Effects of rising CO_2 on the harmful cyanobacterium Microcystis

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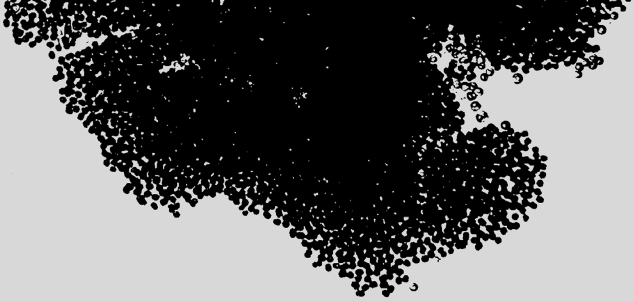

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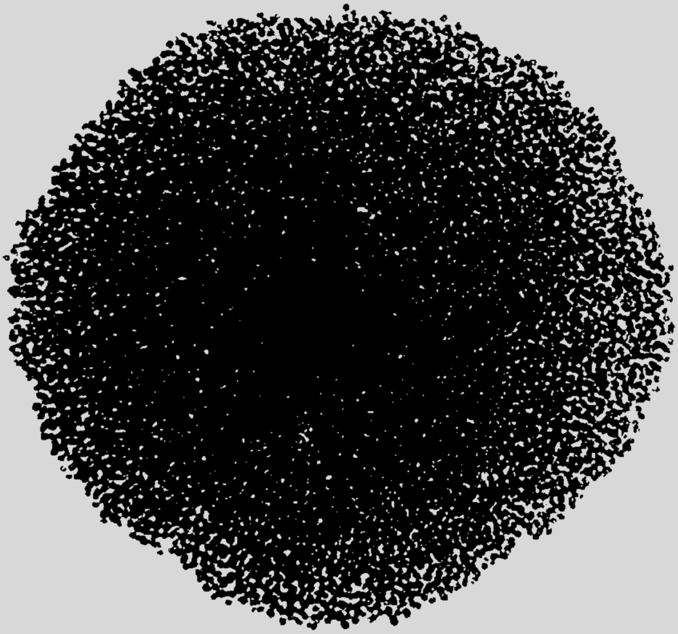

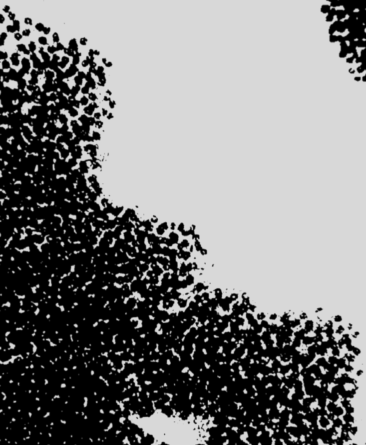

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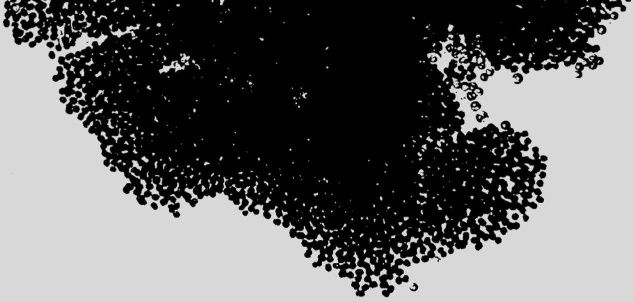
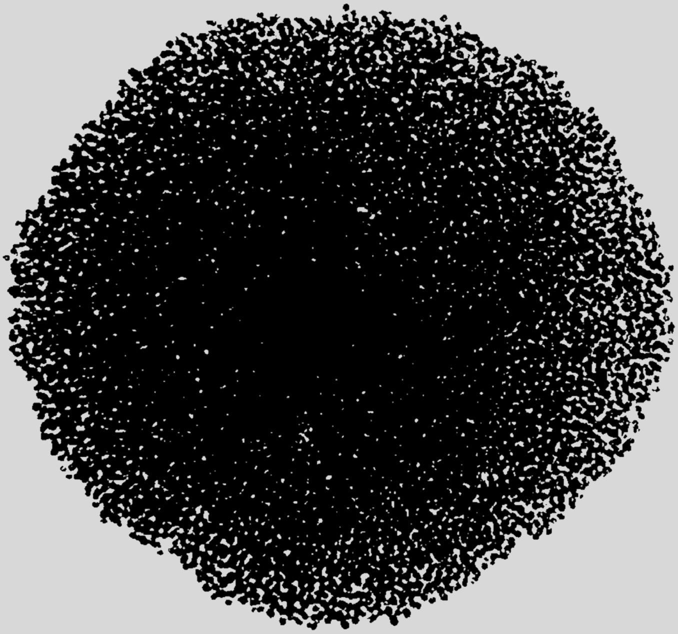
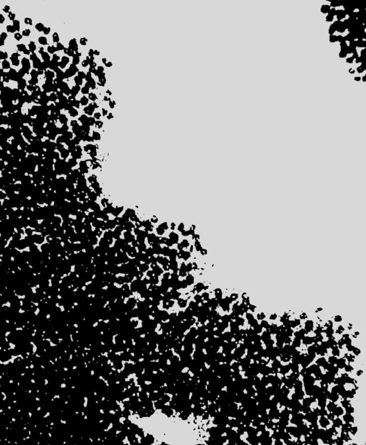


