Mesoscale variability of phosphorus stocks, hydrological and biological processes in the mixed layer in the Eastern Mediterranean Sea in autumn and during an unusually dense winter phytoplankton bloom

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List of abbreviations

BP: heterotrophic prokaryotic production Crypto: cryptophytes-like cells DCM: deep chlorophyll maximum DIP: dissolved inorganic phosphorus DOC: dissolved organic carbon DON: dissolved organic nitrogen DOP: dissolved organic phosphorus EMS: eastern Mediterranean Sea Hprok: heterotrophic prokaryotes H500: dynamic topography relative to 500 dbar L_{DOP}: hydrolysable fraction of DOP LWCC: liquid waveguide capillary cell ML: mixed layer MLD: mixed layer depth MS: Mediterranean Sea Nanoeuk: nanophytoeukaryotes NOx: the sum of nitrate + nitrite PCA: principal component analysis Q10: how many times a biological rate or chemical reaction changes when the temperature shifts by 10°C PDE: phosphodiesterase Picoeuk: picophytoeukaryotes PISO : depth of isopycnal 29.05 kg m^{-3} PME : phosphomonoesterase **PP** : primary production Proc: Prochlorococcus Syn: Synechococcus σ : excess density Tchla: total chlorophyll a ZNcline: nitracline depth ZPcline: phosphacline depth

Material and Methods

Phosphacline and nitracline depths

The phosphacline (nitracline) was defined for each station as the layer with maximum vertical gradient of DIP (NOx) concentration (computed as the highest significant slope of the linear fitting of DIP (NOx) concentration as a function of depth). The set of concentrations selected inside phosphacline (nitracline) included 3 to 9 data points and varied from 38 ± 19 nM to 158 ± 40 nM for DIP and from $1.3 \pm 0.8 \ \mu$ M to $3.5 \pm 1.4 \ \mu$ M for NOx. The depth of the top of the PCline (NCline) was defined as the intercept of the regression line, which is the highest depth at which DIP (NOx) concentration is zero (Moutin and Prieur, 2012). See example Fig. S1b. In the case of DIP versus depth relationship we used the DIP concentrations determined with the LWCC technique for depleted layers and classical DIP measurements for replete layers (> 0.08 \ \muM). When a 'staircase' effects was seen on the plot showing 2 zones of gradients of concentration with depth, we considered the deepest one to calculate the nitracline and phosphacline depths.

DIP and NOx gradients across isopycnals

'DIP and NOx gradients across isopycnals (∂ DIP/ $\partial\sigma$ and ∂ NOx/ $\partial\sigma$) at the nutriclines were calculated as the slope of the linear fitting of the relationship between nutrient concentrations and σ . We identified the maximum gradient of DIP (Nox) across isopycnals (computed as the highest significant slope of the linear fitting of DIP (NOx) concentration as a function of σ (see example Figure S1a). For DIP a second DIP gradient from the surface to the upper boundary of the P-cline (i.e. inside the P-depleted layer, across the ML) was also considered when detectable as suggested in Du et al. (2017) and Pulido-Villena et al. (2021), (i.e. when DIP vs sigma increased linearly). In such cases, the set of concentrations selected varied from 10 ± 4 to 22 ± 8 nM.'

- Du, C., Liu, Z., Kao, S.-J., Dai, M. (2017). Diapycnal fluxes of nutrients in an oligotrophic oceanic regime: The South China Sea. Geophys. Res. Lett. 44, 11,510–11,518. https://doi.org/10.1002/2017GL074921
- Moutin, T. and Prieur, L. (2012). Influence of anticyclonic eddies on the Biogeochemistry from the Oligotrophic to the Ultraoligotrophic Mediterranean (BOUM cruise), Biogeosciences, 9, 3827–3855, https://doi.org/10.5194/bg-9-3827-2012

Table S1. Medians, first and 3rd percentiles (in brackets) of selected physical and biogeochemical parameters among the different groups of stations according to the PCA results (see Fig. 3, Table 1): group A corresponds to PERLE1 cruise (autumn situation, Ierapetra gyre), groups B to F PERLE 2 cruise (winter/spring situation). * In B group, medians at ST50 in the center of the Ierapetra anticyclone, are indicated in italics.

