm{DC}} = 4\pi r S_{\mathrm{h}} D M = \frac{4}{3}\pi r^3 g(q), \quad (8)$$

and membrane uptake and cellular catalysis limitation:

$$J_{\mathrm{VC}} = 4\pi r^2 f(M, q) = \frac{4}{3}\pi r^3 g(q). \quad (9)$$

Uptake of Multiple Resources of Different Molecular Sizes

Formulation (2) can be extended for the uptake of multiple resource species. We consider n resource species that each contains a particular limiting element. Let $J_{\mathrm{DVC}i}$ be fluxes of resource i when the three steps colimit resource uptake; $J_{\mathrm{DVC}i}$ is described by

$$J_{\mathrm{DVC}i} = 4\pi r S_{\mathrm{h}} D_i(M_i - m_i) = 4\pi r^2 f_i(m_1, m_2, \ldots, m_n, q), \quad (10)$$

where symbols with subscript i ($=1, 2, \ldots, n$) denote resource i. At steady state, total resource flux to a cell, $J_{\mathrm{DVC}} = \sum_i J_{\mathrm{DVC}i}$, equates with cellular catalysis:

$$J_{\mathrm{DVC}} = \sum_i J_{\mathrm{DVC}i} = \frac{4}{3}\pi r^3 g(q). \quad (11)$$

Equations (10) and (11) describe the uptake of multiple resources under colimitation by the three steps. Limitations by one or two steps are expressed analogously, using appropriate subscripts. In this article, we assume that resource species of different molecular sizes share the same transporters. Then, membrane uptake of resource i per unit cell surface area is expressed by

$$f_i(m_1, m_2, \ldots, m_n, q) = (1 - q)\frac{\nu \varepsilon_i m_i}{\sum_i \varepsilon_i m_i + K}, \quad (12)$$

where ε_i is relative affinity of transporters to resource i.

Resource-Consumer Dynamics

Let B (cells mL^{-1}) be the cell density of a consumer. We assume that biomass losses can be partitioned into size-independent loss and size-dependent loss (with the allometric exponent ρ). Under a constant supply of resources, the resource-consumer dynamics can be expressed by

$$\frac{dM}{dt} = \kappa(M_{\mathrm{IN}} - M) - JB,$$

$$\frac{dB}{dt} = B\left(\frac{J}{Q} - \theta r^{\rho} - \omega\right), \quad (13)$$

where κ (day^{-1}) is dilution rate, M_{IN} (nmol element mL^{-1}) is the concentration of resource input, ρ and θ ($\mu\mathrm{mol}^{-\rho}$

day^{-1}) are the exponent and constant of size-dependent loss, and ω (day^{-1}) is the size-independent loss. Cells are assumed to be isolated enough to allow no overlaps of diffusive boundary layer (Siegel 1998). Minimum and maximum cell quotas are assumed to be proportional to cell volume: $Q_{min} = \beta \times (4/3)\pi r^3$ and $Q_{max} = \gamma \times (4/3)\pi r^3$.

The numerical examples we present consider heterotrophic bacteria grown in a carbon-limited chemostat (table 1). Respiration loss was assumed to be proportional to (cell volume)$^{3/4}$, resulting in a negative allometric exponent of size-dependent loss, $\rho = -0.75$. We used the molecular diffusion coefficient of nitrate (1.5×10^{-5} cm^2 s^{-1}; Pasciak and Gavis 1974) for reference and assumed that resource molecules are spherical and that the volume is proportional to the molecular weight (Da): D (m^2 d^{-1}) $= 5.13 \times 10^{-4} \times Da^{-1/3}$. The half-saturation constant of membrane uptake (K) was taken to be one order of magnitude smaller than that in Thingstad (1987), in which uptake is a Monod function of resource concentration in the medium. Conversion factors from cell volume to minimum and maximum cell quotas (β and γ) were taken from carbon content per unit volume reported by Scavia and Laird (1987) that are consistent with cell quota used in Thingstad (1987) for a spherical cell of $r = 0.3$ μm. Maximum rates of membrane uptake (ν) and cellular catalysis (α) were chosen so that the maximum growth rate is 3 day^{-1} for a spherical cell of $r = 0.3$ μm and $q = 0.5$. We determined θ so that the maximum growth efficiency is 50% (del Giorgio and Cole 1998) for a spherical cell of $r = 0.3$ μm.

Results

The Existence of Optimal Cell Size

A positive steady state (M^*, B^*) satisfies equalities

$$0 = \kappa(M_{IN} - M^*) - J^*B^*, \tag{14}$$

$$0 = \frac{J^*}{Q^*} - \theta r^{\rho} - \omega, \tag{15}$$

where symbols with an asterisk denote their steady state values. The steady state is calculated explicitly in each limitation case (table 2). Based on the R^* theory of resource competition (Tilman 1982), the optimal cell radius ($\bar{r}$) is defined as the cell radius that minimizes M^* (fig. 1). Depending on the exponent of size-dependent loss (ρ), the optimal cell radius is either 0 or a positive value, except when resource uptake is limited by cellular catalysis; in this case, M^* ($= 0$) is independent of cell radius. The positive optimal cell radii were obtained either explicitly ($\bar{r}_D$, $\bar{r}_V$, $\bar{r}_{DC}$, $\bar{r}_{VC}$; table 2) or implicitly ($\bar{r}_{DV}$, $\bar{r}_{DVC}$; see appendix in the online edition of the *American Naturalist*). When resource uptake is limited by diffusive transport, the exponent of size-dependent loss $\rho < -2$ is necessary for a positive $\bar{r}_D$. In contrast, when resource uptake is limited by cellular catalysis and one or two other steps, a positive $\bar{r}$ exists if loss rate depends negatively on cell radius (i.e., $\rho < 0$), no matter how weak the dependence is. Detailed calculations and conditions for the existence of positive optimal cell radii are shown in the appendix.

