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EFFECTS OF CHRONIC WHOLE-BODY EXPOSURE TO GSM OR UMTS ELECTROMAGNETIC FIELDS ON LEARNING AND MEMORY *IN VIVO*

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Aim

Detection of cognitive effects, i.e. learning ability and memory, eventually induced by chronic exposure to GSM or UMTS electromagnetic fields in three consecutive generations of rats

Specific aim

Quantification of learning ability and memory deficits – if any

Key words

- health hazards
- electromagnetic fields (EMFs), cell-phone
- Central Nervous System (CNS)
- cognition (learning, memory)
- operant-behavior
- microstructures (inter-response intervals, IRIs)
- dynamics of serial properties in operant-behavior performance
- rats

Literature

- **M. Bornhausen and H. Scheingraber**: Prenatal exposure to 900 MHz, cell-phone electromagnetic fields had no effect on operant-behavior performances of adult rats. *Bioelectromagnetics* 21:566-574, 2000

- **C.B. Ferster and B.F. Skinner**: Schedules of Reinforcement. Appleton-Century-Crofts, New York 1957

- **R.P.Jensh**: Behavioral testing procedures: a review. In: E.M. Johnson, D.M. Kochhar (eds.): Handbook of experimental pharmacology, vol. 65. Teratogenesis and reproductive toxicology. Berlin, Heidelberg, New York: Springer Verlag, 1983

- **M.H. Repacholi**: Low-level exposure to radiofrequency electromagnetic fields. Health effects and research needs. *Bioelectromagnetics* 19:1-19, 1998

- **B. Weiss, J.M. Ziriax, M. Christopher Newland**: Serial properties of behavior and their chemical modification. *Animal Learning & Behavior* 17(1):83-93, 1989

Rationale for experimental studies of cognition after chronic exposure to environmental hazards (e.g. GSM- or UMTS-EMFs)

- changes of function are precursors of structural changes
- functions of the Central Nervous System (CNS) are more sensitive than functions of other organs
- CNS functions are most sensitive during prenatal development

Automated operant-behavior tests *vs.* "developmental landmarks"

Various physical signs and neuromuscular reflexes in laboratory rodent pups must be carefully and repeatedly checked by experienced personnel (*cave*: personal bias)

postnatal day	
0	day of birth
2	surface righting
4	pinna detachment
8	cliff avoidance
9	negative geotaxis
11	forelimb grasp
15	bar holding
16	eye opening, forelimb hanging, air righting
17	development of fur
19	ear unfolding
25-30	descent of testis, opening of vagina

Operant-behavior

- Operant-behavior tests were run in a battery of 10 standardized test chambers (“Skinner boxes“).

- Subjects were required to press a lever for food reinforcement (pellets of 45 mg) .

- 15h-nocturnal test sessions (16:00-07:00 CET) were subdivided by alternating
  30 min ON- and 60 min OFF-cycles.

- Final tests required the subjects to respect a blocking interval of 16 sec after a reinforcement.

Operant-behavior test chambers

("Skinner boxes")

Intelligence panel of individual "Skinner box"

Operant-behavior schedules

- Differential Reinforcement of Zero Rate (**DR0**)
- Differential Reinforcement of High Rate (**DRH**)
- Differential Reinforcement of Low Rate (**DRL**)

Sequence of 5 operant-behavior training resp. test sessions

- DR0 5 min (subjects were automatically trained to press a lever for food reinforcement)

- DRH 2/1 (ss. were required to press the lever 2 times in 1 sec for a reinforcement)
- DRH 4/2 (ss. were required to press the lever 4 times in 2 sec for a reinforcement)

- DRL 1/16 (ss. were required to respect a blocking interval of 16 sec after a reinforcement; a precocious bar press reset the interval to its start. The interval was signaled by a green cue light.) **"LEARNING"**

- DRL 1/16 rep. (ss. were required to remember the previous task after a delay of 6 days) **"MEMORY"**

No effects after prenatal exposure

M. Bornhausen and H. Scheingraber:

Prenatal exposure to 900 MHz, cell-phone electromagnetic fields had no effect on operant-behavior performances of adult rats.

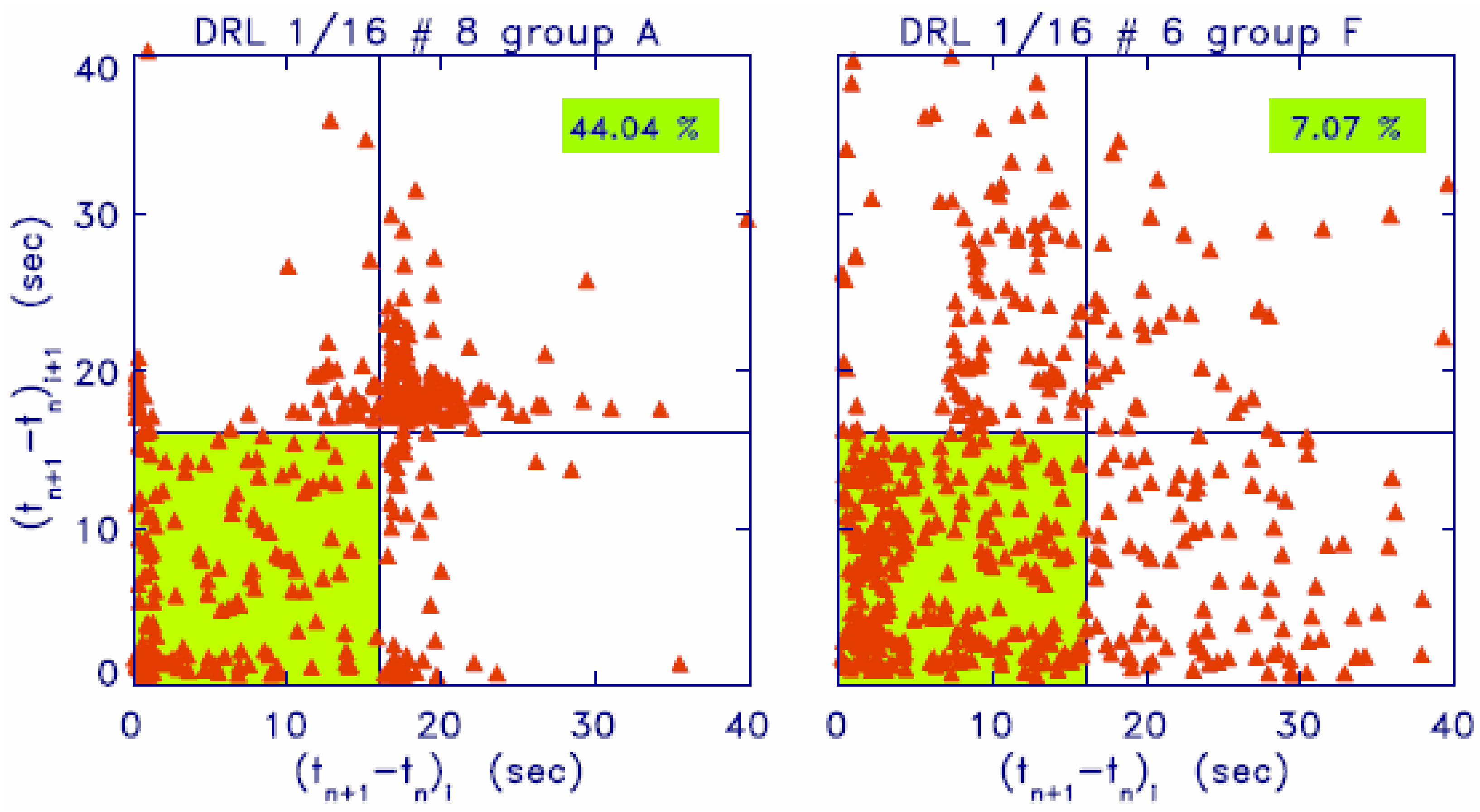
Bioelectromagnetics 21:566-574, 2000

Microstructures

- Microstructures of individual operant-behavior test performance are illustrated by pattern of interresponse intervals (IRIs, i.e. time between consecutive lever presses with a resolution of 1 msec).

- IRI pattern differentiate between “learners“ and “non-learners“.

Superposed scatter plots of the 10 ON-cycles of a DRL test session in two rats



Assessing dynamic *vs.* static changes

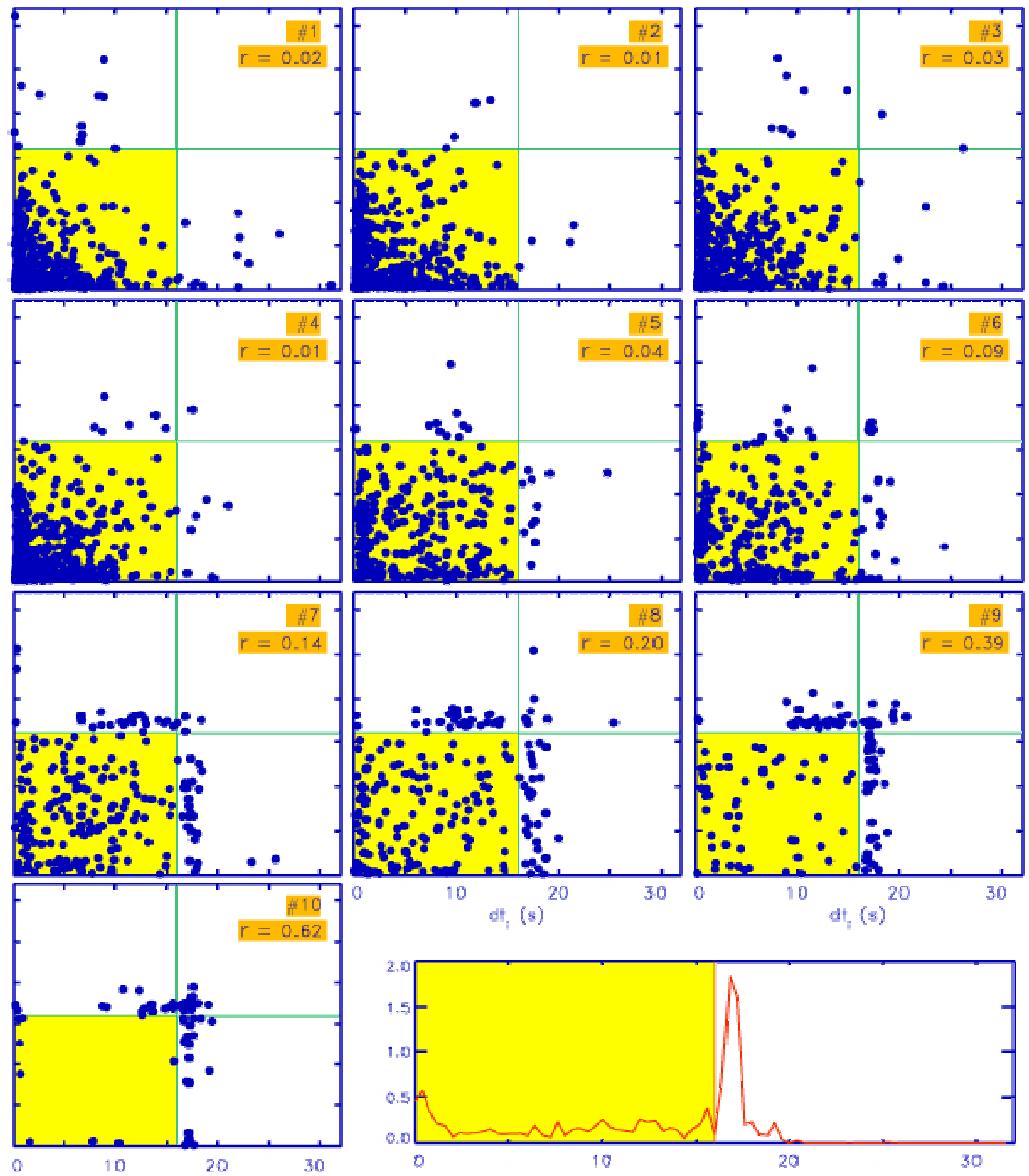
Static results at the end of a test session (f.i. the ratio of correct responses to all responses) do not reflect the dynamics of test requirement acquisition.