parameter	units	А	B*	С	D	Е	F
Mixed layer depth	m	30	103 213	57	50	22	145
		[22-37]	[83-158]	[47-88]	[49-51]	[17-27]	[131-207]
Depth of	m	282	108 108	212	100	88	101
29.05	111	[270-288]	408 408 [401_429]	[193-216]	[86-113]	[40-130]	[95_249]
dynamic height	dun	0.238		0.300	0.416	0.416	0 305
ref 500 dbar	m	-0.238	-0.320 -0.341	-0.390	-0.410	-0.410	-0.395
Temperature	°C	24.0	160.166	15.6	16 1	16 4	15 7
remperature	C	24.7 [24 8-25 8]	[16.5-17.3]	[15.5]	[16.1-16.2]	[15 3-16 6]	[15.7
Salinity	PSU	39.70	30 20 30 28	39.04	30.21	30.22	30.10
Samity	150	[39 68-39 73]	[39 28-39 31]	[38 99-39 16]	[39 21-39 22]	[39 21-39 23]	[39 15-39 25]
depth of	m	123	211 210	<u>[50.57 57.10]</u> 89	<u>[33.21 33.22]</u> 85	21	90
nitracline		[101-139]	[172-225]	[70-109]	[58-93]	[0-46]	[75-139]
depth of	m	145	257 257	94	103	59	163
phosphacline		[120-181]	[217-261]	[72-114]	[74-127]	[31-83]	[122-205]
<u></u> ∂NOx/∂σ	mmol	16	18 /8 9	34	55	51	28
gradient	ko ⁻¹	[15-17]	[16-19]	[33-42]	[52-60]	[42-58]	[27-28]
aDIP/ag	umol	993	800 799	1301	2753	2410	1274
gradient	ko ⁻¹	[935-1003]	[634-841]	[1172-1375]	[2670-3038]	[2315-2726]	[1230-1521]
NOx	иM	0.011	0.48.049	0.77	0 700	0.29	1 10
NOX	μινι	[0 010-0 016]	[0 44-0 50]	[0 40-0 83]	[0 60-0 79]	[0 22-0 40]	[1 09-1 13]
DIP	nM	10.2	8483	9.9	97	91	23.3
		[7.9-12.4]	[8.3-9.2]	[9.1-10.7]	[7.8-11.0]	[8.9-9.5]	[21.9-24.2]
DOP	nM	22	50 63	49	38	49	70
		[20-34]	[30-66]	[44-53]	[29-42]	[37-55]	[65-73]
T	nM	62	11 4 8 7	11.1	12.0	12.5	20.4
LDOP	IIIVI	0.2 [4 0-7 5]	11.4 0.7 [8 6-14 8]	[7 3_13 6]	13.9 [12 4_15 3]	13.5 [10.9_16.5]	29.4 [11.0_33.7]
DON	uМ	5.2	<u>[0.0-14.0]</u>	[7.3-13.0]	[12.4-13.3]	4.6	<u>[11.0-35.7]</u> 4 3
DON	μινι	5.2 [4 8-5 7]	4.5 4.7	4.4 [4 2_4 7]	4.3 [4 1_4 4]	4.0 [4 5_4 7]	4.5
DOC	uМ	[+.0- <i>3</i> .7]	65.64	<u>[۲.2</u> -۲.7]	[+.1 ⁻ +.+]	[+.5 ⁻ +.7]	57
DOC	μινι	50 [78-81]	[62-66]	[58_63]	[59-62]	[58-65]	57
94 I	0/2	23	20	[58-05]	[39-02]	30	[30-38]
∕u ∟DOb	70	∠3 [14_38]	20 [14- 5 0]	10 [14_26]	55 [31_51]	50 [27_33]	+1 [14_53]
NOv·DIP		1 5	[14-J0] 55	67	70	32	[14-33] A7
molar ratio		1.5 [1 3_2 3]	55 [51-59]	[38-75]	7 <i>7</i> [68-87]	52 [25-46]	+/ [43-54]
motal rado		[1.5-2.5]	[31-37]	[30-73]	[00-07]	[23-40]	[+5-54]