Figure 1 shows the dependence of the steady state resource concentration (M^*_{DVC}) on cell radius (r) of heterotrophic bacteria grown in a chemostat. Parameter values used in the numerical calculation are shown in table 1. Quantity M^*_{DVC} is at its minimum at an intermediate cell radius, $\bar{r}_{DVC}$. Figure 2 shows the dependence of $\bar{r}$ on the exponent of size-dependent loss (ρ). The following inequalities hold for optimal cell radii:

$$\bar{r}_D < \bar{r}_{DV} < \bar{r}_V, \tag{16}$$

$$\bar{r}_{DC} < \bar{r}_{DVC} < \bar{r}_{VC}. \tag{17}$$

Derivations of inequalities (16) and (17) are found in the appendix.

The optimal cell radii $\bar{r}_D$, $\bar{r}_V$, $\bar{r}_{DC}$, and $\bar{r}_{VC}$ are independent of diffusion coefficient D, which is inversely correlated with resource molecular radius. Thus, size of resource molecule has no influence on cell size in these cases. They are also independent of the Sherwood number (S_h) and the half-saturation constant (K). Thus, fluid motion or affinity of transporters to resource molecules ($\propto 1/K$) does not affect the optimal cell radius. In contrast, $\bar{r}_{DV}$ and $\bar{r}_{DVC}$ depend positively on D, S_h, and K; the cell size increases with fluid motion and decreases with resource molecule size and the affinity of transporters (fig. 3*A*–3*C*); $\bar{r}_{DVC}$ has its minimum at an intermediate dilution coefficient (κ) and increases with storage capacity (the ratio of maximum and minimum quota; fig. 3*D*, 3*E*).

Competition for Two Resources of Different Molecular Sizes

We examined coexistence of two different-sized consumers on two resources of different molecular sizes. Invasibility criteria were used to determine the outcome of competition. We assume that consumers are identical except their sizes and that resource molecules are spherical and contain the limiting element proportional to their volume.

When resource uptake is limited by diffusive transport (D), membrane uptake (V), diffusive transport and cellular catalysis (DC), or membrane uptake and cellular catalysis (VC), a superior consumer always outcompetes the other, and no coexistence is possible. In these cases, the order

Table 1: Symbols and their interpretations

Symbol	Definition (unit)	Value
Subscripts:		
D	Limitation by diffusive transport	
V	Limitation by membrane uptake	
C	Limitation by cellular catalysis	
Variables:		
B	Cell density (cells mL^{-1})	…
M	Resource concentration (nmol element mL^{-1})	…
J	Resource flux per cell (nmol element day^{-1} $cell^{-1}$)	…
r	Cell radius (μm)	…
m	Resource concentration at cell surface (nmol element mL^{-1})	…
q	Relative cell quota: $(Q - Q_{min})/(Q_{max} - Q_{min})$	…
Q	Cell quota (nmol element $cell^{-1}$)	…
Q_{min}	Minimum cell quota (nmol element $cell^{-1}$)	…
Q_{max}	Maximum cell quota (nmol element $cell^{-1}$)	…
B^*	Steady state cell density (cells mL^{-1})	…
M^*	Steady state resource concentration (nmol element mL^{-1})	…
$\bar{r}$	Optimal cell radius (μm)	…
r_{ESS}	Evolutionarily stable strategy cell radius (μm)	…
Functions:		
$f(m, q)$	Membrane uptake rate per unit area (nmol element μm^{-2} day^{-1})	…
$g(q)$	Cellular catalysis rate per unit volume (nmol element μm^{-3} day^{-1})	…
Parameters:		
M_{IN}	Resource input concentration (nmol element mL^{-1})	…
D	Molecular diffusion coefficient of resource (m^2 day^{-1})	$5.13 \times 10^{-4} \times Da^{-1/3}$
K	Half-saturation constant of membrane uptake (nmol element mL^{-1})	.1
α	Maximum cellular catalysis rate (nmol element μm^{-3} day^{-1})	7.72×10^{-5}
β	Conversion factor from cell volume to minimum quota (nmol element μm^{-3})	8.92×10^{-6}
γ	Conversion factor from cell volume to maximum quota (nmol element μm^{-3})	1.69×10^{-5}
ε_i	Relative affinity of membrane transporters to resource i	1
ν	Maximum membrane uptake rate (nmol element μm^{-2} day^{-1})	7.72×10^{-6}
ρ	Allometric exponent of size-dependent loss (−)	−.75
θ	Factor of size-dependent loss ($\mu m^{-\rho}$ day^{-1})	.608
ω	Size-independent loss rate (day^{-1})	.1
κ	Dilution rate (day^{-1})	.1
S_h	Sherwood number	1

of the steady state resource concentrations (M^*; table 2) with respect to cell radius (r) is independent of molecular diffusion coefficient (D), the Sherwood number (S_h), and the half-saturation constant (K), and hence competitive ability is not affected by them.