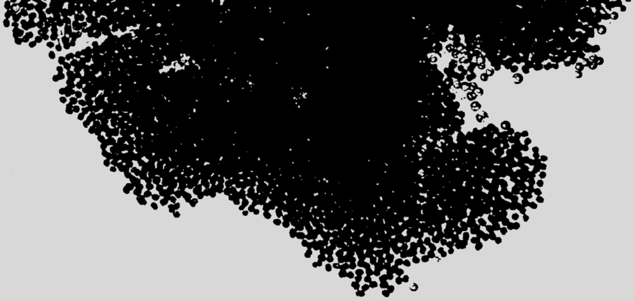
List of frequently used abbreviations, symbols and genes



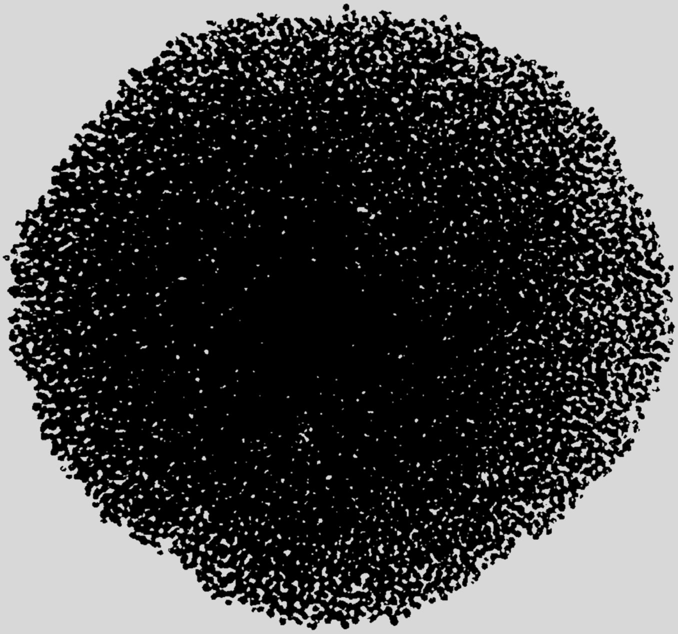


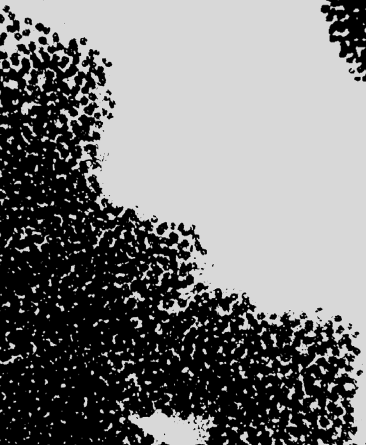
2PG	2-phosphoglycerate
3PG	3-phosphoglycerate
ATP	adenosine triphosphate
BCT1	ATP-dependent bicarbonate uptake system (high affinity, low flux)
bicA	gene encoding sodium-dependent bicarbonate uptake system BicA
BicA	sodium-dependent bicarbonate uptake system (low affinity, high flux)
CA	carbonic anhydrase
CCM	CO_2-concentrating mechanism
ccmR	gene encoding transcriptional regulator CcmR
ccmR2	gene encoding transcriptional regulator CcmR2
cDNA	complementary DNA, synthesized from messenger RNA
C_i	inorganic carbon
Chl *a*	chlorophyll *a* (pigment)
chpY (=cupA)	gene encoding CO_2 hydration subunit of CO_2 uptake system NDH-I$_3$
chpX (=*cupB*)	gene encoding CO_2 hydration subunit of CO_2 uptake system NDH-I$_4$
cmpA	gene encoding bicarbonate-binding subunit of uptake system BCT1
CO_2(aq)	carbon dioxide dissolved in water
CO_3^{2-}	carbonate
DIC	dissolved inorganic carbon
DOC	dissolved organic carbon
HCO_3^-	bicarbonate
g_{CO2}	CO_2 gas influx
gDNA	genomic DNA
flv1-4	genes encoding flavodiiron proteins, involved in oxidative stress protection
I / I_{in} / I_{out}	irriadiance / incident irriadiance / irradiance penetrating through vessel
isiA	gene encoding iron stress-induced protein
$K_{0.5}$	half-saturation constant
K_H	solubility constant of CO_2 gas in water
MC	microcystin (hepatotoxin)
mcyB	microcystin synthetase gene
NADPH	nicotinamide adenine dinucleotide phosphate
NDH-I$_3$	CO_2 uptake system (high affinity, low flux)
NDH-I$_4$	CO_2 uptake system (low affinity, high flux)
nhaS1-6	genes encoding sodium/proton antiporters
PAR	photosynthetically active radiation, spectral range used for photosynthesis
pCO_2	partial pressure of CO_2

PKS	polyketide synthetase
ppm	parts per million
PSI	photosystem I
PSII	photosystem II
rbcX	gene encoding RuBisCO chaperone
ROS	reactive oxygen species, chemically reactive molecules containing oxygen
RT-qPCR	reverse transcription quantitative polymerase chain reaction
RuBisCO	ribulose-1,5-bisphosphate carboxylase/oxygenase
sbtA	gene encoding bicarbonate uptake system SbtA (high affinity, low flux)
SbtA	sodium-dependent bicarbonate uptake system (high affinity, low flux)
sbtB	gene found downstream of *sbtA*, associated with *sbtA*
v	gas transfer velocity (piston velocity) across the air-water interface



Summary





Effects of rising CO_2 on the harmful cyanobacterium *Microcystis*

Harmful cyanobacteria ('blue-green algae') are notorious for causing worldwide ecological and economical problems in eutrophic lakes and reservoirs, where they can produce dense and often toxic blooms. Climate change is foreseen to have large effects on these photosynthetic microorganisms. Yet, while several studies have investigated effects of global warming on harmful cyanobacteria, the implications of rising CO_2 have received relatively little attention. Cyanobacteria are often assumed to be favored at low inorganic carbon conditions, because of the presence of an effective CO_2-concentrating mechanism (CCM) to fix CO_2. But how will they perform at elevated CO_2 levels? This thesis investigates the impact of elevated CO_2 on various strains of the ubiquitous harmful cyanobacterium *Microcystis aeruginosa*.

