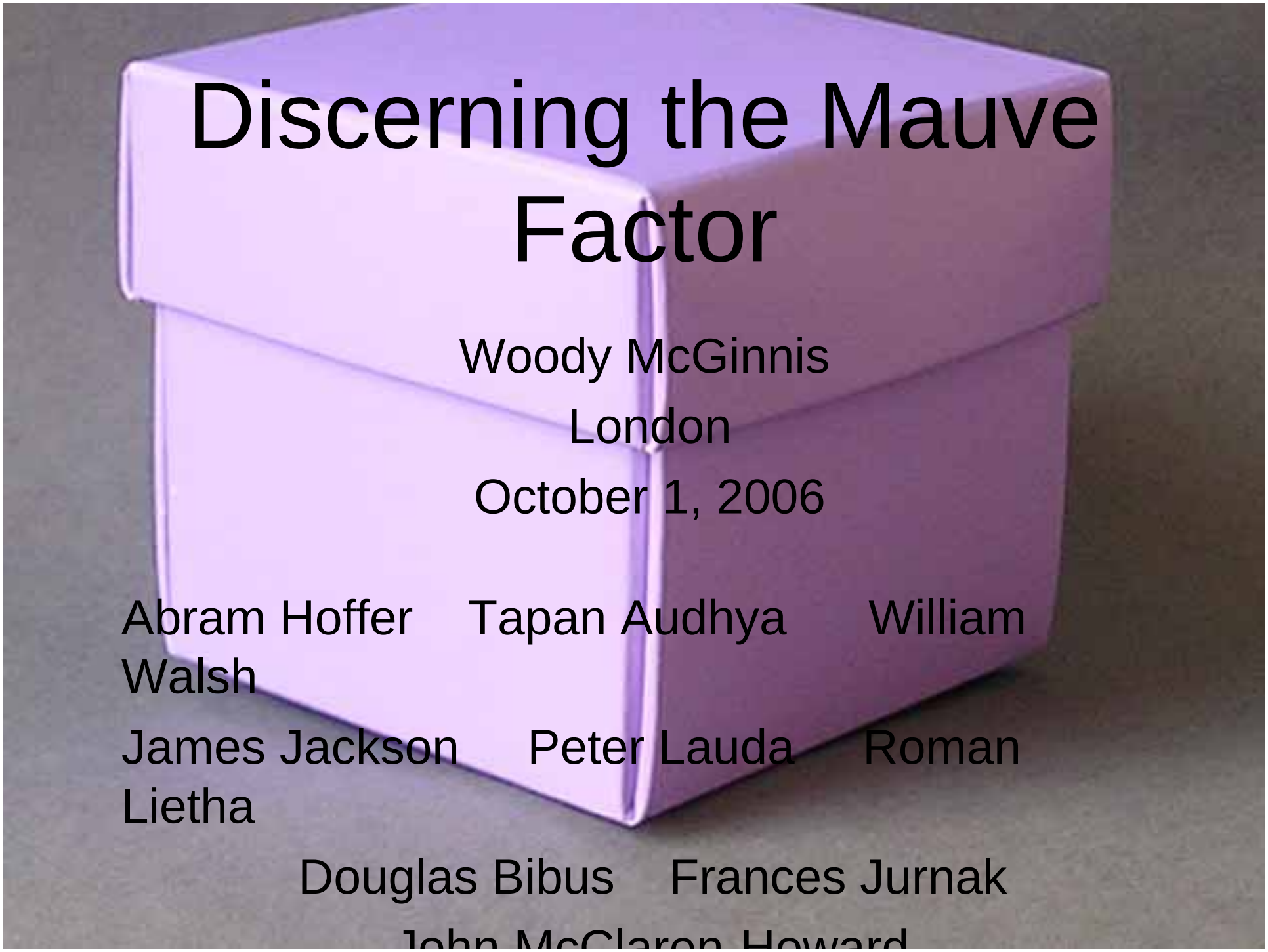


Discerning the Mauve Factor

Woody McGinnis

London

October 1, 2006

Abram Hoffer Tapan Audhya William Walsh

James Jackson Peter Lauda Roman Lietha

Douglas Bibus Frances Jurnak

John McClaren Howard

Irene (Vicky) Colquhoun

1920-2000

David Horrobin

1939-2003

Mauve History

Discovered in urine in 1958

Named for lilac-colored appearance on paper chromatograms developed with Erhlich's reagent