When diffusive transport and membrane uptake (DV) or all three steps (DVC) limit resource uptake, two consumers can coexist on two resources of different molecular sizes if cell sizes of two consumers and inputs of two resources are chosen correctly. The steady-state concentrations of resources 1 and 2 for a consumer j, (M_{1j}^*, M_{2j}^*), rest on a line (zero net growth isocline [ZNGI]),

$$\frac{M_{1j}^*}{\hat{M}_{1j}} + \frac{M_{2j}^*}{\hat{M}_{2j}} = 1, \tag{18}$$

where $\hat{M}_{ij}$ is the intercept of resource i axis, which is equivalent to M^* when consumer j grows on resource i. The direction of the consumption vector (Tilman 1982) on the ZNGI is expressed by

$$\mathbf{u} = \left(\frac{M_{1j}^*}{\hat{M}_{1j}}, \frac{M_{2j}^*}{\hat{M}_{2j}}\right). \tag{19}$$

The derivations of the ZNGI and $\mathbf{u}$ are found in the appendix. The ZNGIs and consumption vectors of two consumers are depicted in figure 4, where consumers 1 and 2, respectively, are superior competitors for resources 1 and 2 (i.e., $\hat{M}_{11} < \hat{M}_{12}$ and $\hat{M}_{21} > \hat{M}_{22}$). From the order of slopes of two consumption vectors (fig. 4*A*), both consumers can invade the other when resource inputs (M_{IN1}, M_{IN2}) are between the two vectors, suggesting the coexistence of the two consumers (Tilman 1982). Figure

4*B* shows a numerical example of ZNGIs and consumption vectors, in which resource 1 is a small molecule (50 Da) and resource 2 is a large molecule (600 Da).

Evolutionarily Stable Strategy (ESS) Cell Size on Two Resources of Different Molecular Sizes

Next, we examined the evolutionary outcome of competition for two resources of different molecular sizes. We numerically generated a pairwise invasibility plot (PIP; fig. 5*A*) that shows regions where a rare species can invade a monoculture of a resident species (marked with a plus sign) or where it cannot (marked with a minus sign). In figure 5*A*, two lines, where the growth rate of an invader is 0, intersect at one point (r_{ESS}) that is classified as an evolutionarily and convergent stable strategy (Geritz et al. 1997). By flipping the PIP around its 45° axis and superimposing it back on itself, we can assess the outcome of competition between two species (fig. 5*B*). Figure 5*B* indicates regions where a pair of two different-sized cells is mutually invasible, that is, regions of coexistence of two species. The coexistence regions move within an area between the dotted lines in fig. 5*B* with changes in inputs of two resources. The ESS cell radius decreases when the relative availability of large resource molecules increases (fig. 6).

Discussion

In this study, we showed conditions for the existence of an optimal cell size when resource uptake is limited by diffusive transport, membrane uptake, and/or cellular catalysis. In previous studies on cell size of microorganisms, resource uptakes were modeled either as a single-step process of diffusive transport or membrane uptake (Laws 1975; Jumars 1993; Jiang et al. 2005; Thingstad et al. 2005) or as a two-step process of membrane uptake and cellular catalysis (Grover 1991; Stolte and Riegman 1996). This is the first study that considers three steps for resource uptake—diffusive transport, membrane uptake, and cellular catalysis. Because those three steps are related to cell size with different exponents, this inclusive analysis is necessary for a fuller understanding of cell size.

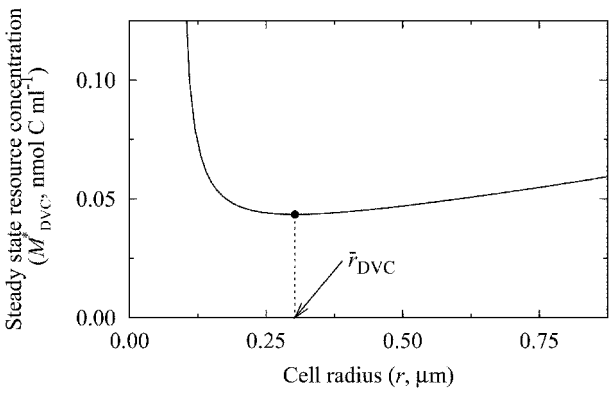

Figure 1: Steady state resource concentration (M^*_{DVC}) against consumer's cell radius (r) when resource uptake is limited by diffusive transport, membrane uptake, and cellular catalysis. The resource molecular weight used in the calculation is 100 Da. Other parameter values are found in table 1. M^*_{DVC} has its minimum value at an intermediate cell radius (optimal cell radius, $\bar{r}_{\mathrm{DVC}}$, marked with a solid circle).