Table S2. Medians, first and 3rd percentiles (under brackets) of abundances of microorganisms: *Synechococcus* (Syn), *Prochlorococcus* (proc) picophytoeucaryotes (Picoeuk), nanophytoeucaryotes (Nanoeuk); heterotrophic bacterial abundances (Hprok); BP rates; PME and PDE kinetic characteristics (Vm, Km) as well as cell specific and biomass specific Vm rates among the different groups of stations according to the PCA results (see Fig. 3; Table 1): group A corresponds to PERLE1 cruise (autumn situation, Ierapetra gyre), groups B to F PERLE 2 cruise (winter/spring situation).*Pigments were not available at some stations, see methods.

parameter	units	А	В	С	D	E	F
Tchla*	µg L ⁻¹	0.047	0.23	0.26	0.45	0.42	0.23
		[0.043-0.054]	[0.23-0.25]	[0.24-0.26]	[0.36-0.47]	[0.42-0.45]	[023-0.24]
Proc	x 10 ³	0.58	1.16	1.95	3.68	3.16	0.89
	cell mL ⁻¹	[0.4-0.7]	[0.8-1.2]	[1.6-2.1]	[3.0-5.1]	[3.0-4.1]	[0.82-0.91]
Syn	x 10 ³	12	2.0	2	3.8	5.6	0.7
	cell mL ⁻¹	[11-13]	[1.7-2.2]	[2.0-2.4]	[3.6-4.6]	[5.2-6.0]	[0.6-0.8]
Picoeuk	cell mL ⁻¹	495	76	70	218	205	208
		[407-592]	[60-106]	[63-81]	[195-259]	[174-269]	[62-251]
Nanoeuk	cell mL ⁻¹	87	21	22	21	49	15
		[65-97]	[12-27]	[19-27]	[20-24]	[39-52]	[12-16]
Hprok	x10 ⁵	3.3	4.1	3.3	6.7	4.2	3.7
	cells mL ⁻¹	[3.0-3.7]	[3.9-4.3]	[3.0-4.3]	[6.5-7.0]	[3.9-5.2]	[3.6-4.0]
BP	$ngC L^{-1} h^{-1}$	ND	7.4	9.6	28.3	22.8	6.7
			[6.2-12.7]	[8.4-11.2]	[24.5-30.9]	[17.1-27.4]	[6.3-7.2]
Vm PME	nmol MUF-P	2.3	3.8	1.9	5.2	11.1	0.34
	hydr $L^{-1} h^{-1}$	[1.9-2.6]	[1.5-4.9]	[1.7-3.7]	[4.7-5.9]	[9.3-16.1]	[0.22-0.41]
Vm PDE	nmol bis MUF-P	2.5	7.2	5.5	7.2	18.3	0.20
	hydr L ⁻¹ h ⁻¹	[1.7-4.2]	[3.4-8.5]	[3.2-7.3]	[6.9-7.4]	[14.4-21.1]	[0.16-0.42]
Km PME	μΜ	0.063	0.14	0.10	0.20	0.22	0.14
		[0.059-0.068]	[0.11-0.19]	[0.093-0.12]	[0.17-0.23]	[0.19-0.27]	[0.12-0.19]
Km PDE	μΜ	2.6	5.8	4.1	6.30	6.6	1.3
		[2.1-4.3]	[3.9-6.8]	[3.2-5.1]	[5.9-6.5]	[6.5-6.8]	[1.0-1.5]
TT PME	days	1.16	1.84	2.16	1.74	0.82	19.9
		[1.05-1.31]	[1.61-2.74]	[1.46-2.28]	[1.21-2.24]	[0.73-0.91]	[15.5-27.9]
TT PDE	days	45	36	25	36	15	230
		[39-52]	[32-44]	[24-41]	[35-42]	[14-19]	[162-326]
cell specific	x10 ⁻¹⁸ mol	7	10	6	7	23	1.0
Vm PME	hydr cell ⁻¹ h ⁻¹	[5-8]	[4-12]	[4-10]	[6-9]	[20-29]	[0.5-1.2]
cell specific	x10 ⁻¹⁸ mol	8	17	14	11	36	0.7
Vm PDE	hydr cell ⁻¹ h ⁻¹	[5-13]	[8-20]	[10-27]	[10-11]	[33-36]	[0.4-1.1]
biomass sp	nmal hydr	0.22	0.16	0 1 2	0 17	0.45	0.017
		0.32	0.10		U.L/		
	[µgC] []	[U.29-U.30]	[0.09-0.19]	[0.09-0.18]	[U.14-U.21]	[U.37-U.39]	0.012
		U.32	0.35	0.39	0.30	U.74	
VIIIPUE		[0.25-0.48]	[U.Z3-U.43]	[0.20-0.00]	[0.20-0.33]	[0.01-0.00]	[0.010-0.027]