Labile and elusive

Abram Hoffer is the father of Mauve

Hoffer *J Neuropsych* 1961

Qualitative Mauve assay

All normals Mauve-negative

27/39 early schizophrenics positive

All 7 who recovered on niacinamide converted to negative

Hoffer 1961

Mauve associates with relapses

Apparent role in other behaviors: ETOH, depression

A "mentally retarded" mauve-positive child responded dramatically to niacinamide

Hoffer and Mauve

Relatives should be tested

Preventive potential

10/14 criminal / deviant positives

740 patients: all recovered schizophrenics negative, unrecovered 50% positive

Mauve in Schizophrenia

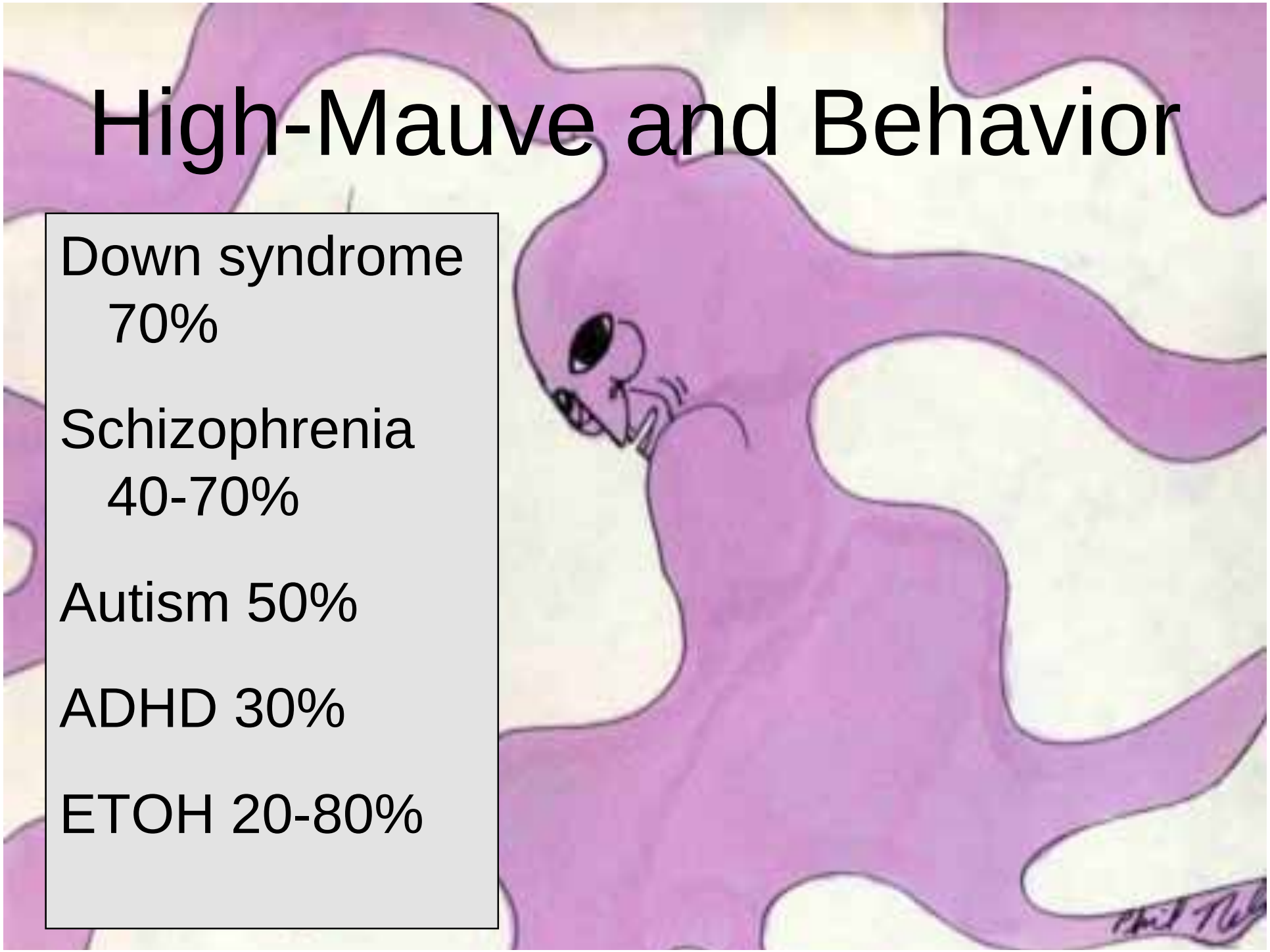
Hoffer 1961, 1963, 1966

Yutwiller 1962

O'Reilly 1965

Sohler 1967 x 2

High-Mauve and Behavior



Down syndrome 70%

Schizophrenia 40-70%

Autism 50%

ADHD 30%

ETOH 20-80%

Donald Irvine and Mauve

Dubbed it “Mauve Factor”