Smaller cells are generally favored under diffusive trans-

Table 2: Steady state resource concentrations (M^*) and optimal cell radii ($\bar{r}$) when resource uptake is limited by diffusive transport (D), membrane uptake (V), and/or cellular catalysis (C)

Limitation			Optimal cell radius (ρ)			
D	V	C	0	Positive	M^*	$\bar{r}$
+			≥ -2	< -2	$\frac{\beta r^2(\theta r^\rho+\omega)}{3S_{\mathrm{h}}D}$	$\left[\frac{2\omega}{-(\rho+2)\theta}\right]^{1/\rho}$
	+		≥ -1	< -1	$\frac{\beta Kr(\theta r^\rho+\omega)}{3\nu-\beta r(\theta r^\rho+\omega)}$	$\left[\frac{\omega}{-(\rho+1)\theta}\right]^{1/\rho}$
		+	…	…	0	…
+	+		≥ -1	< -1	$\frac{\beta r^2(\theta r^\rho+\omega)}{3S_{\mathrm{h}}D}+\frac{\beta Kr(\theta r^\rho+\omega)}{3\nu-\beta r(\theta r^\rho+\omega)}$	†
+		+	≥ 0	< 0	$\frac{\alpha\beta r^2(\theta r^\rho+\omega)}{3S_{\mathrm{h}}D[\alpha-(\gamma-\beta)(\theta r^\rho+\omega)]}$	$\max\left\{\left(\frac{\alpha-\gamma\omega}{\gamma\theta}\right)^{1/\rho}, \left[\frac{\alpha(\rho+2)-4(\gamma-\beta)\omega+\sqrt{\alpha^2(\rho+2)^2-8\alpha(\gamma-\beta)\rho\omega}}{4(\gamma-\beta)\theta}\right]^{1/\rho}\right\}$
	+	+	≥ 0	< 0	$\frac{\alpha\beta Kr(\theta r^\rho+\omega)}{3\alpha\nu-[3\gamma\nu+\alpha\beta r](\theta r^\rho+\omega)}$	$\left[\frac{\alpha(\rho+1)-2\gamma\omega+\sqrt{\alpha^2(\rho+1)^2-4\alpha\gamma\rho\omega}}{2\gamma\theta}\right]^{1/\rho}$
+	+	+	≥ 0	< 0	$\frac{\alpha\beta r^2(\theta r^\rho+\omega)}{3S_{\mathrm{h}}D[\alpha-(\gamma-\beta)(\theta r^\rho+\omega)]}+\frac{\alpha\beta Kr(\theta r^\rho+\omega)}{3\alpha\nu-[3\gamma\nu+\alpha\beta r](\theta r^\rho+\omega)}$	†

Note: The optimal cell radius is either 0 or a positive value depending on the exponent of size-dependent loss (ρ). Optimal cell radii are expressed explicitly except when resource uptake is limited by DV or DVC (marked with a dagger). The implicit calculations of $\bar{r}_{\mathrm{DV}}$ and $\bar{r}_{\mathrm{DVC}}$ are shown in the appendix in the online edition of the *American Naturalist*.

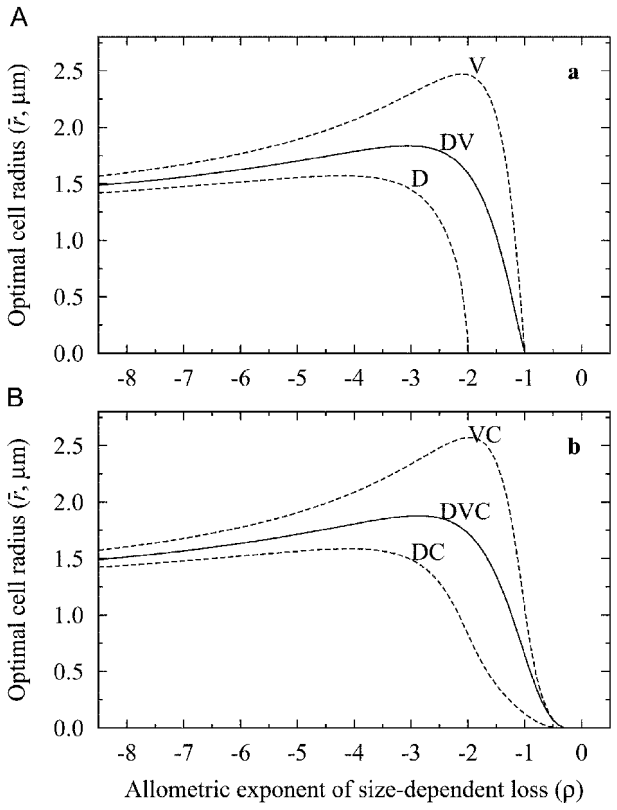

Figure 2: Optimal cell radius ($\bar{r}$) against the allometric exponent of size-dependent loss (ρ) in each case of limitation for resource uptake. *A*, Diffusive transport limitation (*D*), membrane uptake limitation (*V*), and diffusive transport and membrane uptake limitation (*DV*). *B*, Diffusive transport and cellular catalysis limitation (*DC*), membrane uptake and cellular catalysis limitation (*VC*), and diffusive transport, membrane uptake, and cellular catalysis limitation (*DVC*). The resource molecular weight used in the calculation is 100 Da.