The following questions are addressed:

1) How variable are the CCMs within the genus *Microcystis*? (**Chapter 2**)
2) What are the adaptations of *Microcystis* to elevated CO_2? (**Chapter 3**)
3) What are the similarities and differences in CCM gene expression (1) among *Microcystis* strains, and (2) between *Microcystis* and other cyanobacteria? (**Chapters 2 and 4**)
4) How are the *Microcystis* CCM genes regulated *in situ*? (**Chapter 6**)
5) Can genetic variability of the *Microcystis* CCM cause strain-specific differences in growth rate at elevated CO_2 concentrations? (**Chapters 2 and 4**)
6) Does rising CO_2 affect the competition between different *Microcystis* strains, and if so, which strains will benefit most? (**Chapter 5**)
7) What are the effects of rising CO_2 on other harmful cyanobacteria? (**Chapter 7**)
8) Will rising CO_2 concentrations stimulate cyanobacterial blooms and make them more toxic? (**Chapters 2, 3, 5 and 7**)
9) Is potassium ion addition an effective method to combat harmful cyanobacterial blooms? (**Chapter 8**)

To investigate the first question, 20 *Microcystis* strains from different continents were studied at the gene level. Cyanobacteria often use a combination of CO_2 and bicarbonate uptake systems to import inorganic carbon (C_i). Genes encoding the two CO_2 uptake systems, the ATP-dependent bicarbonate transporter BCT1, the CO_2-fixing enzyme RuBisCO and carboxysomes (compartments containing RuBisCO) were detected in all 20 *Microcystis* strains. Eight of the analyzed strains also contain the genes *bicA* and *sbtA*, encoding the sodium-dependent bicarbonate uptake systems BicA and SbtA, respectively. BicA has a low affinity for bicarbonate and high flux rate, whereas SbtA has a high affinity and low flux rate. Affinity refers to the effectiveness of bicarbonate uptake at low bicarbonate concentrations, whereas the flux rate refers to the bicarbonate uptake rate at high bicarbonate concentrations. A unique feature of these *Microcystis* strains is that the genes *bicA* and *sbtA* are present in one operon and are co-transcribed. In contrast to these C_i uptake generalists, 12 of the 20 analyzed *Microcystis* strains lack either the *bicA* or *sbtA* gene. The results show that *Microcystis* strains have adapted differently to the wide natural variation in CO_2 concentrations.

The second question was answered in chemostat experiments with *Microcystis* PCC 7806. Changes in the transcriptome (expression of all genes in the genome) were monitored from 45 minutes up to 2 weeks after increasing the CO_2 concentration. Surprisingly, elevated CO_2 affected the expression of only a small number of genes. The bicarbonate uptake genes were downregulated at elevated CO_2. Other regulated genes were involved in the stress response of the cells, control of the cellular C/N ratio, and the production of two weakly characterized polyketides. Expression of genes encoding the CO_2 uptake systems, carboxysome, RuBisCO, photosystems, C metabolism and microcystin synthetases did not respond significantly to elevated CO_2.

The third question was answered by exposing batch cultures of six different *Microcystis* strains to elevated CO_2. The high-affinity gene *cmpA* (encoding a subunit of the bicarbonate uptake system BCT1) was downregulated at elevated CO_2 in all strains. Most strains also downregulated *bicA* and *sbtA* at elevated CO_2, but two strains showed constitutive expression of these bicarbonate uptake genes. The high-flux BicA uptake system remained active at high CO_2 levels in all strains containing the *bicA* gene. Interestingly, expression of the high- and low-affinity CO_2 uptake genes of *Microcystis* was not affected by elevated CO_2, which deviates from most other cyanobacterial species that downregulate the high-affinity CO_2 uptake genes. The carboxysome and RuBisCO genes were also constitutively expressed in all *Microcystis* strains. We discovered a new CCM transcriptional regulator gene (*ccmR2*), located upstream of the *bicA-sbtA* operon. Both *ccmR2* and the *bicA-sbtA* operon are so far unique for *Microcystis.*

The fourth question was answered with an *in situ* study at Lake Kennemermeer (the Netherlands) of a cyanobacterial bloom that contained *Microcystis*. The lake showed large diel fluctuations in bicarbonate, pH and dissolved oxygen as a consequence of the photosynthetic activity of the bloom. Expression of the bicarbonate uptake genes of *Microcystis* was tuned to the diel variation in bicarbonate concentration. In contrast, expression of the CO_2 uptake genes was constitutive, and expression of the RuBisCO and carboxysomal genes was slightly increased during nighttime.

To address the fifth question, a series of laboratory experiments were carried out in batch culture at different CO_2 concentrations. The results showed that strains with the high-affinity gene *sbtA* perform better at low C_i concentrations, strains with the high-flux gene *bicA* perform better at high C_i concentrations, and *bicA+sbtA* strains containing both genes perform well across the entire range of C_i conditions investigated.