Dynamic signal

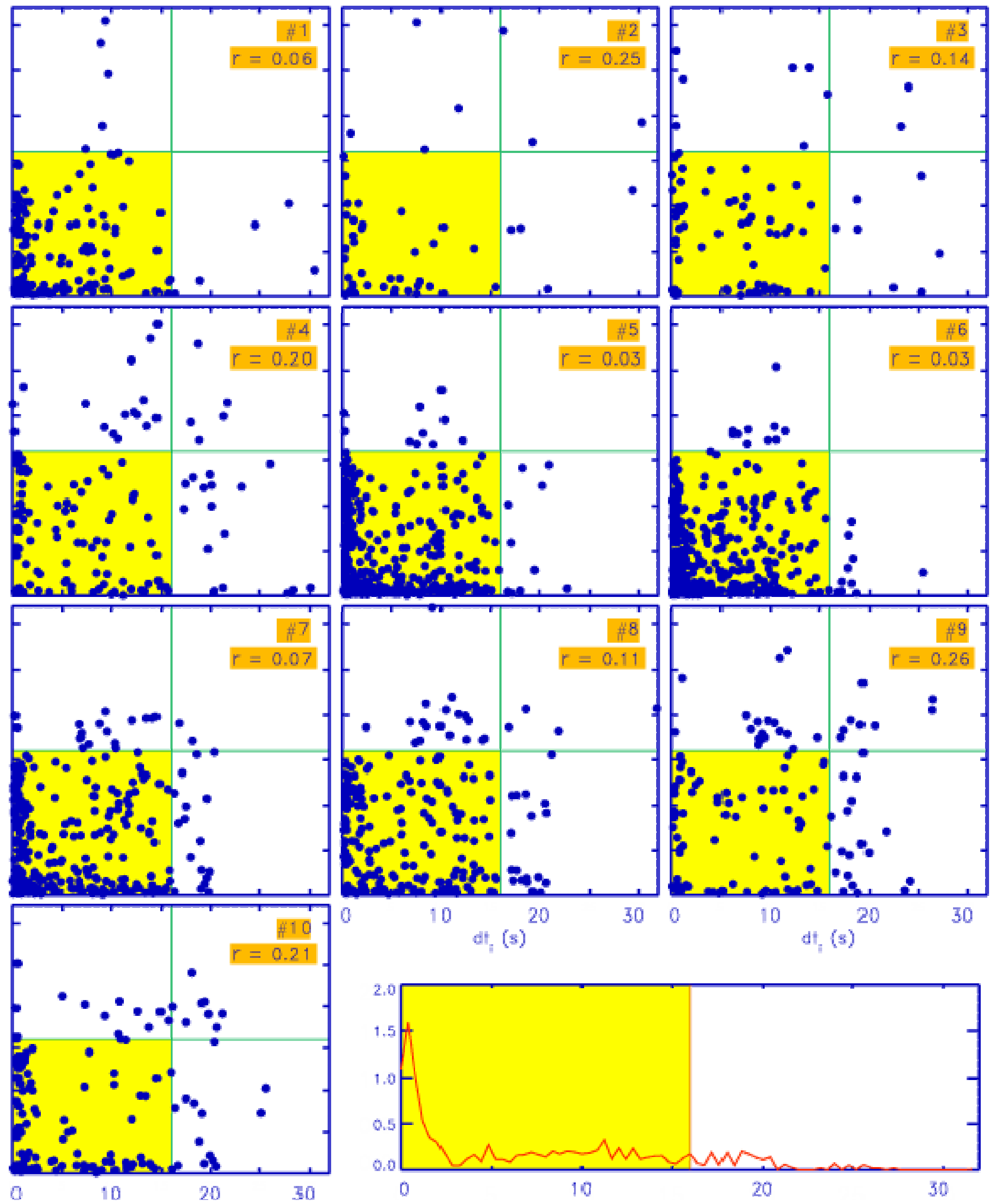
Looking at the sequence of 10 consecutive ON-cycles of a 15h-nocturnal test session -

a signal becomes apparent that is proportional to the ability of the subject to acquire the test requirement

(i.e. to "learn").



#1
r = 0.02
#2
r = 0.01
#3
r = 0.03
#4
r = 0.01
#5
r = 0.04
#6
r = 0.09
#7
r = 0.14
#8
r = 0.20
#9
r = 0.39
#10
r = 0.62
dt_i (s)
dt_i (s)



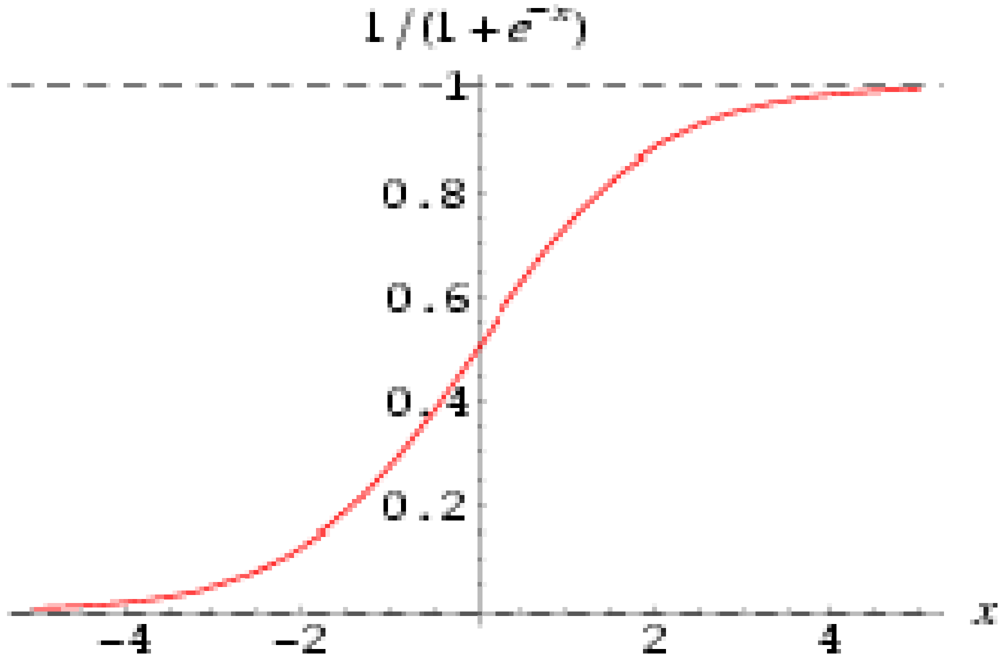
#1
r = 0.06
#2
r = 0.25
#3
r = 0.14
#4
r = 0.20
#5
r = 0.03
#6
r = 0.03
#7
r = 0.07
#8
r = 0.11
#9
r = 0.26
#10
r = 0.21
0 10 20 30
dt_i (s)
2.0 1.5 1.0 0.5 0.0

Measuring and scaling of "learning" ability and "memory"

- We are not only interested in the fact whether a subject has acquired the test requirement (i.e. has finally "learnt" the task) ---
- we go further, measure the intrinsic serial properties of the "learning" and/or the "memory" process itself, and thus are able to scale individual performances.

The phenomenon of learning

- can be appropriately described by an
  S-shaped curve



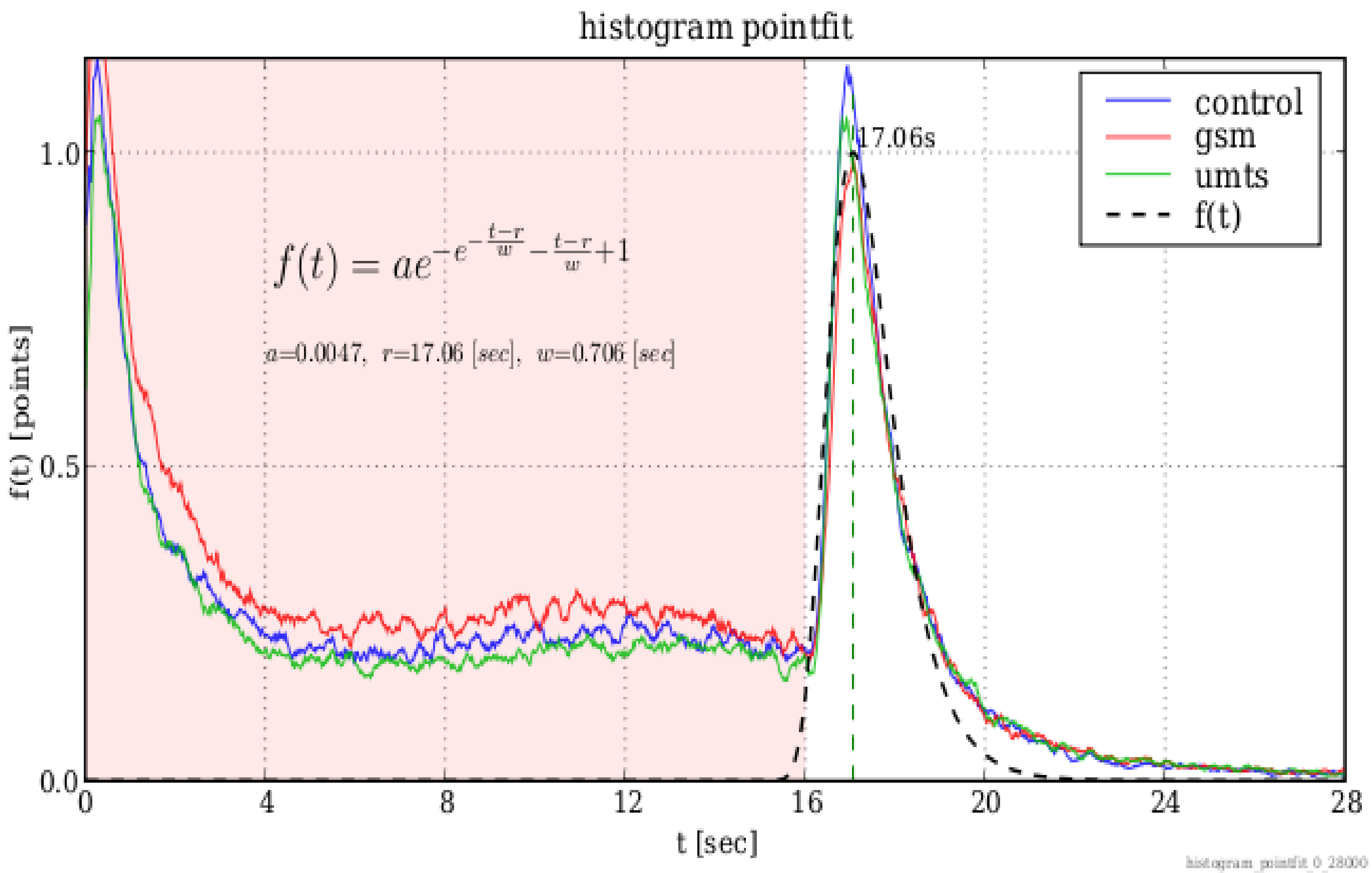
parameters:

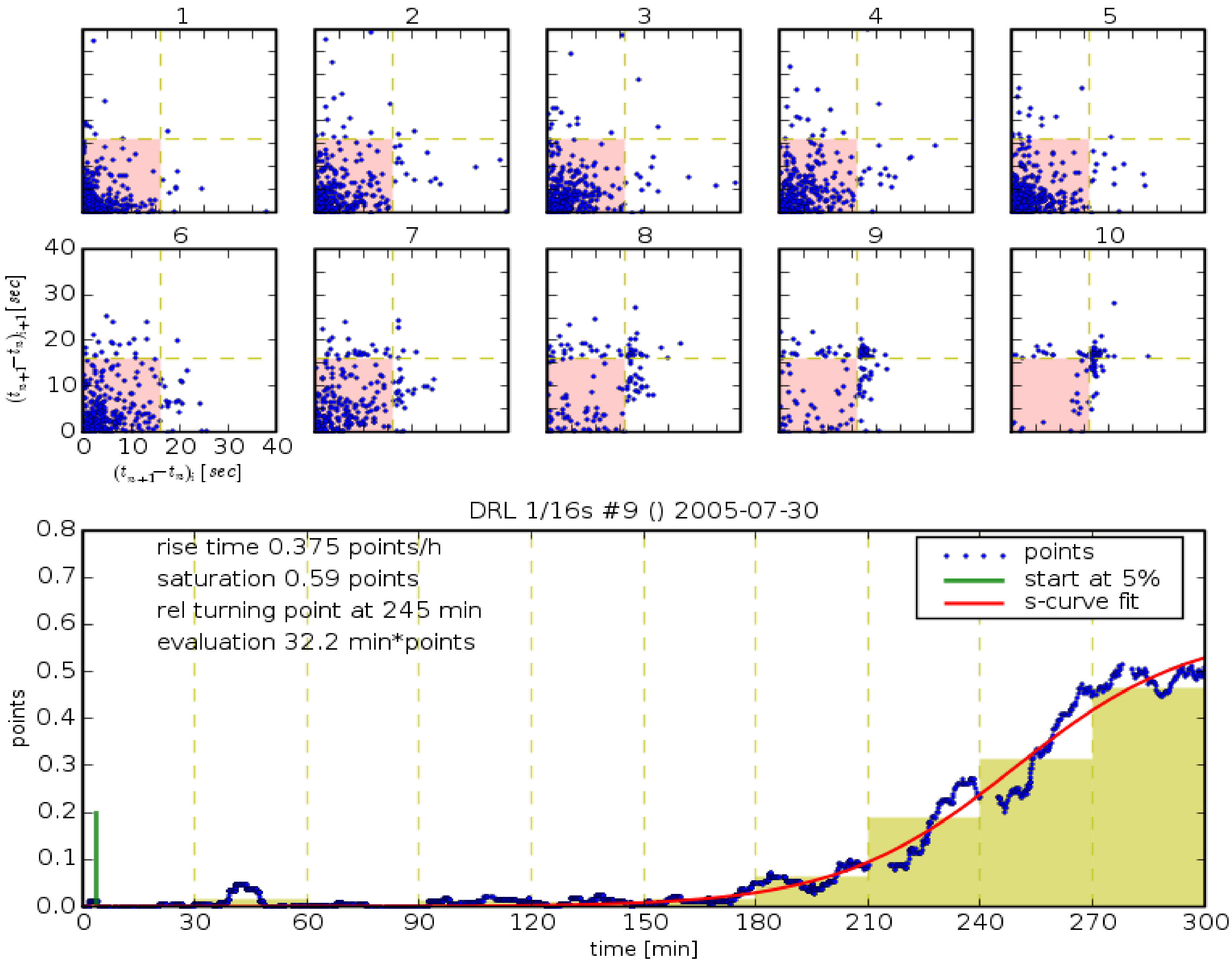
- start time
- base line
- rise time
- saturation
- turning point

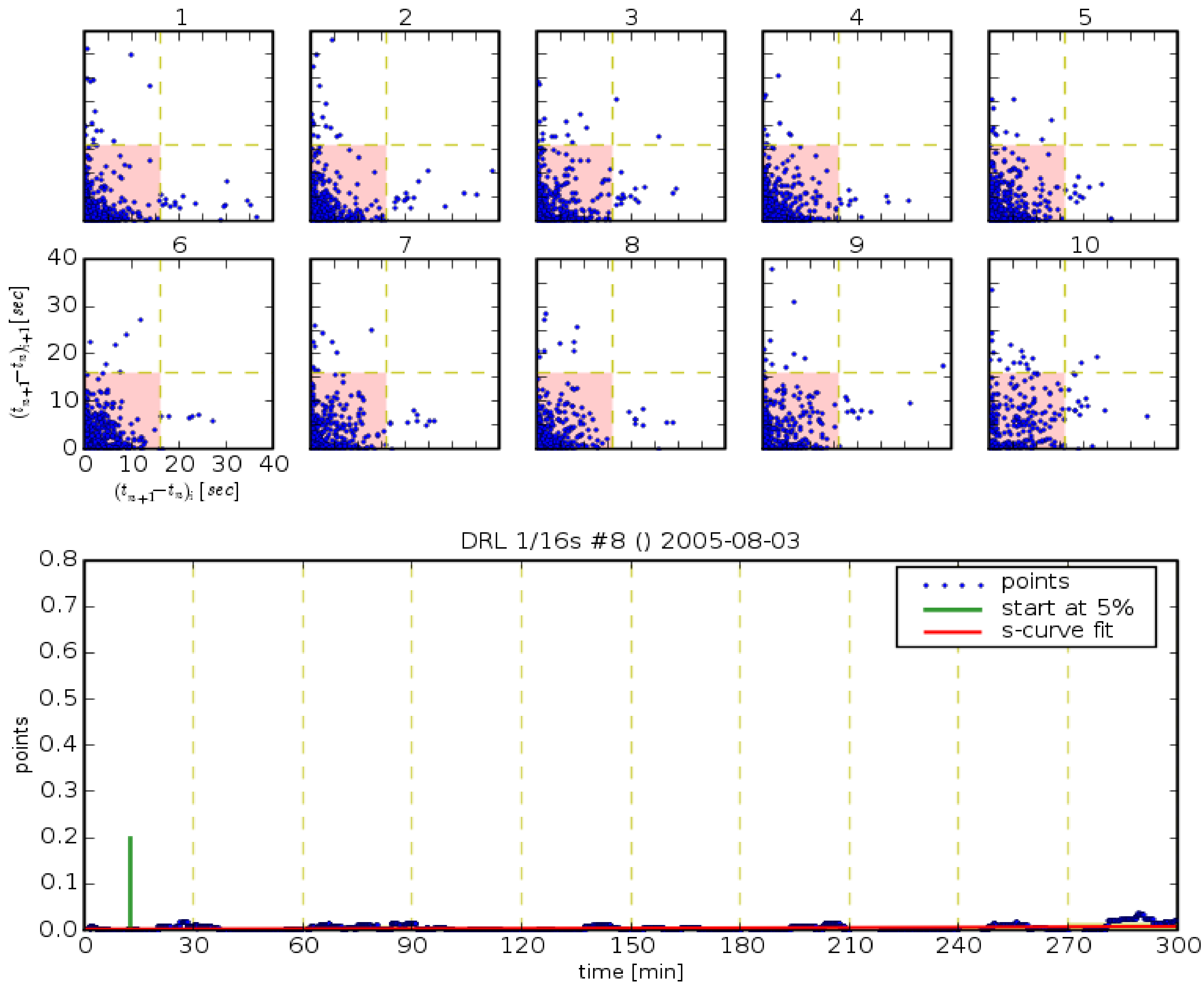
Measuring serial properties of operant-behavior

Inter-response intervals (IRIs) between consecutive lever presses are recorded (in multiples of 1 msec), weighed and normalized relative to an empirically determined standard IRI distribution, and expressed as "points".

The sequence of points, then, is fitted to an S-shaped curve by an appropriate algorythm.


histogram pointfit
control
gsm
umts
f(t)
17.06s
$f(t) = ae^{-e^{-\frac{t-r}{w}}-\frac{t-r}{w}+1}$
a=0.0047, r=17.06 [sec], w=0.706 [sec]
f(t) [points]
t [sec]
0.0
0.5
1.0
0
4
8
12
16
20
24
28
histogram_pointfit_0_28000


1
2
3
4
5
6
7
8
9
10
$(t_{n+1}-t_n)_{i+1}$ [sec]
$(t_{n+1}-t_n)_i$ [sec]
DRL 1/16s #9 () 2005-07-30
rise time 0.375 points/h
saturation 0.59 points
rel turning point at 245 min
evaluation 32.2 min*points
points
start at 5%
s-curve fit
time [min]

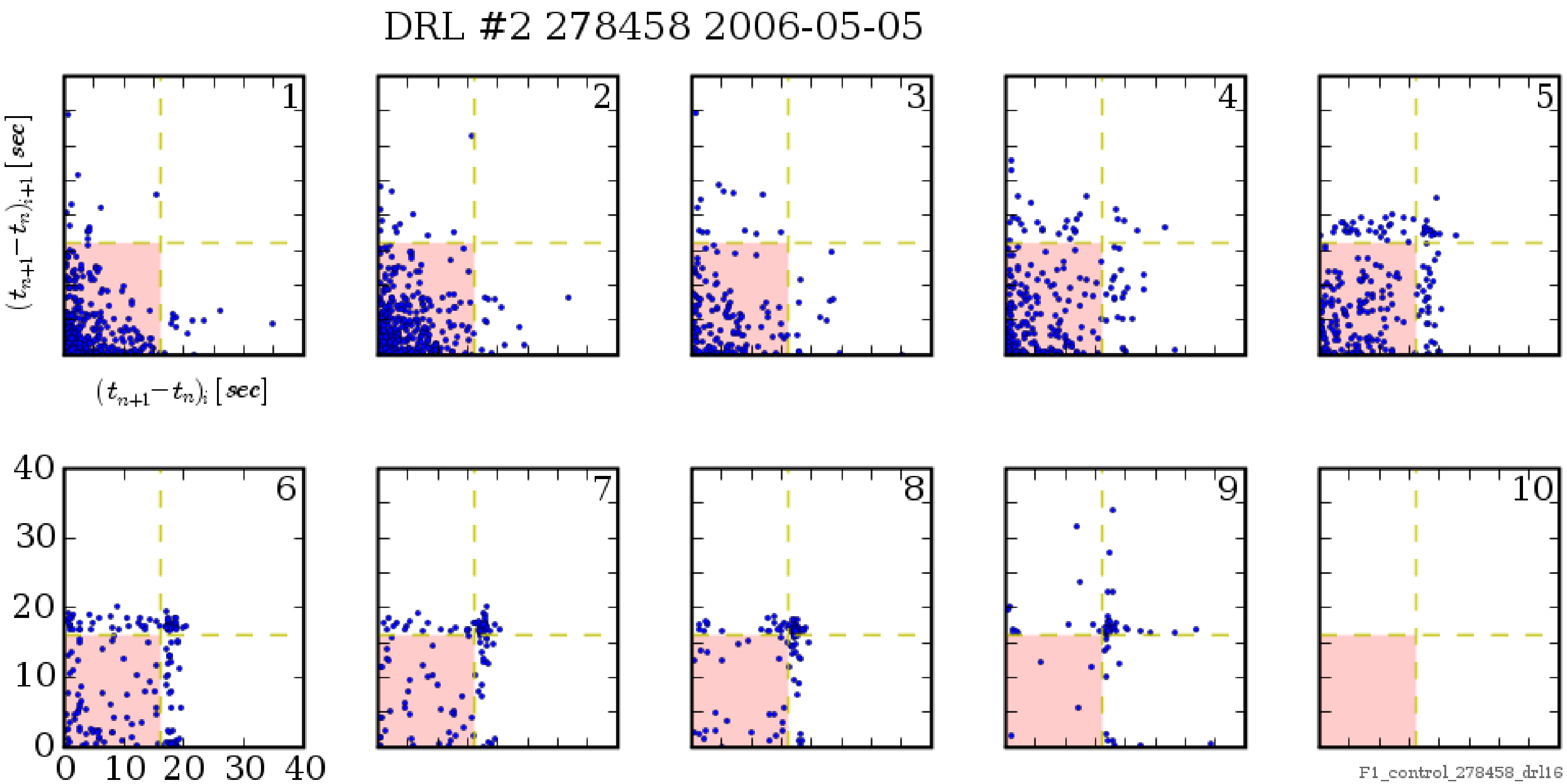


1
2
3
4
5
6
7
8
9
10
40
30
20
10
0
$(t_{n+1}-t_n)_{i+1}$ [sec]
0
10
20
30
40
$(t_{n+1}-t_n)_i$ [sec]
DRL 1/16s #8 () 2005-08-03
points
start at 5%
s-curve fit
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
points
0
30
60
90
120
150
180
210
240
270
300
time [min]