First to extract Mauve from urine

First to suggest pyrrole structure

Mis-identified Mauve twice

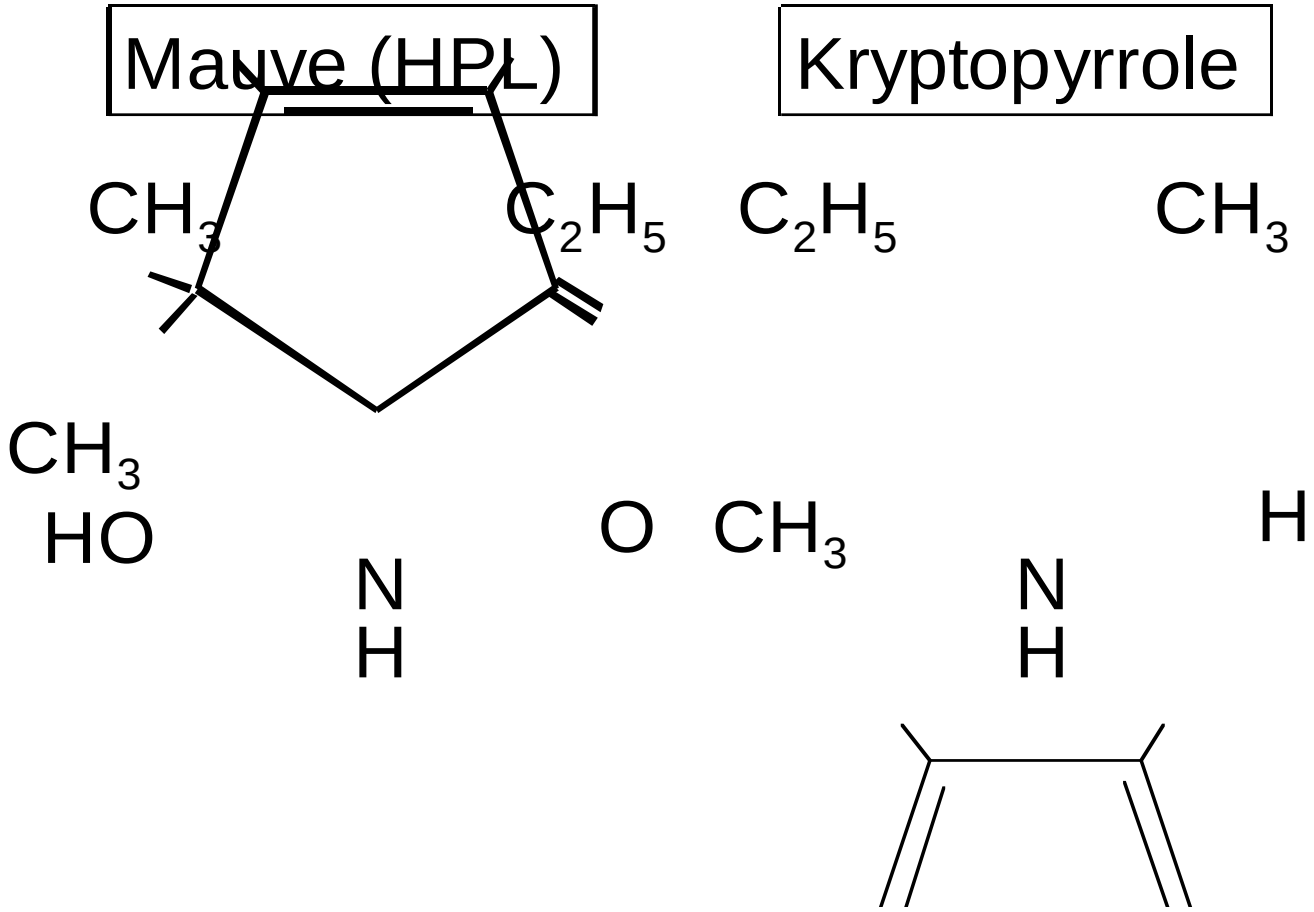
Animal experiments