port limitation (Koch 1996; Raven 1998). Jumars (1993) showed that an intermediate cell size can maximize resource gain per cell under diffusive transport limitation; however, smaller cells always show higher specific growth rate, hence fitness, unless cell quota scales to a power ≤ 1 with cell radius (Thingstad et al. 2005). Inequalities derived from our model, $\bar{r}_{\mathrm{D}} < \bar{r}_{\mathrm{DV}} < \bar{r}_{\mathrm{V}}$ and $\bar{r}_{\mathrm{DC}} < \bar{r}_{\mathrm{DVC}} < \bar{r}_{\mathrm{VC}}$, confirm the above statement. The optimal cell radius $\bar{r}_{\mathrm{DV(C)}}$ increases from $\bar{r}_{\mathrm{D(C)}}$ to $\bar{r}_{\mathrm{V(C)}}$ with increasing molecular diffusion coefficient. Because the diffusion coefficient is inversely correlated with the molecular radius, $\bar{r}_{\mathrm{DV(C)}}$ depends negatively on the size of resource molecule. Smaller resource molecules relax the diffusive transport limitation, resulting in selection for larger cells. An important observation is that the dependence on the size of resource molecules is realized only when a model incorporates both diffusive transport and membrane uptake for the resource uptake process.

Likewise, the sizes of resource molecules affect competition outcome under diffusive transport and membrane uptake limitations (fig. 4). The ZNGI (fig. 4) is similar to that of substitutable resources (Leon and Tumpson 1975; Tilman 1982; Vincent et al. 1996). For two substitutable resources in a homogeneous habitat, Vincent et al. (1996) showed that consumers can coexist if there are trade-offs in encounter efficiency or if consumers can selectively take up a particular resource. In our model, two consumers coexisted on two resources without explicit trade-offs or selectivity for resource uptake. Variation in the size of consumers implicitly generates a trade-off between uptakes of two resources of different molecular sizes via diffusive transport. Coexistence was shown analytically by assuming that different resources share the same transporters. When consumers utilized specific transporters for different resources, coexistence was confirmed numerically (result not shown).

Coexistence is possible when cell sizes of two consumers and inputs of two resources are chosen appropriately (figs. 4*B*, 5*B*). However, the region of coexistence is extremely narrow (fig. 4*B*). In the numerical example, we assumed 50 and 600 Da for molecular weights of two resources, and consumers that were identical except for their sizes. One way to expand this region is to increase the difference between two molecular weights, although 50 Da is the lower end of molecular weight of dissolved organic matter (DOM) observed in aquatic systems (Seitzinger et al. 2005) and 600 Da is the upper limit of resource molecules that pass through an outer membrane (Schirmer 1998). Uptake of resource molecules larger than 600 Da can be considered; however, to do so we may need to include additional factors such as corporate hydrolyzation by extracellular enzymes as another step of resource uptake (Ames 1986) and the dependence of the Sherwood number on cell radius and the diffusion coefficient of resource molecules (Confer and Logan 1991; Karp-Boss et al. 1996). This region is also expanded if each consumer can selectively take up resource molecules either by changing the affinity of membrane transporters to resources (when different resources are taken up by the same transporters) or by changing the ratio of specific transporters (when different resources are taken up by their specific transporters).

If cell size can adapt either evolutionarily or physiologically, a dimorphic population converges on a monomorphic population with cells of $r = r_{\mathrm{ESS}}$ (fig. 5*A*). Therefore, size diversity is predicted to diminish under a constant resource supply over a timescale of adaptive change in cell size. Whether variation in sizes of resource molecules promotes diversity in cell size in natural environments may