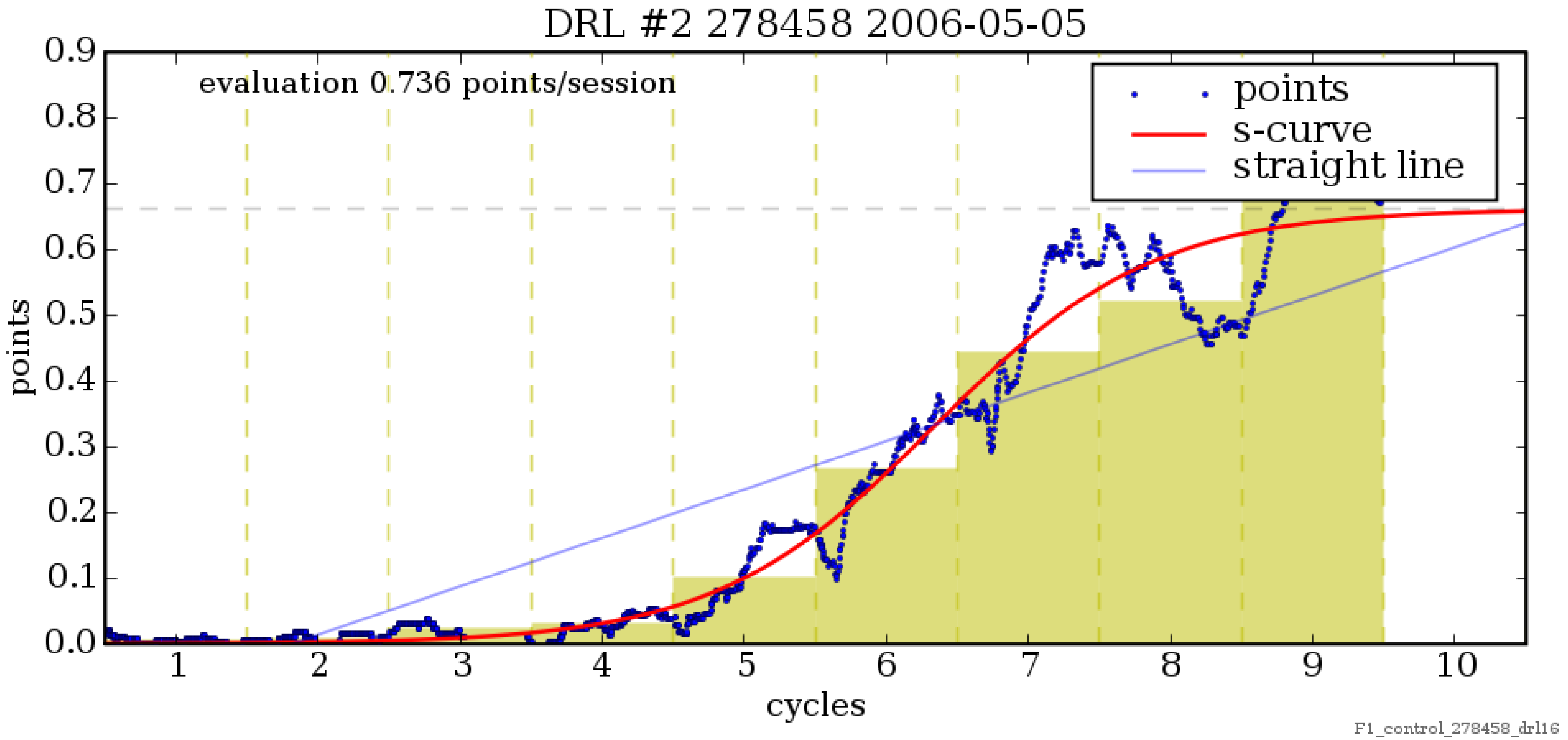
Assessing changes of CNS functions

Obviously, the ability of an animal subject to acquire an operant-behavior test requirement (i.e. to "learn") can be mathematically assessed (in terms of points, rise time, turning point, saturation, start time, etc.) and used to quantify subtle deficits of CNS functions.

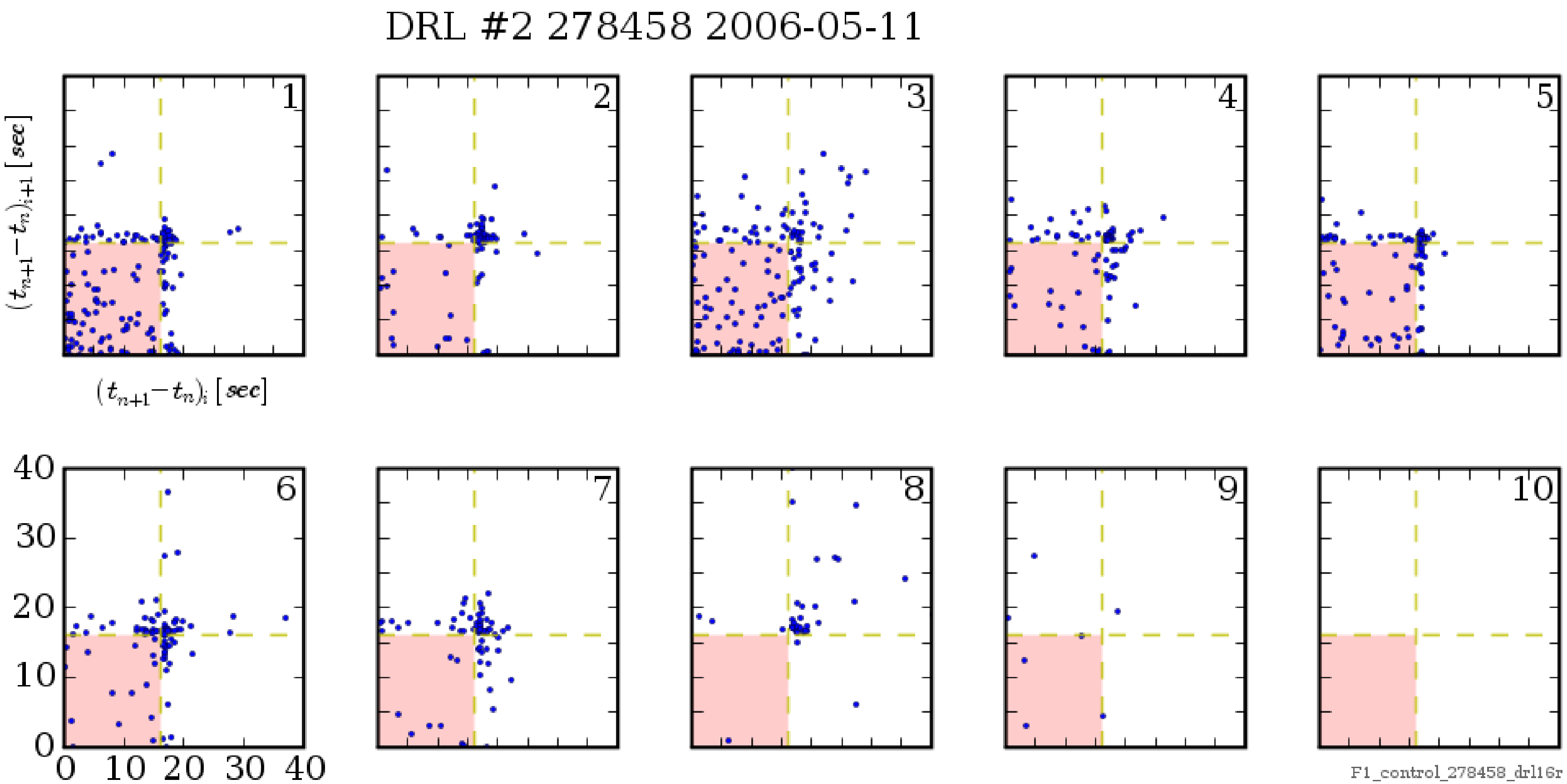
Scatter plot of the 1st DRL-test



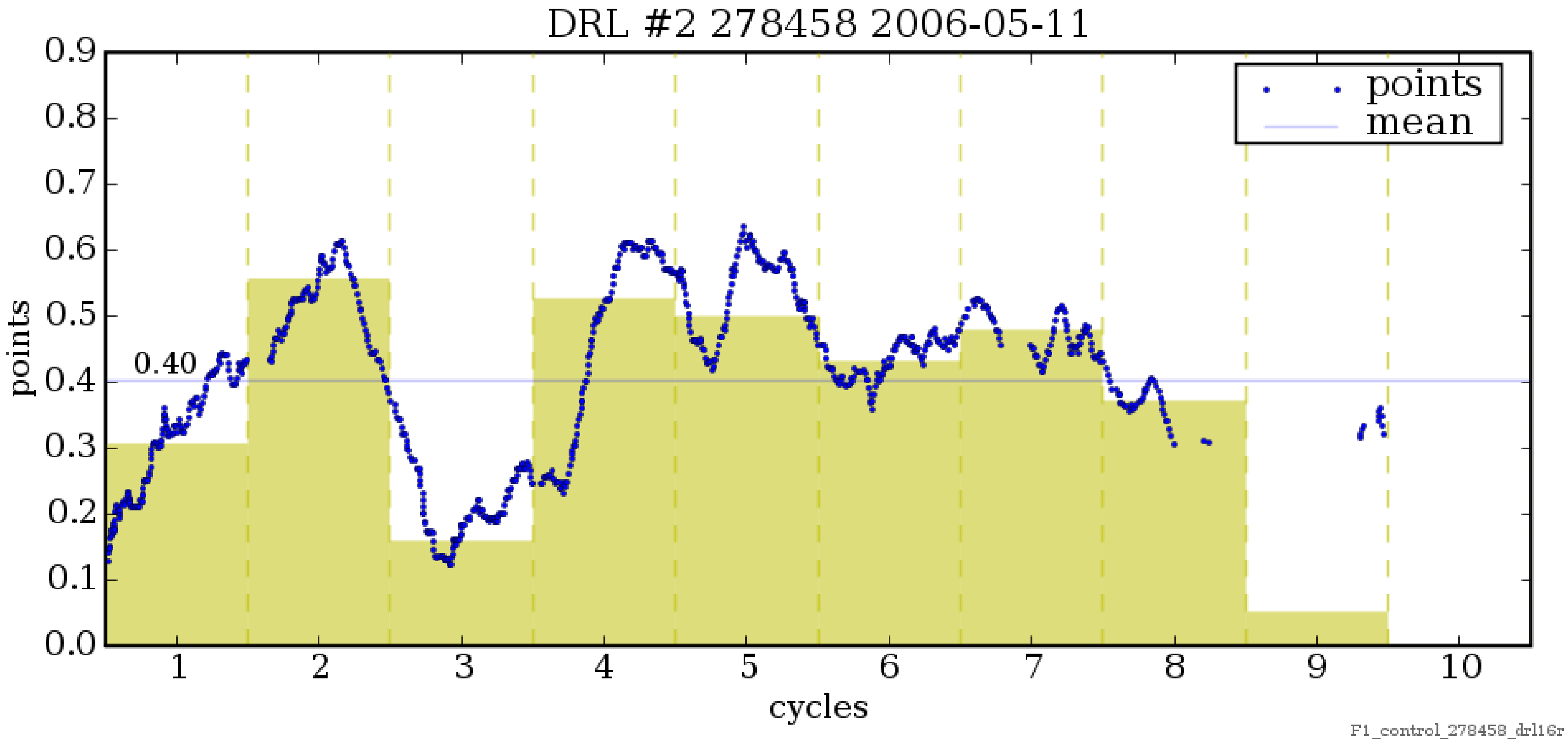
Evaluation of "learning" ability



Scatter plot of the 2nd DRL-test



Evaluation of "memory"