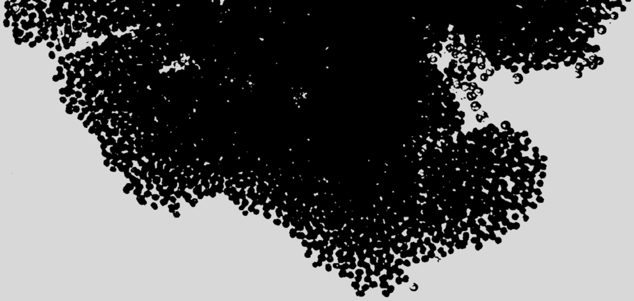
The sixth question was addressed by investigating mixtures with multiple *Microcystis* strains in laboratory competition experiments and a lake study. The competition experiments and lake study both showed that strains with the high-flux gene *bicA* have a selective advantage at elevated C_i levels. These results provide laboratory and field evidence that changes in C_i availability induce rapid adaptive changes in the genotype composition of harmful cyanobacterial blooms. Hence, future cyanobacterial blooms may have a genetic composition that differs from contemporary blooms.

The seventh question was answered by analyzing recently sequenced genomes of other harmful cyanobacteria, including *Anabaena*, *Aphanizomenon* and *Planktothrix* strains. These cyanobacteria also showed intraspecific variation in the presence of the *bicA* and *sbtA* genes, similar to *Microcystis*, suggesting that they are well adapted to a wide range of CO_2 conditions. However, in *Anabaena*, *Aphanizomenon* and *Planktothrix*, *bicA* and *sbtA* are not organized in one operon, and in some strains both *bicA* and *sbtA* are absent. Presumably, these harmful cyanobacteria display a similar phenotypic variation as *Microcystis*, with a selective advantage for strains with the high-affinity uptake systems SbtA and/or BCT1 at low C_i conditions and a selective advantage for strains with the high-flux uptake system BicA at high C_i conditions.

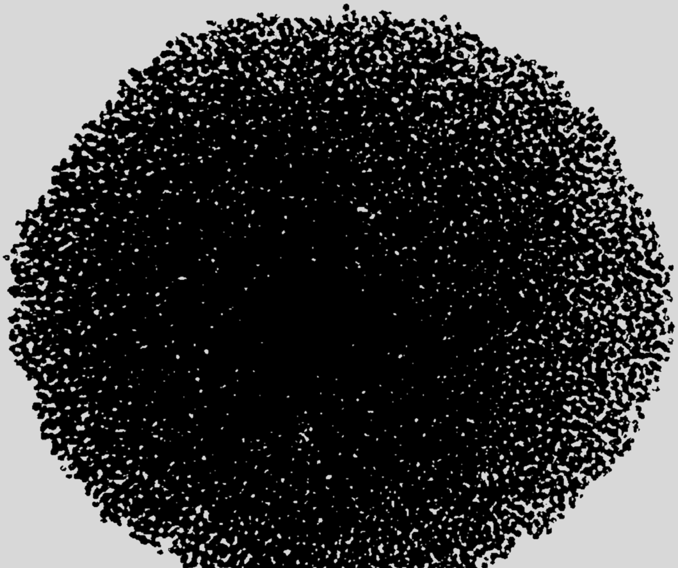
To address the eighth question, it was shown that there was no direct connection between the presence of the C_i uptake genes *bicA* or *sbtA* and the microcystin synthetase genes. In chemostat experiments with *Microcystis* PCC 7806, elevated CO_2 levels led to a shift from carbon- to light-limited conditions. The strain contained ~2.5 times more unbound microcystins per cell at elevated CO_2, indicating that the cells can become more toxic at elevated CO_2 levels. Biomass of this strain increased strongly at elevated CO_2, suggesting that cyanobacterial blooms will intensify in eutrophic lakes. Furthermore, the dry weight of the cells was reduced twofold, indicating that elevated CO_2 can promote buoyancy of the cells, and thus scum layer formation in lakes. Hence, elevated CO_2 is foreseen to worsen the problems with *Microcystis* blooms in eutrophic lakes.

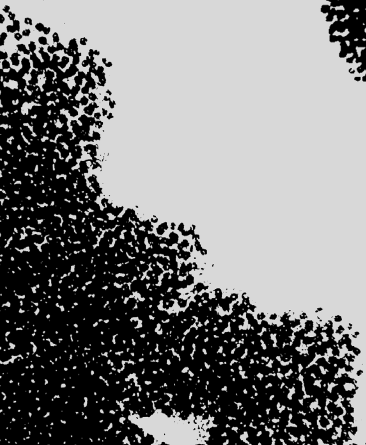
The ninth question was answered by investigating the potassium ion sensitivity of selected laboratory *Microcystis* strains. Strain PCC 7806, originating from brackish water, was not affected by the increased potassium ion concentration, while the growth of two freshwater *Microcystis* strains was strongly reduced. The potassium ion sensitivity of the freshwater strains was linked to the absence of specific salt tolerance genes. These results show that the salt tolerance and potassium sensitivity of *Microcystis* differ between strains. Hence, on the short run, potassium ion addition might be a successful remediation strategy to combat *Microcystis* blooms in freshwater lakes, but over time more tolerant *Microcystis* strains or other cyanobacteria are likely to become dominant.