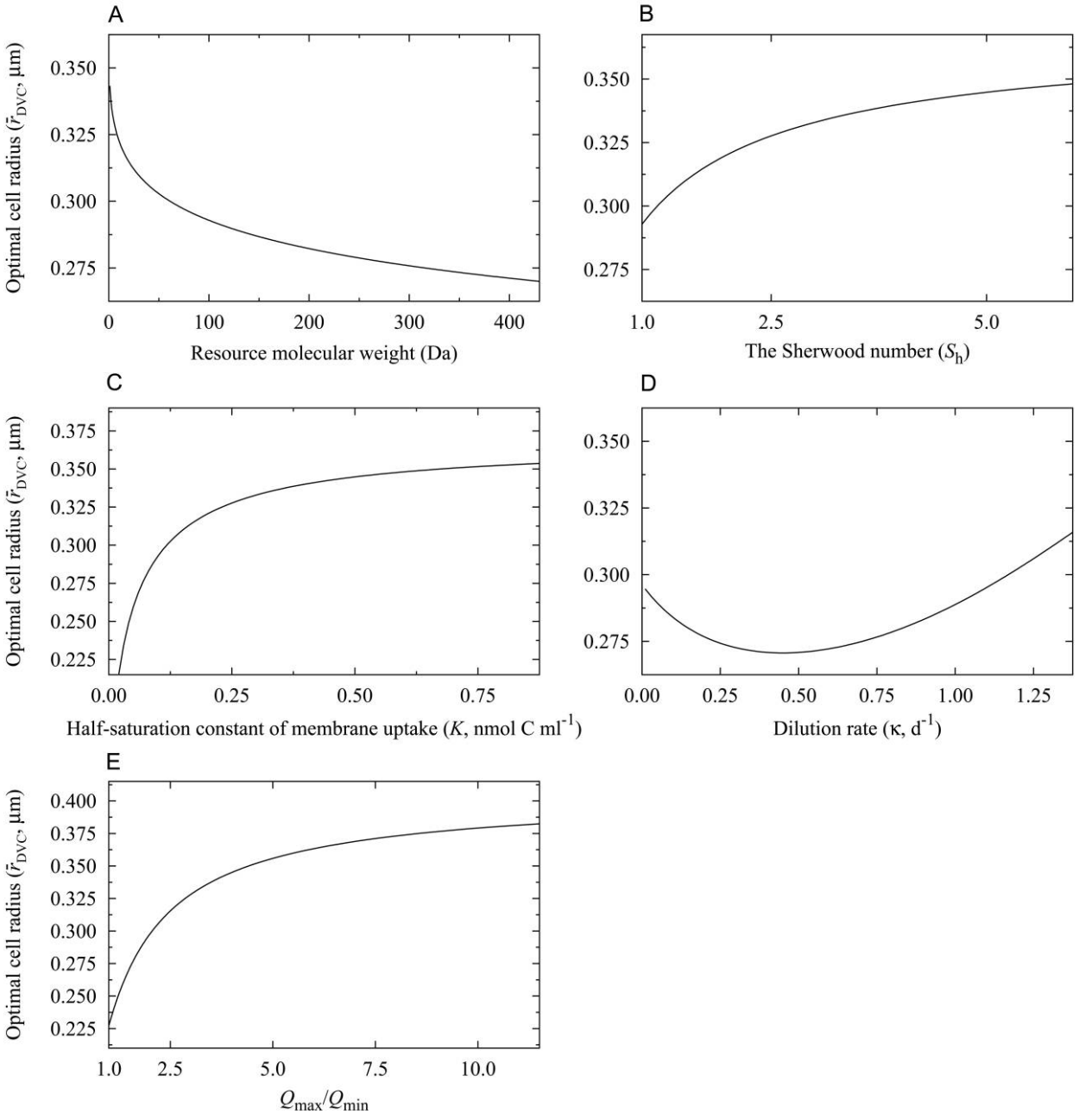

Figure 3: Dependence of the optimal cell radius ($\bar{r}_{DVC}$) on resource molecular weight (*A*), the Sherwood number (S_h; *B*), half-saturation constant of membrane uptake (K; *C*), dilution rate (κ; *D*), the ratio of maximum quota (Q_{max}) and minimum quota (Q_{min}) keeping the sum of Q_{max} and Q_{min} constant (*E*).

depend on the rate of adaptive change in cell size and degree of fluctuation in resource supply.

Our model makes two predictions that are experimentally testable. Natural bacteria live in a mixture of dissolved organic carbon (DOC) molecules, most of which are larger than glucose molecules (Seitzinger et al. 2005). Therefore, the first prediction is that natural bacteria will grow large when incubated on glucose under carbon limitation in the absence of grazers. Numerous experiments already support this prediction (e.g., Mongold and Lenski 1996; Nishimura et al. 2005). However, experiments explicitly designed to test this prediction have not been done. The second pre-

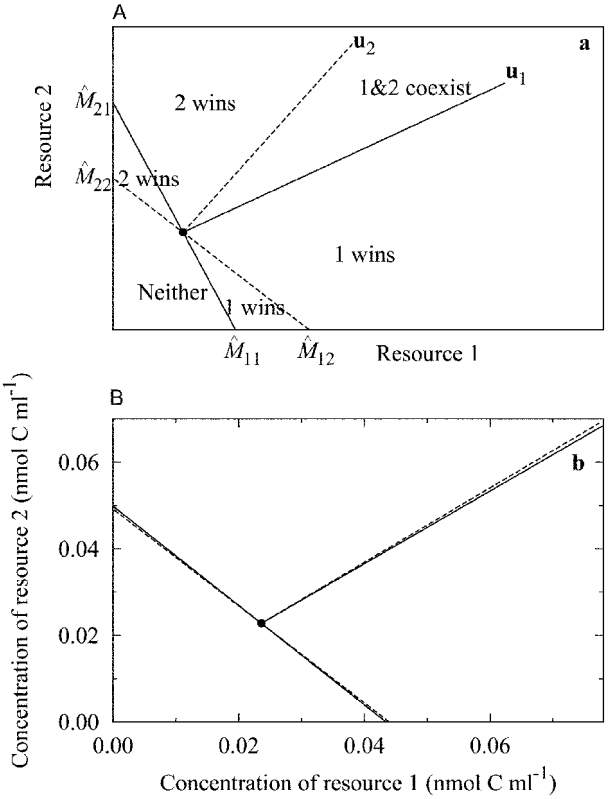

Figure 4: Zero net growth isocline (ZNGI) and consumption vectors ($\mathbf{u}_1$ and $\mathbf{u}_2$) of two consumers. Consumer 1 (*solid lines*) is assumed to be a better competitor for resource 1, while consumer 2 (*dashed lines*) is a better competitor for resource 2. The two consumers coexist when resource inputs (M_{IN1}, M_{IN2}) are between the two consumption vectors (indicated by $\mathbf{u}_1$ and $\mathbf{u}_2$). The conceptual picture of ZNGI, consumption vectors, and the outcome of competition are shown in *A*. A numerical example is shown in *B*, where resource 1 is a small molecule of 50 Da and resource 2 is a large molecule of 600 Da.