Parameters of operant-behavior performance

static

- activity = no. of <u>l</u>ever <u>p</u>resses (lp)
- reinforcements = no. of <u>r</u>einforcements (r)
- rel. performance = test specific ratio of lp/r

dynamic

- points = conformance of each IRI with standard IRI

Test specific calculation of "rel. performance" in DRH- and DRL-tests

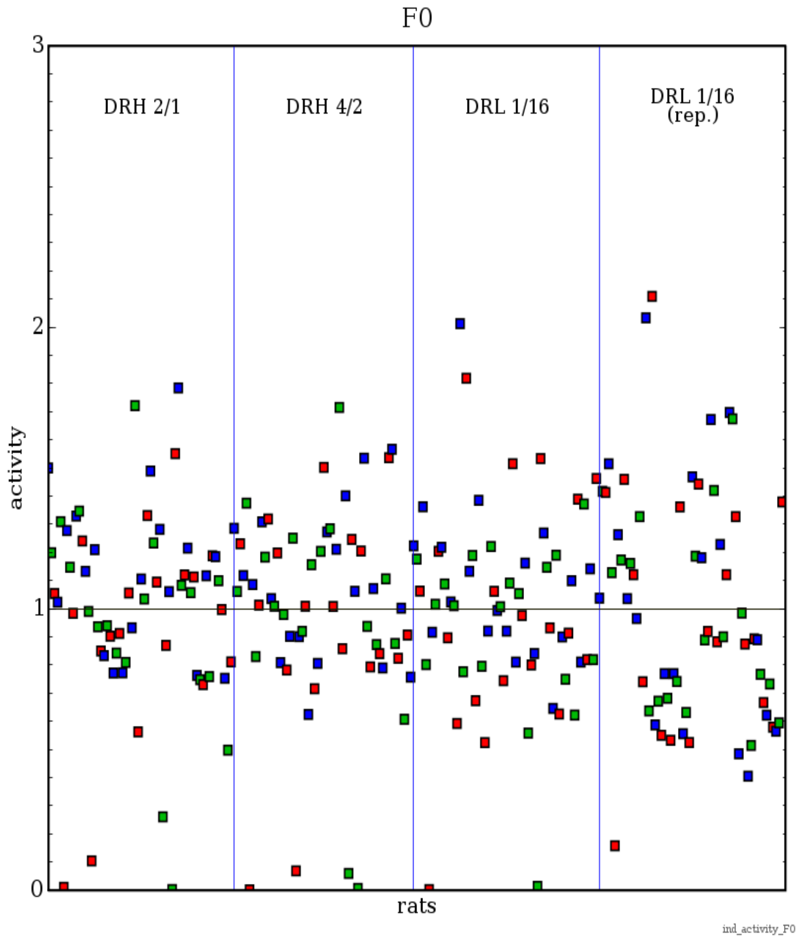
$$\textbf{DRH}\ [\%] = \frac{\text{no. of reinforcements x 100 x DRH requirement}}{\text{no. of lever presses during ON-cycles}}$$

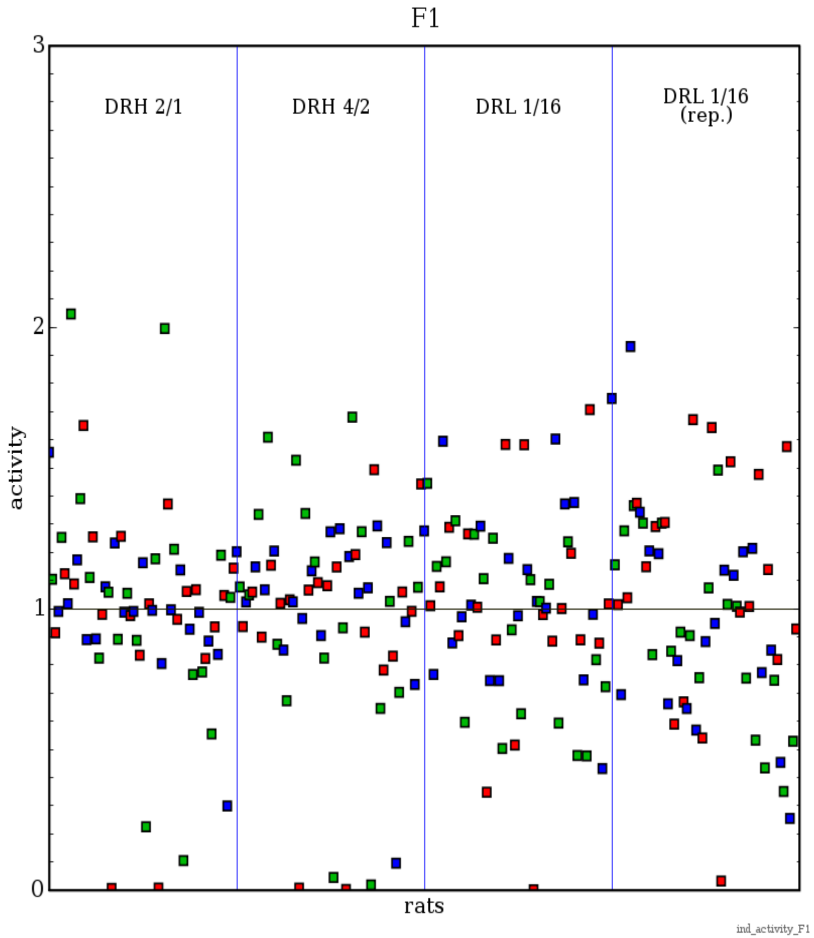
(DRH requirement: 2 or 4)

$$\textbf{DRL}\ [\%] = \frac{\text{no. of reinforcements x 100}}{\text{DRL requirement x no. of ON-cycles}}$$

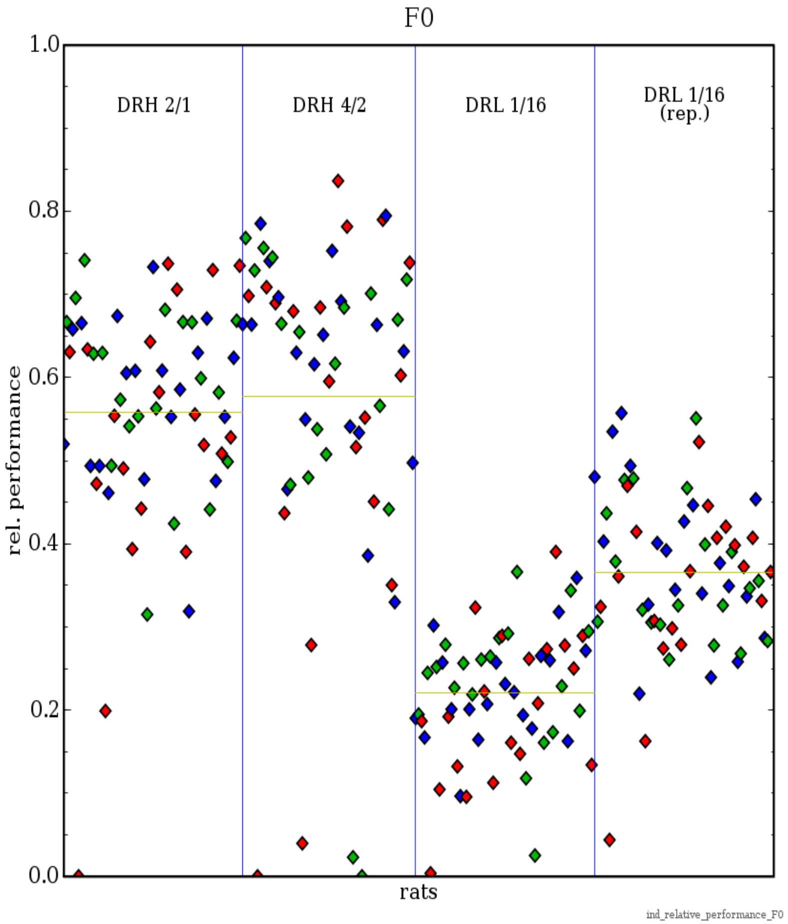
(DRL requirement: Maximal available no. of reinforcements in an ON-cycle with respect to the duration of the blocking interval)

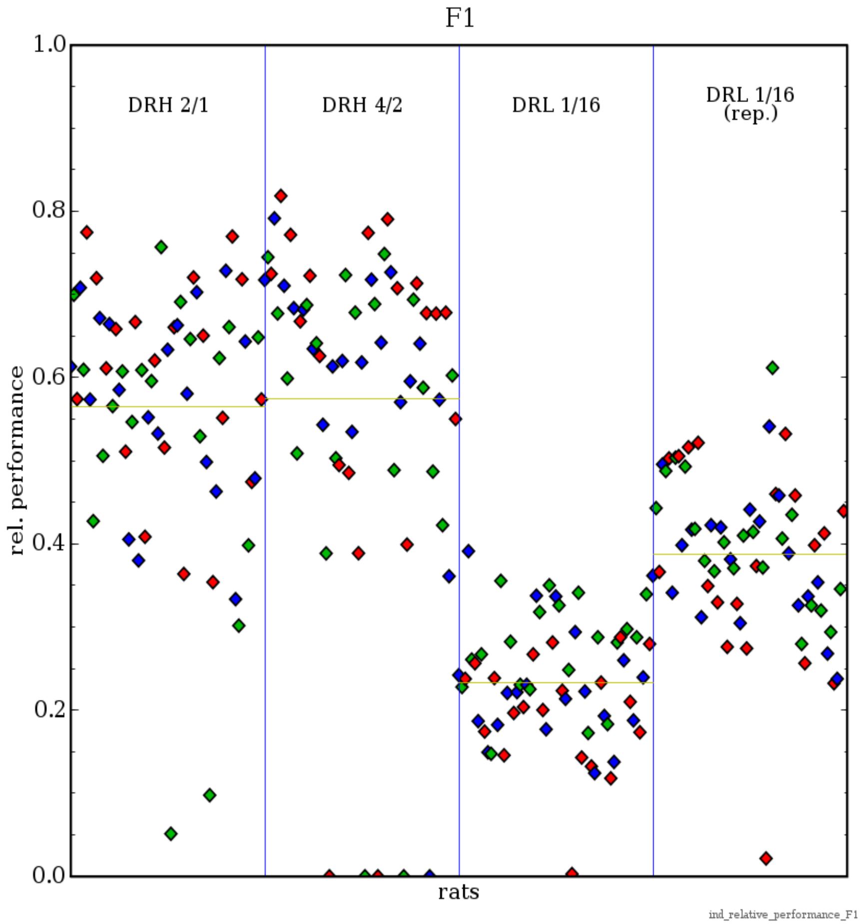
Examples of normalizations of operant-behavior parameters (activity)