This thesis contributes to a better understanding of how harmful cyanobacteria respond to climate change. The results show how cyanobacteria subtly adjust their cells at the molecular and physiological level to changes in C_i availability. Furthermore, the results demonstrate how genetic diversity in the C_i uptake systems provide cyanobacteria with the potential for rapid microevolutionary adaptation to changes in CO_2 conditions, with a selective advantage for strains with the high-flux bicarbonate uptake gene *bicA* at elevated CO_2 levels. Hence, one of the key lessons of this work is that future studies of climate change effects should keep in mind the large genetic and physiological variation within species. In total, the results indicate that a further rise of the atmospheric CO_2 concentration is likely to increase the frequency and intensity of cyanobacterial blooms in eutrophic waters, and possibly may also increase their toxicity. The predicted intensification of cyanobacterial blooms should be countered by the reduction of CO_2 emissions and the development of effective methods to combat and prevent harmful cyanobacterial blooms.



Samenvatting





Effecten van stijgend CO_2 op de schadelijke cyanobacterie *Microcystis*

Schadelijke cyanobacteriën ('blauwalgen') zijn bekende veroorzakers van wereldwijde ecologische en economische problemen in oppervlaktewateren zoals voedselrijke meren, waar ze dichte en vaak toxische bloeien kunnen vormen. Het is voorzien dat klimaatverandering grote effecten zal hebben op deze fotosynthetische microorganismen. Terwijl verschillende studies de effecten van stijgende temperaturen hebben onderzocht, hebben de mogelijke gevolgen van stijgende CO_2-concentraties tot nog toe weinig aandacht gekregen. Vaak wordt aangenomen dat cyanobacteriën voordeel hebben bij lage CO_2-condities, door de aanwezigheid van een effectief CO_2-concentreermechanisme (CCM) om CO_2 te fixeren. Maar hoe presteren ze bij verhoogde CO_2-niveaus? Dit proefschrift onderzoekt de effecten van stijgende CO_2-concentraties op verschillende stammen van de wijdverspreide schadelijke cyanobacterie *Microcystis aeruginosa*.

De volgende vragen worden behandeld:

1) Hoe variabel zijn de CCM's binnen het genus *Microcystis*? (**Hoofdstuk 2**)
2) Wat zijn de aanpassingen van *Microcystis* bij verhoogde CO_2-concentraties? (**Hoofdstuk 3**)
3) Wat zijn de overeenkomsten en verschillen in CCM-genexpressie (1) tussen *Microcystis* stammen onderling, en (2) tussen *Microcystis* en andere cyanobacteriën? (**Hoofdstukken 2 en 4**)
4) Hoe worden de CCM-genen van *Microcystis* gereguleerd? (**Hoofdstuk 6**)
5) Kan genetische variatie in de CCM's leiden tot verschillen in groeisnelheid van *Microcystis* stammen bij verhoogde CO_2-concentraties? (**Hoofdstukken 2 en 4**)
6) Heeft stijgende CO_2 invloed op de competitie tussen verschillende *Microcystis* stammen, en zo ja, welke stammen hebben het meeste voordeel? (**Hoofdstuk 5**)
7) Wat zijn de effecten van stijgend CO_2 op andere schadelijke cyanobacteriën? (**Hoofdstuk 7**)
8) Zullen stijgende CO_2-concentraties bloeien van schadelijke cyanobacteriën stimuleren en hun toxiciteit verhogen? (**Hoofdstukken 2, 3, 5 en 7**)
9) Is toevoeging van kaliumionen een effectieve methode om schadelijke cyanobacteriën te bestrijden? (**Hoofdstuk 8**)

Om de eerste vraag te onderzoeken zijn 20 *Microcystis* stammen uit verschillende delen van de wereld op genniveau onderzocht. Cyanobacteriën gebruiken vaak een combinatie van CO_2- en bicarbonaat-opnamesystemen om anorganische koolstof (C_i) te importeren in hun cellen. Alle

20 stammen bevatten genen die coderen voor de twee CO_2-opnamesystemen, de ATP-afhankelijke bicarbonaattransporter BCT1, het CO_2-fixatie-enzym RuBisCO en carboxyzomen (compartimenten die RuBisCO bevatten). Acht van de onderzochte stammen hadden ook de genen *bicA* en *sbtA*, die coderen voor de natrium-afhankelijke bicarbonaatopnamesystemen BicA en SbtA. BicA heeft een lage affiniteit voor bicarbonaat en een hoge opnamesnelheid, terwijl SbtA een hoge affiniteit heeft en een lage opnamesnelheid. Met affiniteit wordt hier bedoeld de effectiviteit van bicarbonaatopname bij lage bicarbonaatconcentraties, terwijl de opnamesnelheid refereert naar de bicarbonaatopname bij hoge bicarbonaatconcentraties. Een unieke eigenschap van deze *Microcystis* stammen is dat de genen *bicA* en *sbtA* zich bevinden op hetzelfde operon en dus gezamenlijk worden getranscribeerd (co-transcriptie). In tegenstelling tot deze C_i-opnamegeneralisten, misten 12 van de 20 *Microcystis* stammen het *bicA* of *sbtA* gen. De resultaten laten zien dat *Microcystis* stammen zich op verschillende wijze hebben aangepast aan de natuurlijke variatie in CO_2-concentraties.

De tweede vraag is beantwoord met behulp van chemostaatexperimenten met *Microcystis* PCC 7806. Veranderingen in het transcriptoom (expressie van alle genen in het genoom) van deze stam werden bekeken van 45 minuten tot 2 weken na het verhogen van de CO_2-concentratie. De verhoogde CO_2-concentratie had slechts effect op de expressie van een verrassend klein aantal genen. De bicarbonaatopnamegenen waren omlaag gereguleerd bij verhoogde CO_2. Andere gereguleerde genen waren betrokken bij de stress respons van cellen, controle van de cellulaire C/N ratio en de productie van twee nader te karakteriseren polyketides. De verhoogde CO_2-concentratie leidde niet tot significante veranderingen in genexpressie van de CO_2-opnamesystemen, het carboxysoom, RuBisCO, de fotosystemen, het C metabolisme en de microcystine synthetases.