Table S3. DIP $(\partial DIP/\partial \sigma)$ and NOx $(\partial NOx/\partial \sigma)$ gradients accross isopycnals, values ± standard deviation and corresponding significance of the regressions (p). Gradients were estimated from nitracline for NOx and from phosphacline for DIP. In some cases, it was also possible to determine a secondary DIP gradient inside P depleted layer (across the ML), when detectable (see supplementary information - material and methods for details); nd: not determined, in italics p > 0.05.

			from nitracline		from phosphac	line	inside P-depleted layer		
			mmol kg ⁻¹		µmol kg ⁻¹		µmol kg ⁻¹		
cruise	group	st	∂NOx/∂σ	р	∂DIP/∂σ	р	∂DIP/∂σ	р	
PERLE1	А	2	12.1 ± 0.9	< 0.01	887 ± 161	0.03	2.5 ± 1.3	0.16	
PERLE1	А	5	15.8 ± 0.4	< 0.01	994 ± 53	0.03	3.8 ± 1.1	0.02	
PERLE1	А	12	15.3 ± 0.8	< 0.01	766 ± 73	< 0.01	9.0±5.9	0.37	
PERLE1	А	15	16.1 ± 0.8	< 0.01	973 ± 110	0.013	6.2 ± 1.4	0.04	
PERLE1	A*	16	15.0 ± 1.4	< 0.01	1011 ± 58	< 0.01	2.8 ± 0.8	0.04	
PERLE1	А	19	16.2 ± 0.4	< 0.01	993 ± 37	< 0.01	5.8 ± 3.6	0.35	
PERLE1	А	20	18.3 ± 0.9	< 0.01	1187 ± 70	< 0.01	nd		
PERLE1	А	23	15.7 ± 1.1	< 0.01	919 ± 90	< 0.01	3.6 ± 0.8	0.02	
PERLE1	А	25	17.4 ± 0.6	< 0.01	995 ± 105	0.011	3.0 ± 0.8	0.02	
PERLE1	А	27	15.5 ± 1.7	< 0.01	1334 ± 77	< 0.01	nd		
PERLE1	А	30	17.4 ± 1.2	< 0.01	952 ± 89	< 0.01	10.3 ± 1.5	0.09	
PERLE2	F	1	26.5 ± 4.0	0.02	1186 ± 83	< 0.01	nd		
PERLE2	F	13	28.5 ± 1.4	< 0.01	1768 ± 198	0.07	385 ± 84	0.02	
PERLE2	F	15	28.3 ± 1.4	< 0.01	1275 ± 68	0.03	nd		
PERLE2	С	21	42.3 ± 3.1	< 0.01	3406 ± 770	0.05	102 ± 7	0.04	
PERLE2	С	26	32.7 ± 1.4	< 0.01	1301 ± 21	< 0.01	nd		
PERLE2	С	35	34.5 ± 2.8	0.05	1375 ± 83	0.04	nd		
PERLE2	С	44	18.4 ± 0.8	< 0.01	1172 ± 51	< 0.01	nd		
PERLE2	В	50	18.9 ± 0.6	< 0.01	800 ± 25	0.020	nd		
PERLE2	D*	58	50.0 ± 0.3	< 0.01	2754 ± 45	0.010	nd		
PERLE2	Е	68	38.1 ± 5.6	< 0.02	2370 ± 525	0.139	310 ± 127	0.14	
PERLE2	С	75	44.3 ± 3.3	< 0.03	700 ± 219	0.085	nd		
PERLE2	E	80	59.7 ± 4.1	< 0.01	3549 ± 301	< 0.01	nd		
PERLE2	E	90	57.5 ± 7.7	0.02	2451 ± 305	0.079	97 ± 62	0.36	
PERLE2	E	94	43.8 ± 1.4	0.02	2150 ± 185	0.055	nd		
PERLE2	В	104	19.2 ± 4.0	0.13	883 ± 206	0.146	429 ± 133	0.05	
PERLE2	В	108	13.3 ± 1.0	0.05	469 ± 92	0.123	100 ± 21	0.13	
PERLE2	D	111	55.0 ± 1.5	< 0.01	3322 ± 124	0.024	nd		
PERLE2	D	116	64.5 ± 1.2	0.01	2587 ± 458	0.112	268 ± 60	0.02	