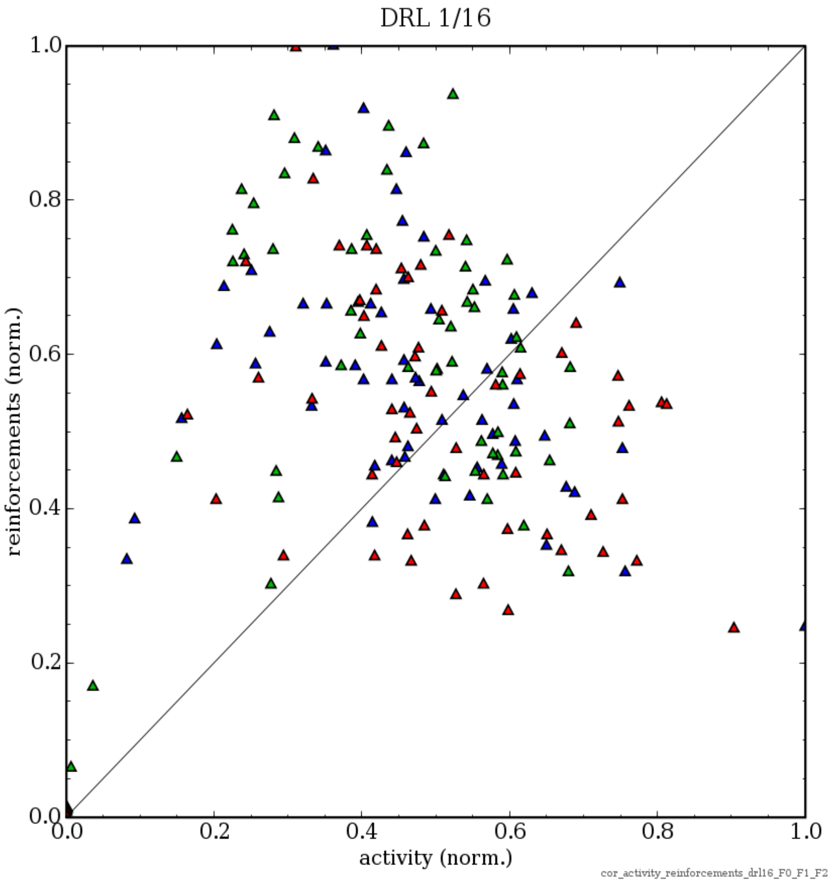


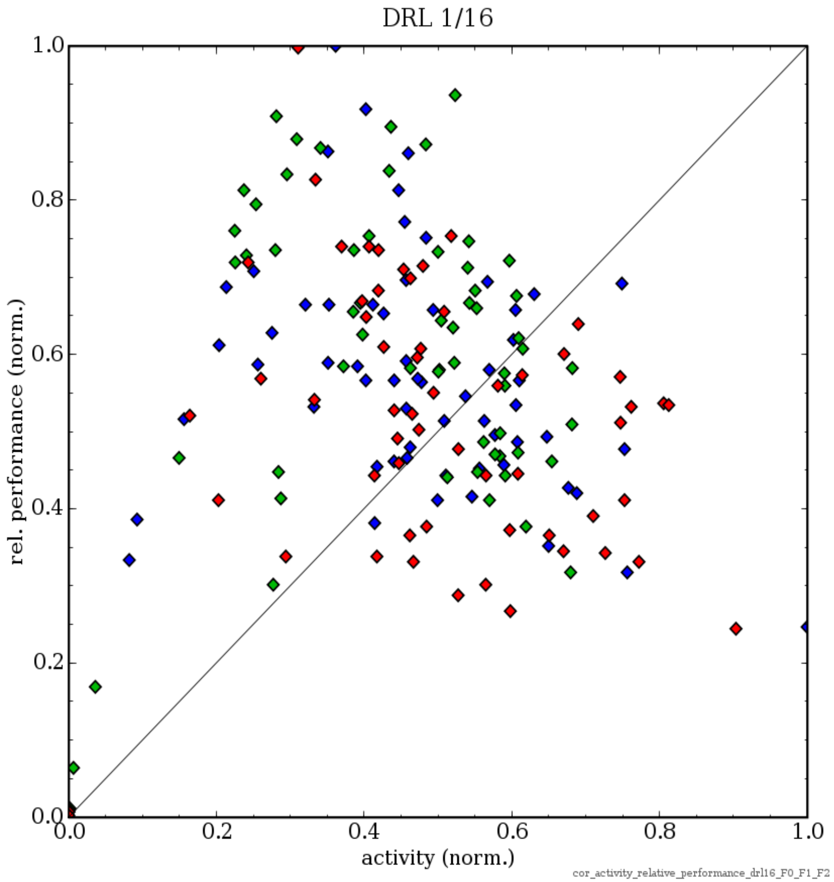
Examples of normalizations of operant-behavior parameters (rel. performance)



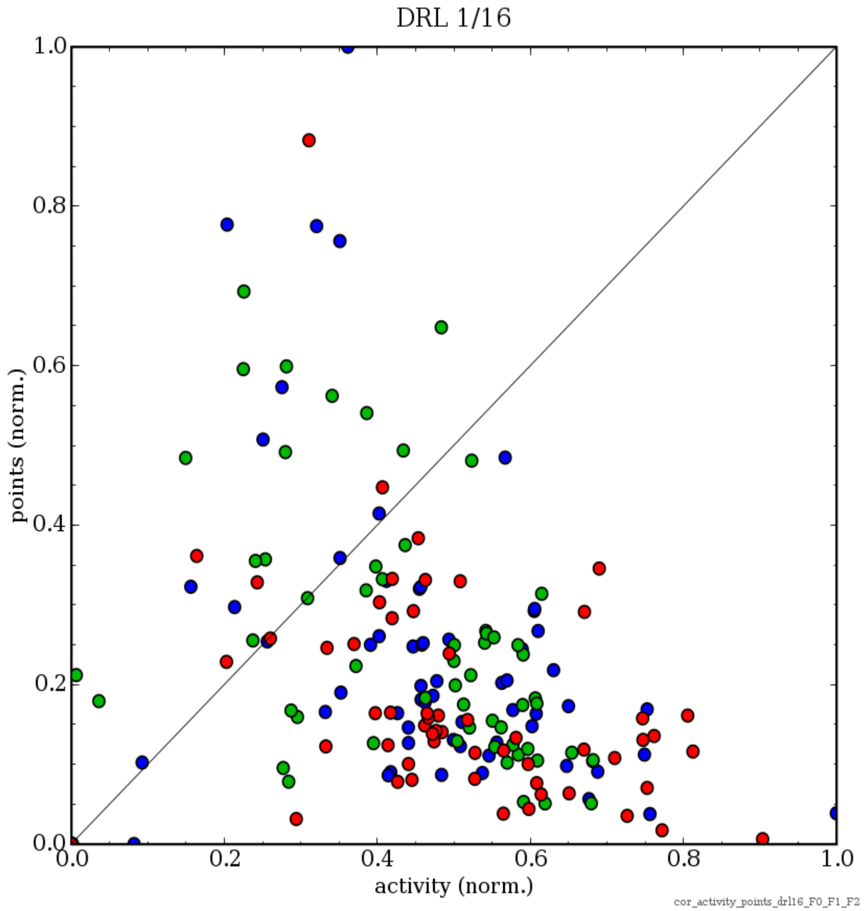


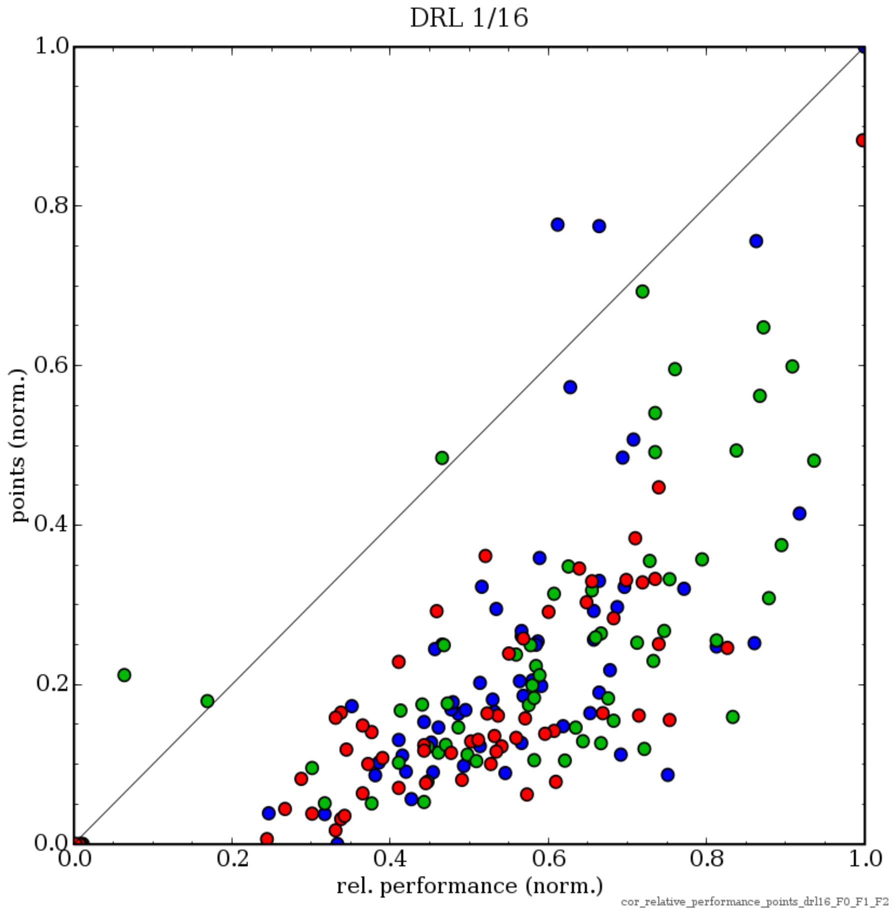
Examples of multiple correlations between parameters of DRL test performance I