De derde vraag is beantwoord door batch culturen met zes verschillende *Microcystis* stammen bloot te stellen aan verhoogde CO_2-concentraties. Het hoge-affiniteit-gen *cmpA* (coderend voor een subunit van het bicarbonaatopnamesysteem BCT1) werd in alle stammen omlaag gereguleerd. De meeste stammen verlaagden ook de genexpressie van *bicA* en *sbtA* bij verhoogde CO_2-concentraties, terwijl in twee stammen de expressie van deze bicarbonaatopnamegenen niet werd aangepast. Het hogesnelheidsopnamesysteem BicA bleef actief bij hoge CO_2-concentraties in alle stammen met het *bicA* gen. Opvallend genoeg werd de expressie van de hoge- en lage-affiniteit-CO_2-opnamegenen van *Microcystis* niet beïnvloed door verhoogde CO_2-concentraties, in tegenstelling tot de meeste andere cyanobacteriën die de expressie van hun hoge-affiniteit-CO_2-opnamegenen verlagen. Expressie van de carboxysoom en RuBisCO genen werd in geen van de *Microcystis* stammen aangepast. We ontdekten een nieuw CCM transcriptioneel regulatorgen (*ccmR2*), dat zich stroomopwaarts van het *bicA-sbtA* operon bevindt. Zowel *ccmR2* als het *bicA-sbtA* operon zijn tot nu toe uniek voor *Microcystis.*

De vierde vraag is beantwoord met een veldstudie in het Kennemermeer (Nederland) van een cyanobacteriële bloei met *Microcystis*. Het meer vertoonde grote dagelijkse schommelingen in bicarbonaat, pH en opgelost zuurstof als een gevolg van de fotosynthese-activiteit van de bloei. Expressie van de bicarbonaatopnamegenen van *Microcystis* was afgestemd op de dagelijkse variatie in de bicarbonaatconcentratie. Expressie van de CO_2-opnamegenen vertoonde echter geen dagelijkse variatie en expressie van de RuBisCO- en carboxysoomgenen was iets verhoogd tijdens de nacht.

Om de vijfde vraag te onderzoeken zijn een serie van laboratoriumexperimenten uitgevoerd in batch-culturen bij verschillende CO_2-concentraties. De resultaten laten zien dat stammen met het hoge-affiniteit-gen *sbtA* beter presteren bij lage C_i-concentraties, stammen met het hogesnelheids-gen *bicA* beter presteren bij hoge C_i-concentraties, terwijl stammen die beschikken over beide genen goed presteren over het hele bereik van onderzochte C_i-condities.

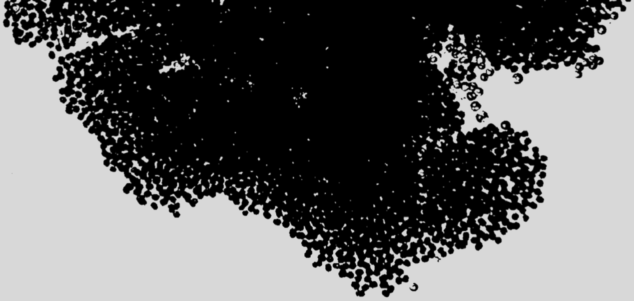
De zesde vraag is onderzocht door mengsels van verschillende *Microcystis* stammen te bestuderen in laboratorium competitie-experimenten en in een veldstudie van een cyanobacteriële bloei in een eutroof meer. De competitie-experimenten en de veldstudie laten beide zien dat stammen met het hogesnelheids-gen *bicA* een selectief voordeel hebben bij verhoogde C_i-concentraties. De resultaten leveren zowel experimenteel als observationeel bewijs dat veranderingen in de C_i beschikbaarheid leiden tot snelle adaptieve veranderingen in de genotypesamenstelling van schadelijke cyanobacteriën. Dit suggereert dat cyanobacteriële bloeien in de toekomst waarschijnlijk een genetische samenstelling zullen hebben die verschilt van de huidige bloeien.

De zevende vraag is beantwoord door recent gesequencede genomen van andere schadelijke cyanobacteriën te analyseren, waaronder *Anabaena*, *Aphanizomenon* en *Planktothrix* stammen. Deze cyanobacteriën lieten ook intraspecifieke variatie zien in de aanwezigheid van *bicA* en *sbtA*, net als bij *Microcystis*, wat suggereert dat ze goed zijn aangepast aan een wijde range van CO_2-condities. Echter, in *Anabaena*, *Aphanizomenon* en *Planktothrix* zijn *bicA* en *sbtA* niet ondergebracht in hetzelfde operon, en in sommige stammen zijn zowel *bicA* als *sbtA* afwezig. Waarschijnlijk laten deze schadelijke cyanobacteriën een vergelijkbare fenotypische variatie zien als *Microcystis*, met een selectief voordeel voor stammen met de hoge-affiniteit-opnamesystemen SbtA en/of BCT1 bij lage C_i-concentraties en een selectief voordeel voor stammen met het hogesnelheids opname systeem BicA bij hoge C_i-concentraties.