Table S4. Correlation coefficients (Pearson) between hydrological and biotic variables. Abiotic variables are mixed layer depth (MLD), depth of isopycnal 29.05 kg m⁻³ (PISO), dynamic topography relative to 500 dbars (H500), DIP gradient across isopycnals (∂ DIP/ $\partial\sigma$), phosphacline depth, NOx gradient across isopycals (∂ NOx/ $\partial\sigma$) and nitracline depth. Biotic variables are medians within the mixed layer for nutrient concentrations (DIP, NOx, Si), dissolved organic matter (L_{DOP}, DOP, DOC), Total chlorophyll a (Tchla) abundances of cells (*Prochlorococcus* (Proc), *Synechococcus* (Syn), picophytoeukaryotes (Pico-euk), nanophytoeukaryotes (Nano-euk), Cryptophytes-like cells (Crypto), heterotrophic prokaryotes (hprok) with high and low nucleic acid content (HNA, LNA, respectively), and kinetic parameters of phosphomonoesterase (Km PME, Vm PME) and phosphodiesterase (Vm PDE, Km PDE). n = 27 stations, no data = insignificant correlations (p > 0.05), in red positive correlations, in blue negative correlations, in bold r > 0.7 or < -0.7.

	DIP	NOx	Si	L _{DOP}	DOP	DOC	Tchl a	Proc	Syn	Pico- euk	Nano- euk	Crypto	LNA	HNA	Hprok	Vm PME	Km PME	Vm PDE	Km PDE
MLD	0.51	0.70			0.57	-0.42			-0.50	-0.39	-0.46					-0.40		-0.40	-0.43
H500		-0.62	-0.75	-0.49	-0.67	0.85	-0.73	-0.57	0.76	0.71	0.78		-0.55		-0.52	-0.39	-0.69	-0.40	
PISO			-0.66		-0.41	0.48	-0.49	-0.53				-0.54	-0.51		-0.53	-0.48	-0.50	-0.44	
∂DIP/∂σ			0.72			-0.46	0.67	0.67				0.62	0.49	0.44	0.67	0.61	0.65	0.52	
ZPcline			-0.40					-0.54				-0.46			-0.39	-0.47		-0.46	
∂ΝΟx/∂σ			0.74			-0.62	0.73	0.63	-0.43	-0.38	-0.44	0.60	0.67		0.71	0.67	0.73	0.64	
ZNcline			-0.52				-0.42	-0.56				-0.44	-0.43		-0.42	-0.49		-0.46	

Table S5. Correlation coefficients (Pearson) between hydrological variables and pigments concentrations or ratios, taken at the median values within the mixed layer. Pigment data were 19' butanoyloxyfucoxanthin (19'BF), fucoxanthin (fuco), 19' hexanoyloxyfucoxanthin (19'HF), zeaxanthin (zea), totalchlorophyll b (Tchlb) and total chlorophylla (Tchla). Correlation with some pigment's ratios were also determined: Fuco:Tchla, Chlb:Tchla and 19'BF:Tchla. n = 17 stations, no data = insignificant correlations (p > 0.05), in red positive correlations, in blue negative correlations, in bold r > 0.7 or < -0.7

	19'BF	Fuco	19'HF	Zea	Tchlb	TChla	Fuco :Tchla	chl b :Tchla	19'BF :Tchla
MLD	0.49						0.49	0.63	0.70
H500	-0.81	-0.83	-0.78	-0.75	-0.76	-0.76	-0.51	-0.64	
PISO		-0.79	-0.54	-0.67	-0.80	-0.70		-0.62	
∂DIP/∂σ		0.66	0.69	0.82	0.71	0.79			
ZPcline		-0.51		-0.68		-0.56			0.57
9NOx/9α		0.69	0.73	0.89	0.73	0.82			
ZNcline		-0.65	-0.50	-0.68	-0.60	-0.64			0.48

Table S6. Correlation coefficients (Pearson) between hydrological variables and biotic variables taken as integrated stocks. Integrated (0-200 m) abundances of *Prochlorococcus* (I Proc), *Synechococcus* (I Syn), picophytoeukaryotes (I Picoeuk), nanophytoeukaryotes (I Nanoeuk), Cryptophytes-like cells (I Crypto), heterotrophic prokaryotes (I hprok)). Integrated DIP, L_{DOP}, NOx (0-200m) and total chlorophyll a (I Tcha, 0-250 m). n = 27 stations, no data = insignificant correlations (p > 0.05), in red positive correlations, in blue negative correlations, in bold r > 0.7 or < -0.7.