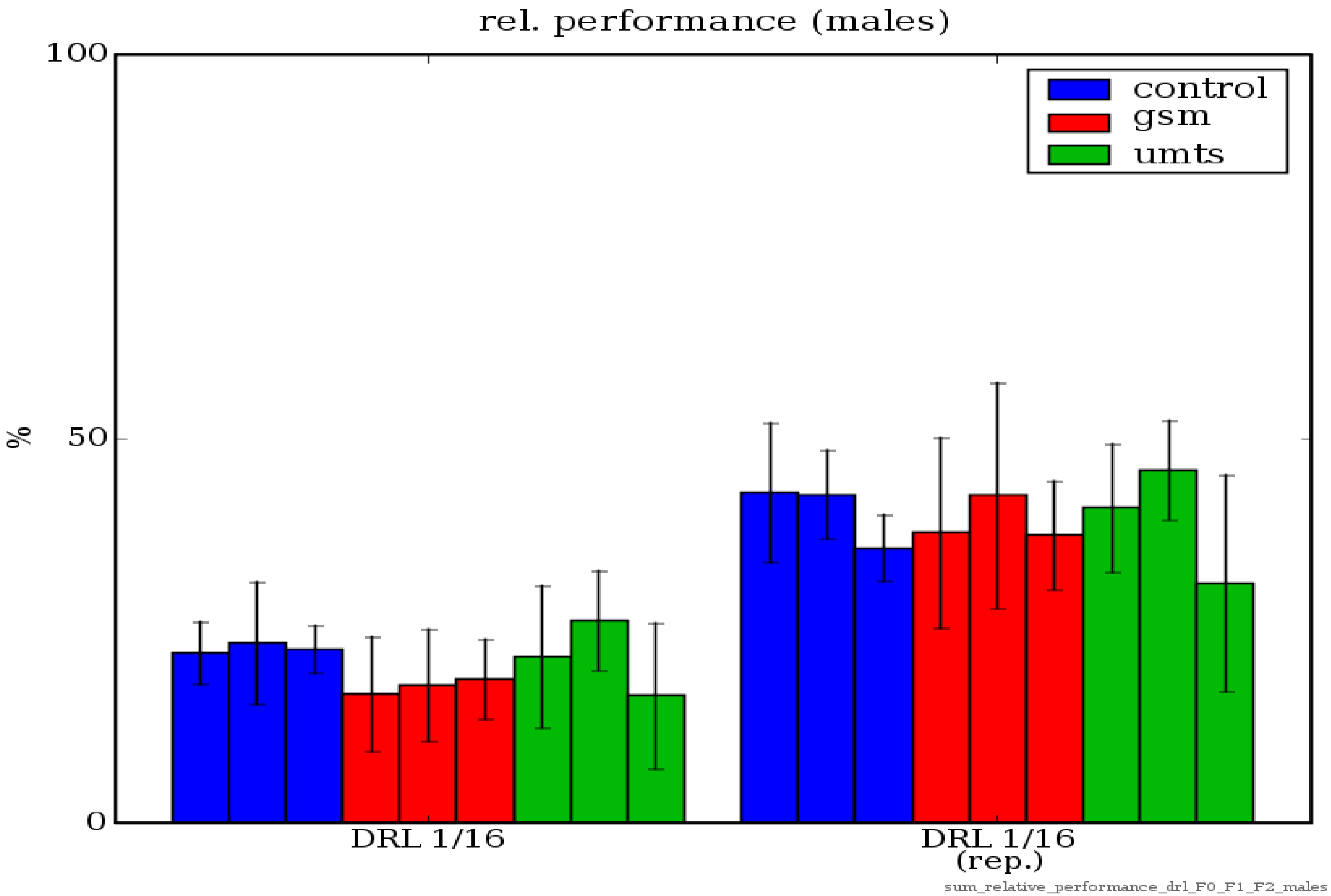


Examples of multiple correlations etween parameters of DRL test performance II

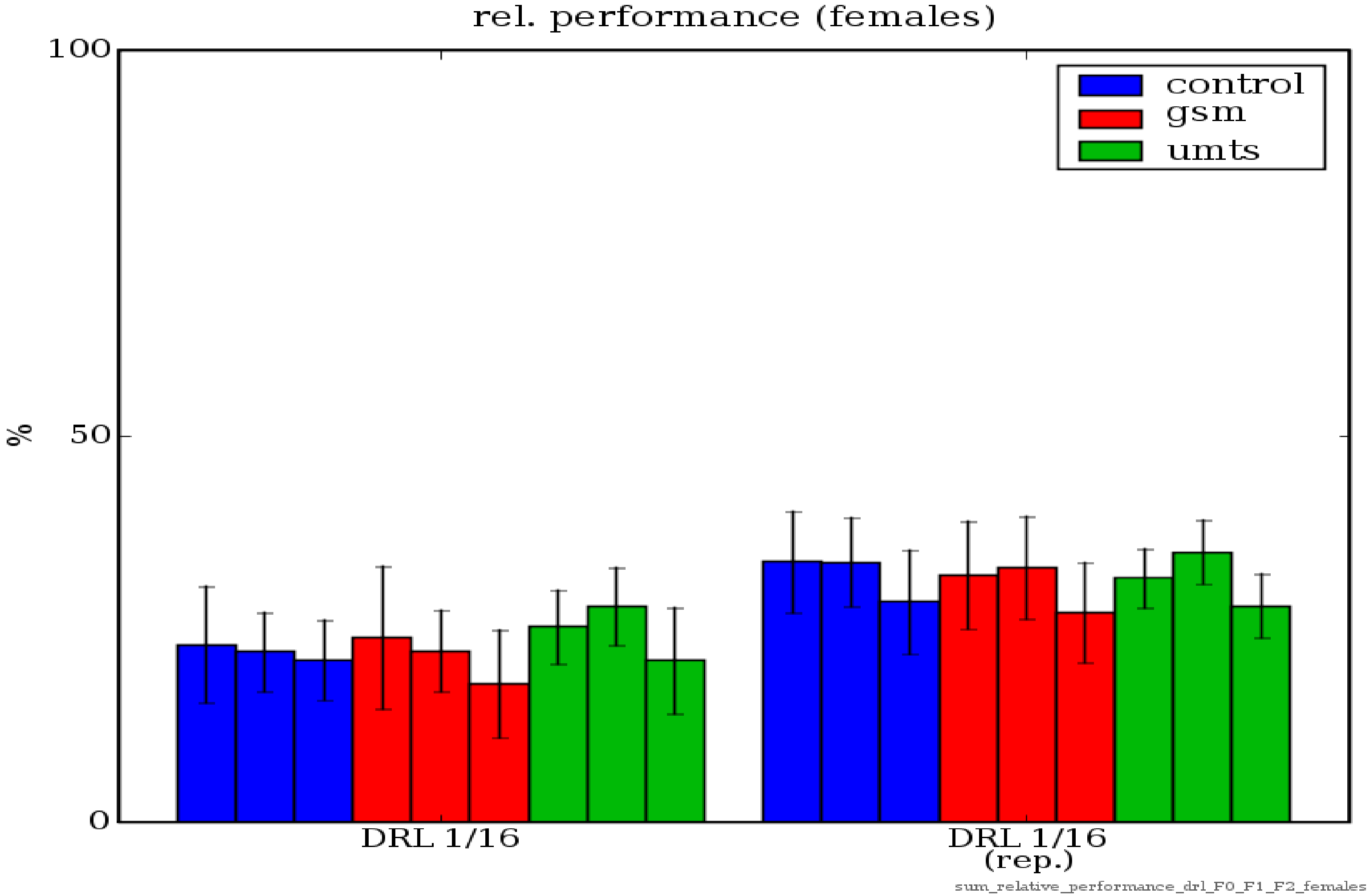




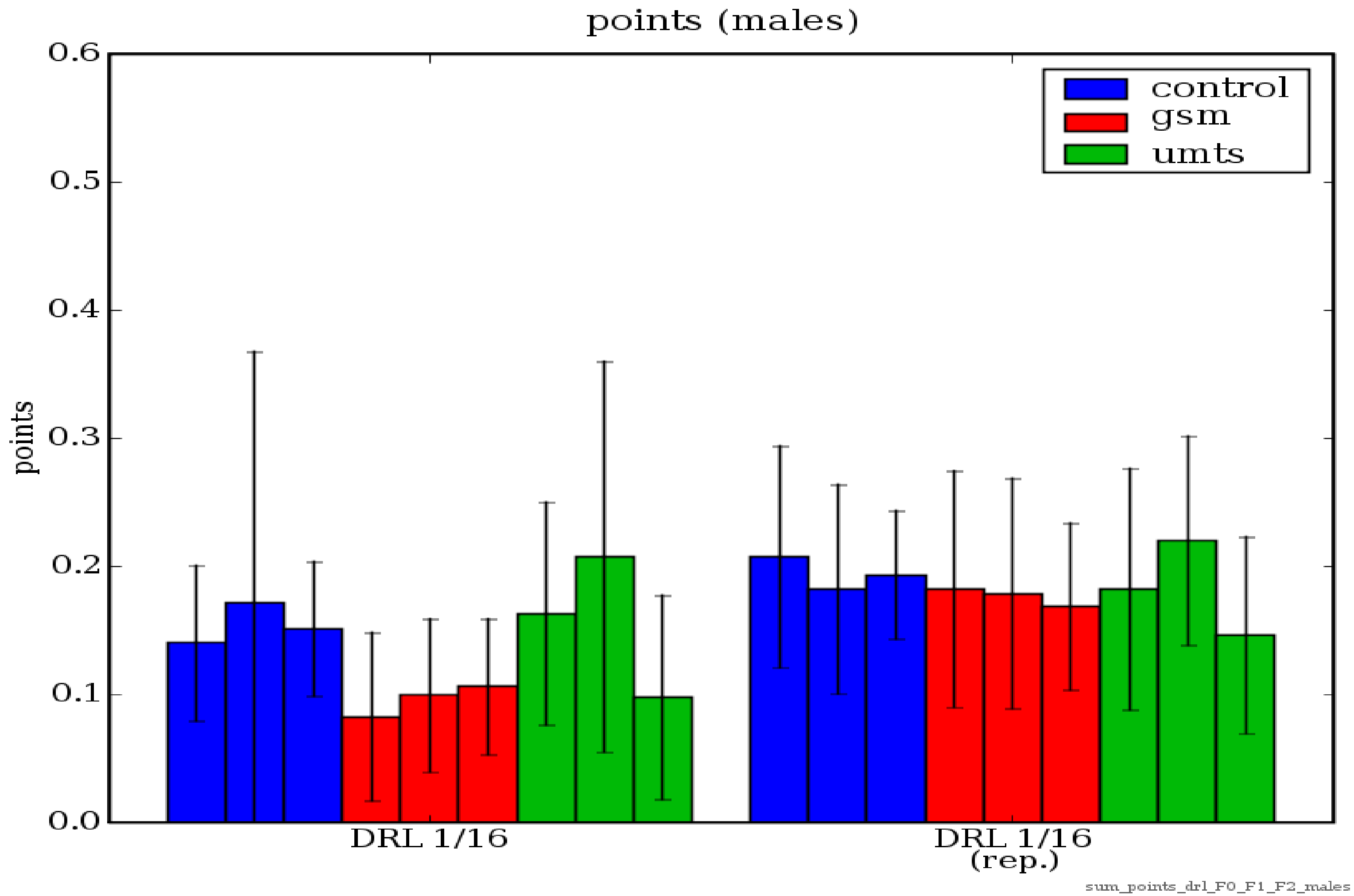
Relative performance (males) in F0, F1, and F2 rats



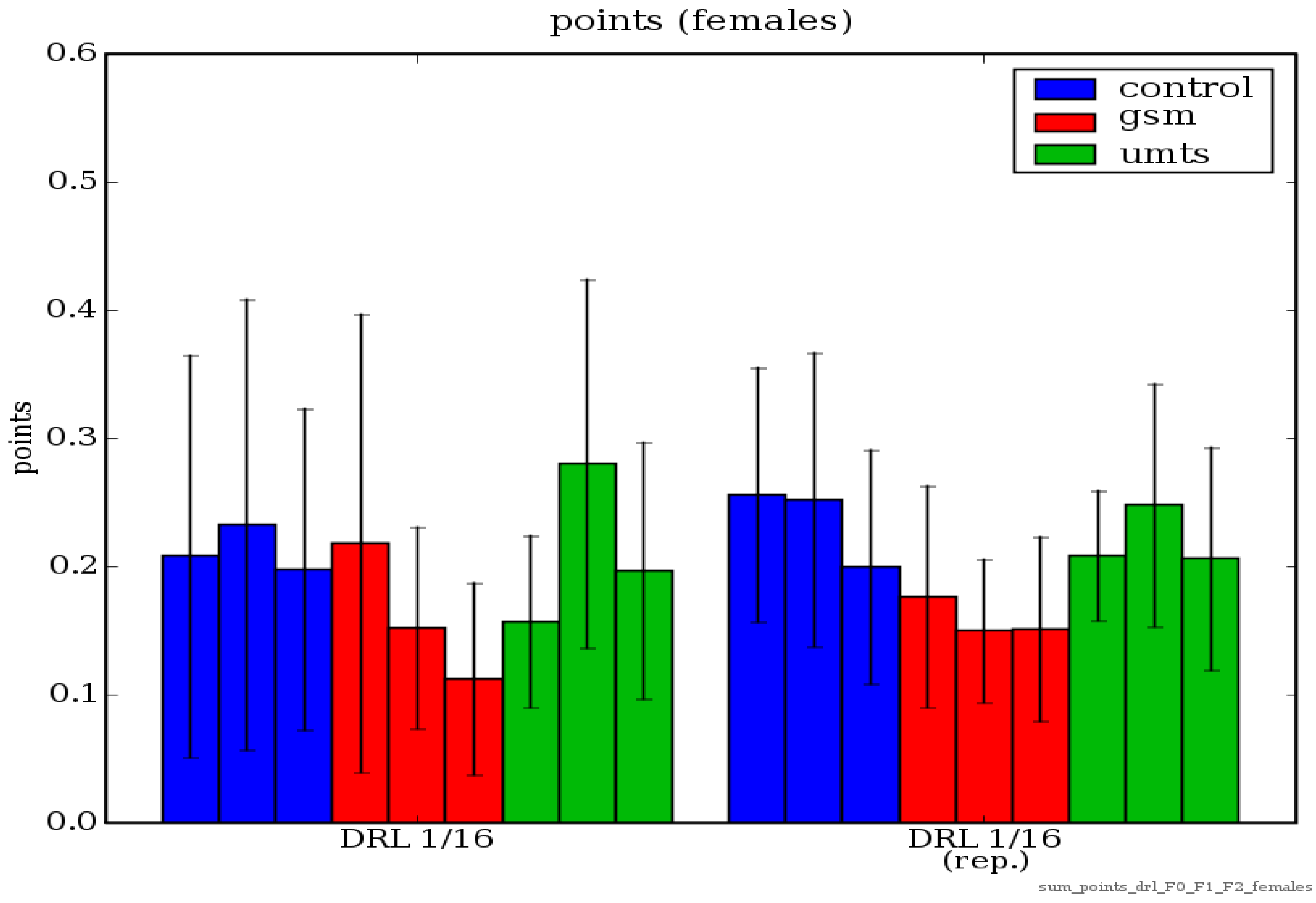
Relative performance (females) in F0, F1, and F2 rats