De achtste vraag is beantwoord door aan te tonen dat er geen direct verband is tussen de aanwezigheid van de C_i-opnamegenen *bicA* of *sbtA* en de microcystine-synthetase-genen. In chemostaatexperimenten met *Microcystis* PCC 7806 leidde verhoogde CO_2-concentraties tot een verschuiving van koolstof-gelimiteerde naar licht-gelimiteerde condities. De stam bevatte ~2.5 keer meer ongebonden microcystine per cel bij verhoogde CO_2-concentraties, wat aangeeft dat de cellen toxischer kunnen worden bij stijging van het CO_2-niveau. De biomassa van de stam was sterk toegenomen bij verhoogde CO_2-concentraties, wat suggereert dat cyanobacteriële bloeien in eutrofe meren intenser worden. Daarnaast was het drooggewicht van de cellen gehalveerd, wat doet vermoeden dat verhoogde CO_2-concentraties het drijfvermogen van cellen kan bevorderen en daarmee de vorming van drijflagen in meren kan stimuleren. Deze resultaten geven aan dat stijgende CO_2-concentraties de problemen met *Microcystis* in eutrofe meren waarschijnlijk zullen verergeren.

De negende vraag is beantwoord door onderzoek naar de kaliumgevoeligheid van geselecteerde *Microcystis* stammen. Stam PCC 7806, die oorspronkelijk is geïsoleerd uit brak water, werd niet beïnvloed door verhoogde kalium concentraties, terwijl de groei van twee zoetwater *Microcystis* stammen sterk gereduceerd werd. De kaliumgevoeligheid van de zoetwater stammen lijkt samen te hangen met de afwezigheid van specifieke genen betrokken bij zoutwatertolerantie. Dit laat zien dat *Microcystis* stammen verschillen in hun zoutwatertolerantie en kaliumgevoeligheid. Het gevolg is dat kaliumtoevoeging op korte termijn een succesvolle beheersmethode kan zijn om *Microcystis* bloeien in zoet water te bestrijden, maar dat op de langere termijn waarschijnlijk minder kaliumgevoelige *Microcystis* stammen of andere tolerante cyanobacteriën de dominantie zullen overnemen.

Dit proefschrift draagt bij aan een beter begrip van hoe schadelijke cyanobacteriën reageren op klimaatverandering. De resultaten laten zien hoe cyanobacteriën hun cel op moleculair en fysiologisch niveau op subtiele wijze kunnen aanpassen aan de C_i beschikbaarheid. Ook laten de resultaten zien dat de genetische diversiteit in C_i-opnamesystemen van cyanobacteriën kan leiden tot een snelle micro-evolutie, waarbij de genotype samenstelling van de bloei zich aanpast aan veranderingen in de CO_2-concentratie. Hierbij hebben stammen met het hogesnelheids-bicarbonaatopnamegen *bicA* een selectief voordeel bij hoge C_i-concentraties. Een van de belangrijkste lessen van dit werk is daarom dat toekomstige studies naar de effecten van klimaatsverandering attent moeten zijn op de genetische en fysiologische variatie binnen soorten. Alles samenvattend geven de resultaten aan dat verdere stijging van de CO_2-concentratie waarschijnlijk zal leiden tot een toename van de frequentie en intensiteit van cyanobacteriële bloeien in eutrofe wateren, en mogelijk ook de toxiciteit van deze bloeien zal verhogen. De voorspelde toename van cyanobacteriële bloeien zou kunnen worden beperkt door reductie van de CO_2-uitstoot en door de verdere ontwikkeling van effectieve methoden om schadelijke cyanobacteriën te bestrijden.



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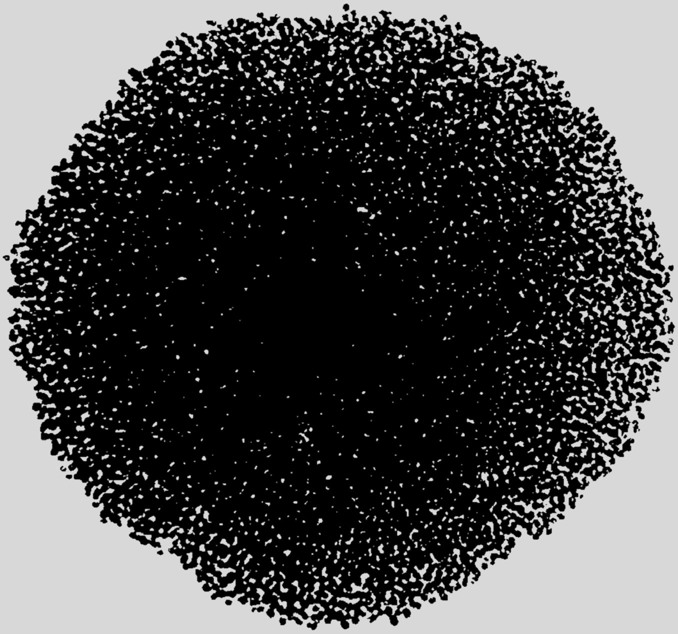

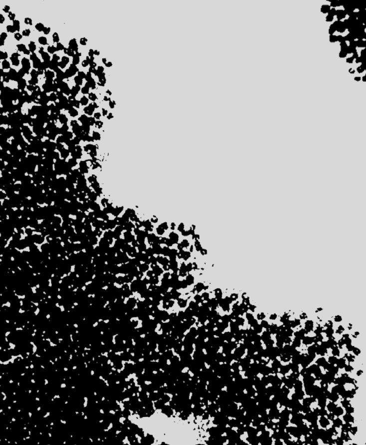

Luctor et Emergo
Ik worstel en kom boven

After several years of hard work it is finally done! Time went by very fast and so much changed since I started working here at the Science Park of Amsterdam in February 2011. I really enjoyed being part of the Aquatic Microbiology (AMB) group and I learned a lot. Yet, I could not have done the work presented in my thesis without the help of several other people. Also many people made my stay at the University of Amsterdam more pleasant, or supported me outside working hours.