Pfeiffer and Mauve

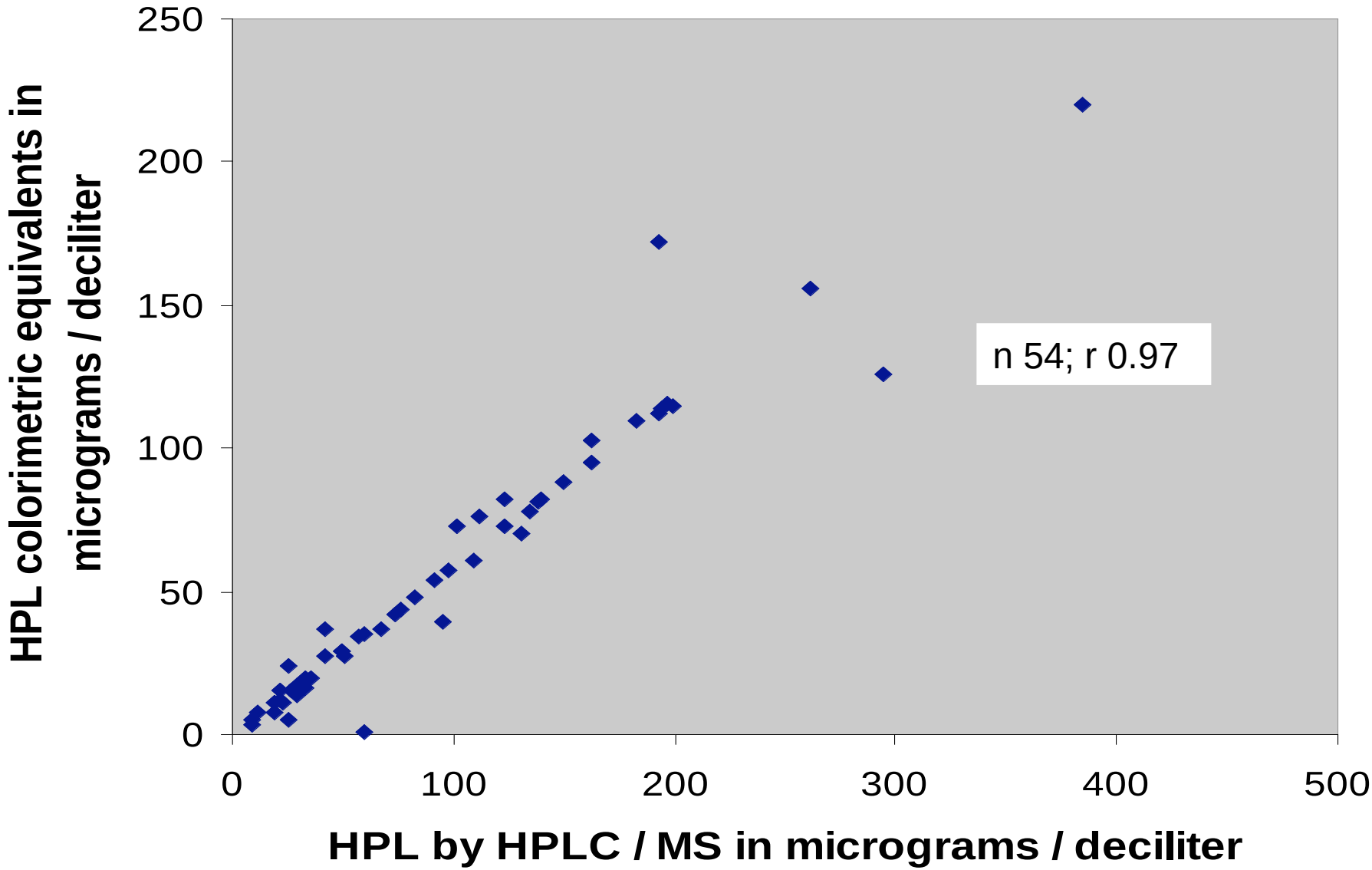
Introduced the colorimetric assay for Mauve using kryptopyrrole as surrogate standard