diction is that bacterial size distribution will be different when bacteria are incubated on DOC sources of varying sizes, such as glucose, maltose, and polysaccharides; the average size will be smaller when bacteria are grown on larger DOC. We do not know of experimental evidence that supports the second prediction, but it is testable by a simple chemostat experiment. Similar experiments can be done on a nitrogen-limited bacterial community, by supplying various-sized dissolved organic nitrogen species such as urea, amino acids, and polypeptides, or on a phosphorus-limited bacterial community, by supplying phosphate and dissolved organic phosphorus. These predictions can also be applied to phytoplankton. Because phytoplankton can utilize organic phosphorus and nitrogen (Antia et al. 1991; Dyhrman and Ruttenberg 2006), the size variety of DOM might have a substantial effect on phytoplankton community composition.

To our knowledge, this is the first theoretical study that relates the size of microbial consumers to the size of their abiotic resources. The obtained resource-consumer size relationship (fig. 3*A*) is the opposite of what is expected from the general predator-prey size relationships (Cohen et al. 1993; Layman et al. 2005); we find that larger resource molecules favor smaller consumers. This discrepancy can be explained by differences between predator-prey and resource uptake processes. In the former, interactions can be scaled to predator-prey size ratio (Weitz and Levin 2006), while in the latter, because the resource is taken up by membrane transporters, resource sizes are not directly

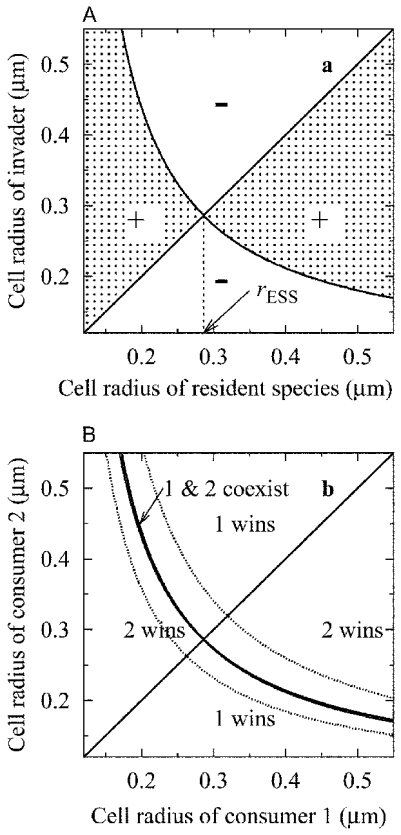

Figure 5: Competition between two different-sized consumers for two resources (molecular weights, 50 and 600 Da; input concentrations, $M_{IN1} = M_{IN2} = 5$ nmol C mL^{-1}). *A*, Pairwise invasibility plot. Cell radii of resident and invader species are on the *X*- and the *Y*-axis, respectively. Solid lines separate the regions where invader has positive (marked with a plus sign) or negative (marked with a minus sign) growth rate. The evolutionarily stable strategy cell radius is indicated by r_{ESS}. *B*, Outcome of competition of two consumers. Solid lines separate regions where consumer 1 outcompetes consumer 2 (indicated by *1 wins*) and consumer 2 outcompetes consumer 1 (indicated by *2 wins*). The region indicated by "1 & 2 coexist" is where two of consumers coexist. The area between two dotted lines represents an envelop of the region of coexistence; the region moves within the envelope with changing resource input concentrations.

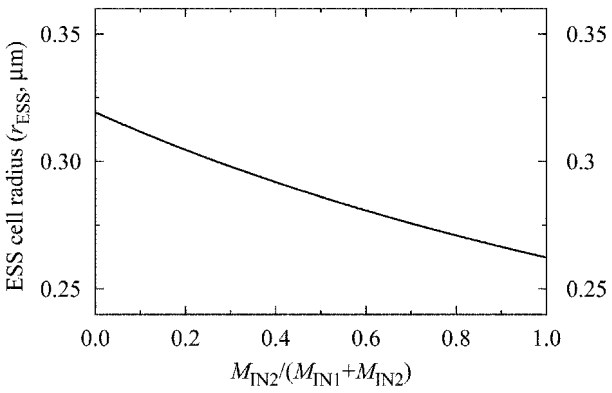

Figure 6: Dependence of the evolutionarily stable strategy (ESS) cell radius (r_{ESS}) on the ratio of inputs of two resources (molecular weights, 50 and 600 Da). The *X*-axis is the input concentration of resource 2 relative to total input. The r_{ESS} varies monotonously between the optimal cell radii for resources 1 and 2.

related to consumer sizes. In our theory, resource sizes are related to consumer sizes indirectly by altering the relative significance of diffusive transport. The size relationships may be affected by other factors that we did not consider here. For example, if affinity of membrane transporters systematically decreases with size of resource molecule, both diffusive transport and membrane uptake slow down with molecular size, resulting in ambiguous or reverse size relationships. Though there are numerous studies that relate cell sizes to resource concentrations, no study has compared size distributions of microorganisms and resources. Thus, empirical test of this prediction is difficult with existing data. Recent developments in chemical analysis allow us to obtain size distributions and characteristics of DOM in aquatic environments (Seitzinger et al. 2005). It is of great interest to test our prediction by comparing size distributions of DOM with those of phytoplankton and bacteria obtained by flow cytometry (Li 2002; Nishimura et al. 2005). Our prediction can best be tested in environments with a relatively constant DOM composition, such as the open ocean, but not in environments, such as coastal waters, where the effect of fluctuations in resources on cell size may be significant (Malone 1980).