First I would like to thank Jef. As my promoter, supervisor of the TOP project and group leader, you guided my research into the right direction and I really learned a lot from you. With my molecular background, ecology was a relatively new aspect for me, and I thank you for introducing me to this field. I also admire your aim for perfection, and your enthusiasm for and dedication to the research of this thesis.

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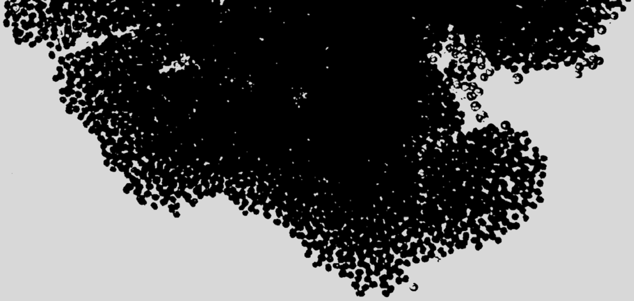
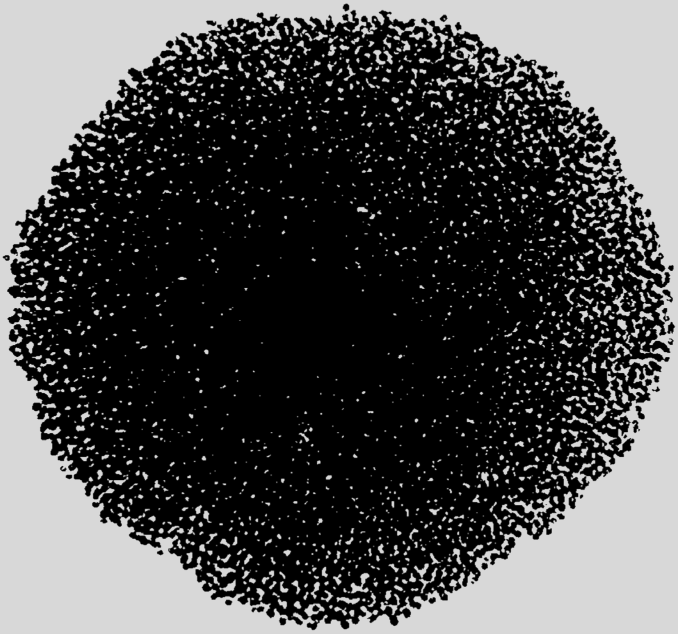
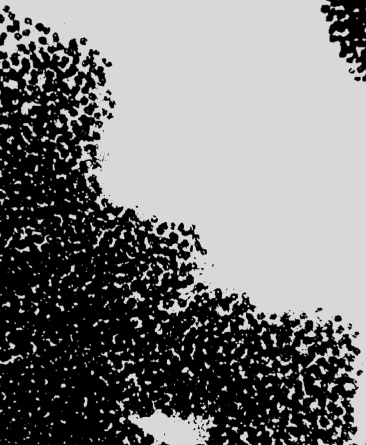


Curriculum Vitae





Giovanni Sandrini was born on the 16th of June 1986, in Terneuzen, the Netherlands. After completing secondary school at the Zeldenrust-Steelant College in Terneuzen in 2004, he completed the bachelor and master program of Life Science & Technology organized by a collaboration between Leiden University and Delft University of Technology. During his bachelor internship he worked on the isolation and genetic analysis of novel streptomycetes from soil samples, in the Microbial Development group of prof. dr. Gilles van Wezel at Leiden University. During his masters he did his industrial internship at the Netherlands Organisation for Applied Scientific Research (TNO) in Delft, in the group of dr. Harald J. Ruijssenaars, where he used genetic engineering on the solvent tolerant soil bacterium *Pseudomonas putida* S12 to allow it to grow on lignocellulose hydrolysate. He did his master research internship at the nidrovirus group of prof. dr. Eric J. Snijder, at the Leiden University Medical Center (LUMC), under supervision of dr. Clara C. Poshuma and dr. Sjoerd van den Worm, where he investigated the presence of an RNA proofreading mechanism in coronoviruses. He graduated in 2010, with the major Functional Genomics. Early 2011, he started his PhD in the group of Aquatic Microbiology of prof. dr. Jef Huisman at the University of Amsterdam, under supervision of dr. Hans C.P. Matthijs. The work of his PhD is described in this thesis and resulted in several publications. He also presented the results of this thesis at national and international conferences.

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Sandrini G, Matthijs HCP, Verspagen JMH, Muyzer G, Huisman J. (2014). Genetic diversity of inorganic carbon uptake systems causes variation in CO_2 response of the cyanobacterium *Microcystis*. *ISME Journal* **8**: 589–600.

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Attended conferences

ESF-EMBO symposium on Molecular Bioenergetics of Cyanobacteria: From Cells to Community. Sant Feliu de Guixols, Spain, April 2011.

14th International Symposium on Phototrophic Prokaryotes. Porto, Portugal, August 2012.

15th International Symposium on Microbial Ecology. Seoul, South-Korea, August 2014.

9th European Workshop on the Molecular Biology of Cyanobacteria. Texel, the Netherlands, September 2014.

15th International Symposium on Phototrophic Prokaryotes. Tübingen, Germany, August 2015.