Vitamin B6 and zinc to suppress Mauve and improve clinical outcome, irrespective of behavioral diagnosis

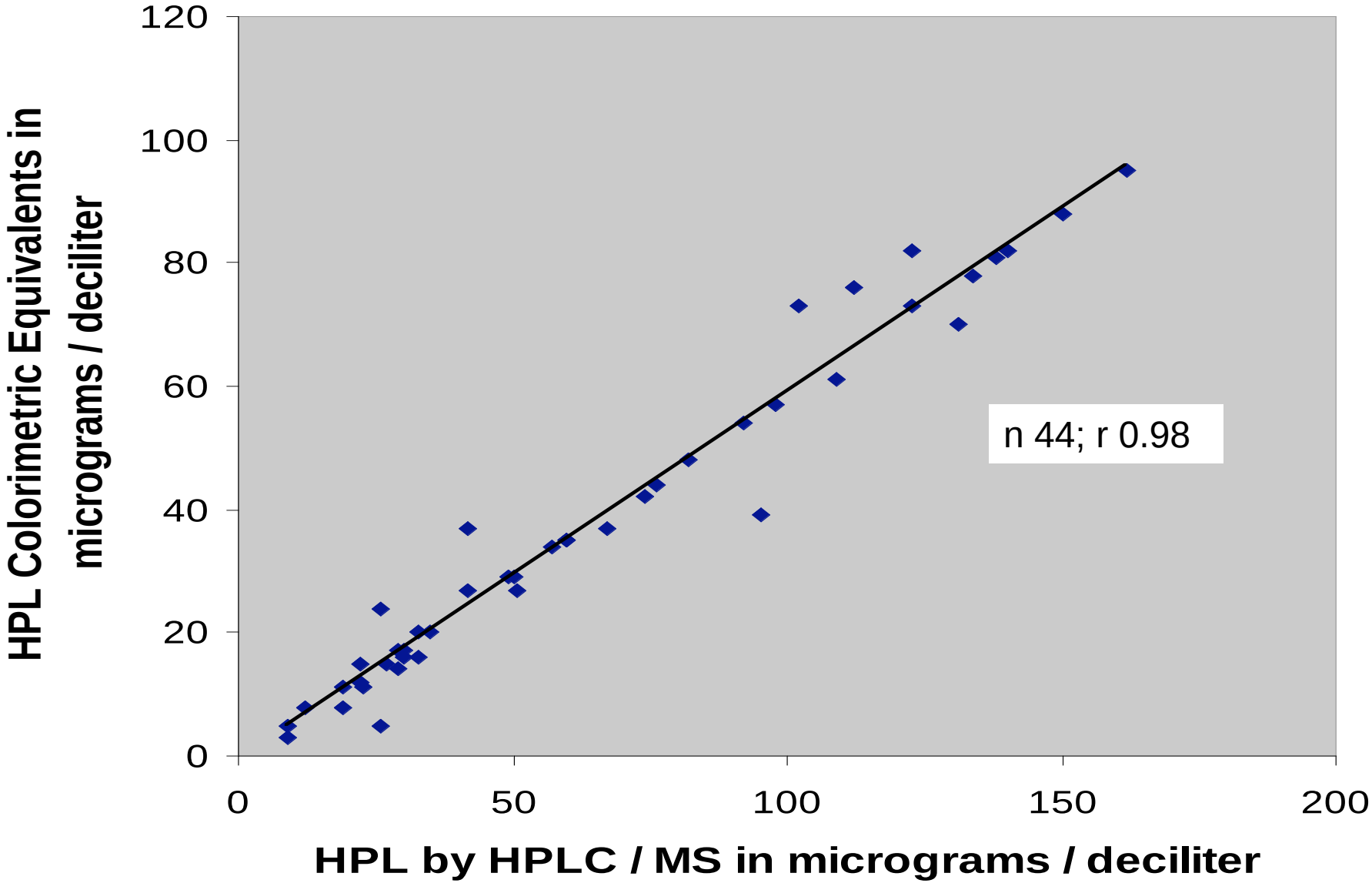
Mauve is hydroxyhemopyrrolin-2-one (HPL), not kryptopyrrole