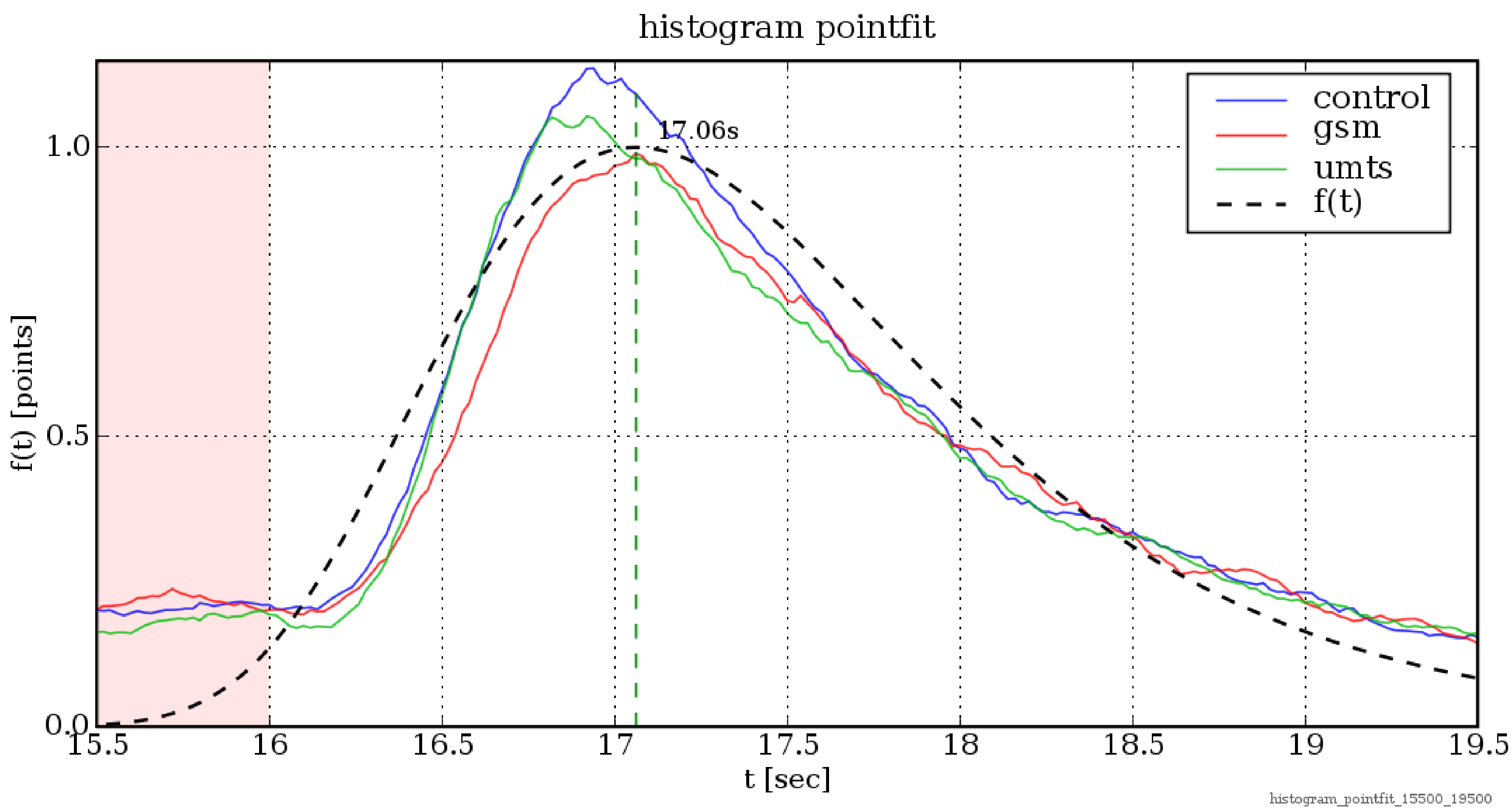


Evaluation of the dynamics of DRL test acquisition (males) in F0, F1, and F2 rats

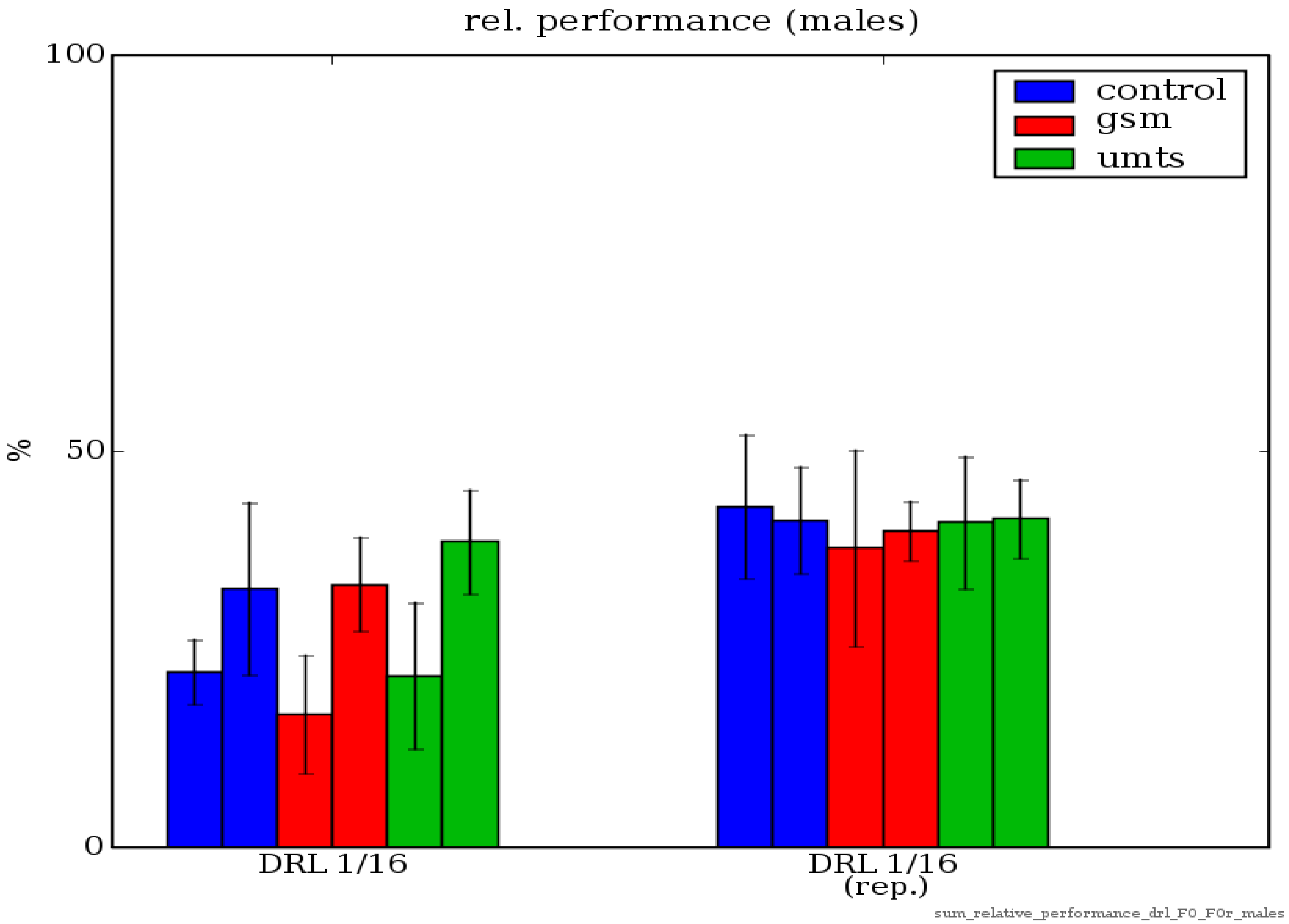


Evaluation of the dynamics of DRL test acquisition (females) in F0, F1, and F2 rats

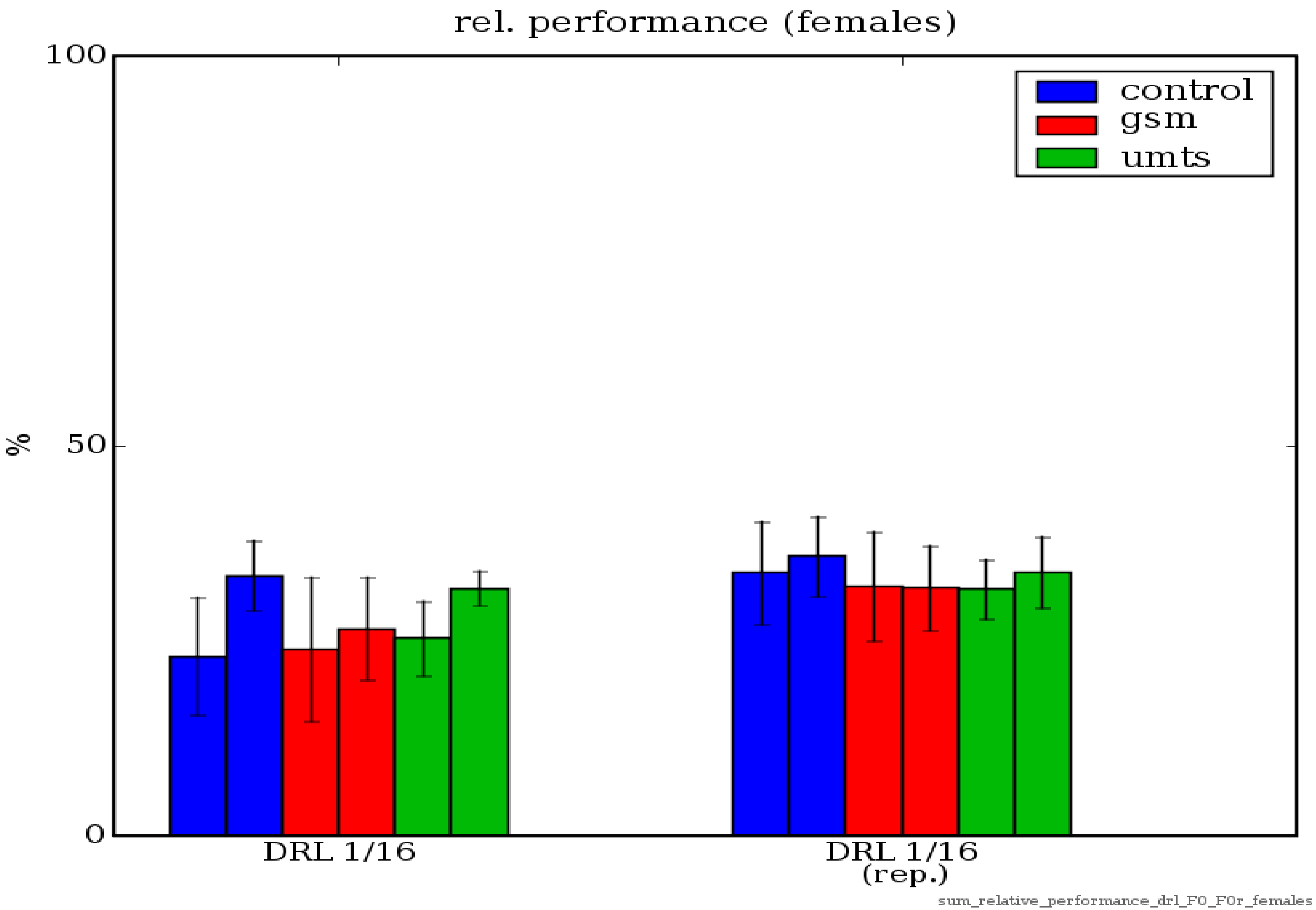



histogram pointfit
control
gsm
umts
f(t)
17.06s
1.0
0.5
0.0
f(t) [points]
15.5
16
16.5
17
17.5
18
18.5
19
19.5
t [sec]
histogram_pointfit_15500_19500

Repetition of DRL-tests in F0 rats



Repetition of DRL-tests in F0 rats



Conclusions I

- Operant-behavior contingencies are useful in the assessment of potential health risks, in toxicology, environmental protection, etc.

- The analysis of microstructures of operant-behavior test performance is a powerful tool to demonstrate changes of CNS functions.

- The dynamics of test acquisition (i.e. "learning") can be measured by S-curve fits and used to enhance test sensitivity of CNS functions in situations of potential health hazards.

Conclusion II

The analysis of the results of this double-blind experiment of continuously EMF-exposed rats (WISTAR, N = 180, males and females, 3 generations, GSM or UMTS, SAR 0.4 W/kg) - featuring multiple correlations of various test parameters - did not show any significant deviations of learning ability or memory in operant-behavior tests when compared to sham-exposed controls.