Although the allometric relation between metabolic rate and body mass has been intensively examined for a wide range of organisms (Gillooly et al. 2001), it is less clear and still controversial for microorganisms (Laws 1975; Banse 1976; Blasco et al. 1982; Makarieva et al. 2005). Patterson (1992) hypothesized that the variation in the mass exponents of growth and respiration rates of aquatic organisms (0.47 ~ 1.28; Patterson 1992) can be explained by the diffusive transfer of metabolically important molecules between cells of different shapes (sphere, cylinder, or plate) and environments in different flow conditions (laminar or turbulent). Makarieva et al. (2005) suggested that metabolic rate has a universal size-independent component that is more prominent for smaller organisms such as prokaryote species. We suggest that cell growth is a multistep process that consists of size-dependent and size-independent subprocesses. In our model, growth rate is an outcome of diffusive transport (mass exponent: 1/3) and biological uptake (mass exponent: 2/3 or 1). Thus, the resulting mass exponent varies from 1/3 to 1, depending on environmental conditions and cell physiological states that determine which subprocesses limit cell growth more. Mass exponents greater than 1 cannot be explained by our model because we considered spherical cells only (Patterson 1992).

We assumed a constant allometric exponent for the size-dependent loss (ρ) rather than considering the mechanistic detail of a specific process. The above simplification allowed us to clarify the condition for the existence of a positive optimal cell radius. Our model can be extended to include the mechanistic detail of respiration or realistic functions of grazing loss. The numerical example assumed that a mass exponent of respiration loss is 3/4 (Banse 1976; Gillooly et al. 2001), which corresponds to $\rho = -0.75$ ($=3/4 \times 3 - 3$ for a spherical cell). This assumption affects our numerical results considerably because the optimal cell radius is relatively sensitive around this value (fig. 2*B*).

Though the analytical expressions allow optimal cell sizes to be infinitely large (e.g., $\bar{r}_{D,V,DV} \to \infty$ for $\omega \to 0$; table 2), optimal cell sizes in our numerical example are limited to relatively narrow range of small cells (figs. 2, 3). This may be because our model lacks important characteristics common for giant cells (Villareal 1992; Villareal et al. 1999; Schulz and Jørgensen 2001). We assumed isometric storage capacity (Q_{min}, Q_{max}, $\propto r^3$); however, both the biggest bacteria (*Thiomargarita namibiensis*) and phytoplankton (*Ethmodiscus* spp.) are suggested to have disproportionally large vacuoles to store nitrate to cope with opposing gradients of two resources (hydrogen sulfide and the oxidizer [nitrate] for *Thiomargarita namibiensis*; light and nitrate for *Ethmodiscus* spp.). We did not consider fluctuations in resource supply, which are generally suggested to favor larger cells (Grover 1991; Stolte and Riegman 1996). We assumed that S_h is a constant parameter, although it depends on cell size and molecular diffusion coefficient of resource as well as fluid motion (Karp-Boss et al. 1996). For a spherical cell of $r < 5$ μm, with the swimming speed <10 diameters s^{-1} (Dusenbery 1997) taking up resource molecules <600 Da ($D > 0.61 \times 10^{-4}$ m^2 d^{-1} $= 7.06 \times 10^2$ μm^2 s^{-1}; table 2), S_h is less than 1.1 (according to eq. [18] in Karp-Boss et al. 1996). While our results may be valid as long as S_h is close to unity, the dependence of S_h on cell size and diffusion

coefficient may affect our results substantially when sizes of cells and resource molecules are large (Confer and Logan 1991).

Using a simple model, we investigated optimal cell size for resource uptake in fluids where diffusive transport of resources is an inherent factor in acquiring resources. An important implication is that resources of different molecular sizes favor different-sized cells; size variations of resource molecules affect the outcome of competition and may promote size diversity of consumers. In the model, trade-offs for resource uptake were not explicitly incorporated but derived from the biophysical mechanisms. On one hand, the model simplicity enabled us to perform analyses on optimal cell size and coexistence of different-sized consumers, but on the other hand, our model does not include important details that may affect cell size, such as resource fluctuations (Grover 1991; Stolte and Riegman 1996), changes in cell sizes during the cell cycle (Ward and Glaser 1971; Mitchison 2003), and swimming behavior that can enhance resource uptake in chemical gradients at the expense of energetic cost (Dusenbery 1997; Mitchell 2002; Berg 2003). Our model can be further extended by including those factors explicitly. This theory links sizes of microorganisms and their resource molecules, and it adds a new dimension to the concept of "resource" in aquatic environments.

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