_	I Proc	l Syn	I Pico	l Nano	I Crypto	l Hprok	I DIP	I L _{DOP}	I DOP	I NOx	I Tchla
MLD	-0.41					0.40			0.63		0.59
H500	0.75	0.91	0.75	0.87			-0.62	-0.49	-0.60	-0.78	-0.64
PISO		0.40			-0.47		-0.76			-0.77	
∂DIP/∂σ	-0.40	-0.43		-0.42	0.47		0.71			0.76	
Z Pcline							-0.74			-0.72	
∂NOx/∂σ	-0.57	-0.58	-0.41	-0.57	0.54	0.51	0.72			0.80	0.46
ZNcline					-0.39		-0.76			-0.76	

Supplement Figure captions

Fig. S1 Computation of $\partial DIP/\partial \sigma$ (a) and ZPcline depth (a) at ST26 of PERLE2 cruise.

Fig S2 Vertical profile of NOx versus depth at ST1, showing to possible modes of estimation of ZNcline

Fig. S3. Vertical distributions (0-300 m) of a, d, g: density excess (σ , dotted lines) and fluorescence (continuous lines); b,e,h: dissolved inorganic phosphorus (DIP); and c,f,i: phosphomonoesterase and phosphodiesterase maximum rates (Vm PME, Vm PDE) for A (a, b, c), B (d,e,f) and C (g, h, i) groups. Groups are organized according the principal component analysis results: Group A clusters stations of the autumn cruise in Ierapetra Gyre, group B stations of the winter cruise more anticyclonic, group C stations of the winter cruise being not clearly under mesoscale influence.

Fig. S4. Vertical distributions (0-300 m) of a, d, g: density excess (σ , dotted lines) and fluorescence (continuous lines); b, e, h: dissolved inorganic phosphorus (DIP); and c, f, i: phosphomonoesterase and phosphodiesterase maximum rates (Vm PME, Vm PDE), for D (a, b, c), E (d,e,f) and F (g, h, i) groups. Groups are organized according the principal component analysis results. Group D and E clusters stations of the winter cruise influenced by the cyclonic Rhode gyre, group F clusters stations of the Cretan sea in the beginning of the cruise.

Fig. S5. Vertical profiles of primary production (PP, in mg C m⁻³ d⁻¹, black upper scale), heterotrophic prokaryotic production (BP, in mg C m⁻³ d⁻¹, red upper scale) and chlorophyll derived from fluorescence profiles (Tchl, μ g L⁻¹, lower scale) at the ST15, 35, 75, 83, 90, 116 during the winter cruise (PERLE2)

Fig. S6. Vertical profiles of primary production (PP, in mg C m⁻³ d⁻¹, upper scale) and total chlorophyll a derived from fluorescence profiles (Tchl, μ g L⁻¹, lower scale) at the ST3, 14, 24 and 26 during the autumn cruise (PERLE1)

Fig. S7. Box plots distribution of some pigments to Tchla ratios calculated for: fucoxanthin (fuco:Tchla), peridinin (peri:Tchla), zeaxanthine (zea:Tchla), divinyl-chlorophyll a (dv-chla:Tchla), chlorophyll b (chlb:Tchla), 19'butanoylfucoxanthin (19'BF:Tchla), alloxanthin (allo:Tchla) and degradation index. Group A gathers stations of the autumn cruise and, groups B to F gather stations of the winter cruise.

Fig. S8. Time series of potential density anomaly values between 20 m and 250 m, and chlorophyll fluorescence at 50 m and 100 m from Nov 2018 to June 2019 at the E1-M3A site in the Cretan Sea (35°47.16' N, 24°55.19' E, 1440 m depth). The shaded area shows the period of PERLE 2 cruise.







Fig. S3



Fig. S4



BP PP

chl









Fig. S7