Validation of Colorimetric Assay

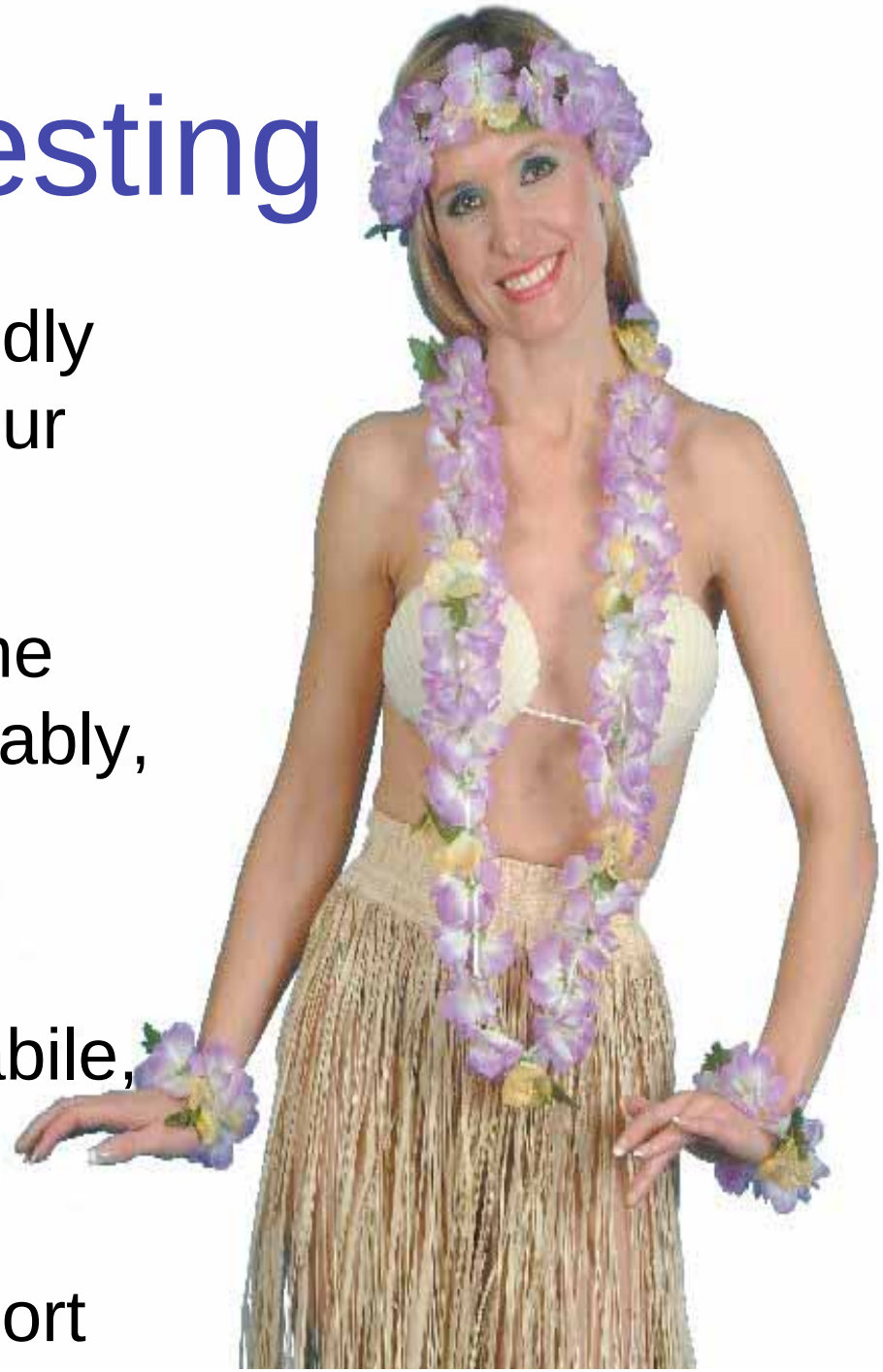


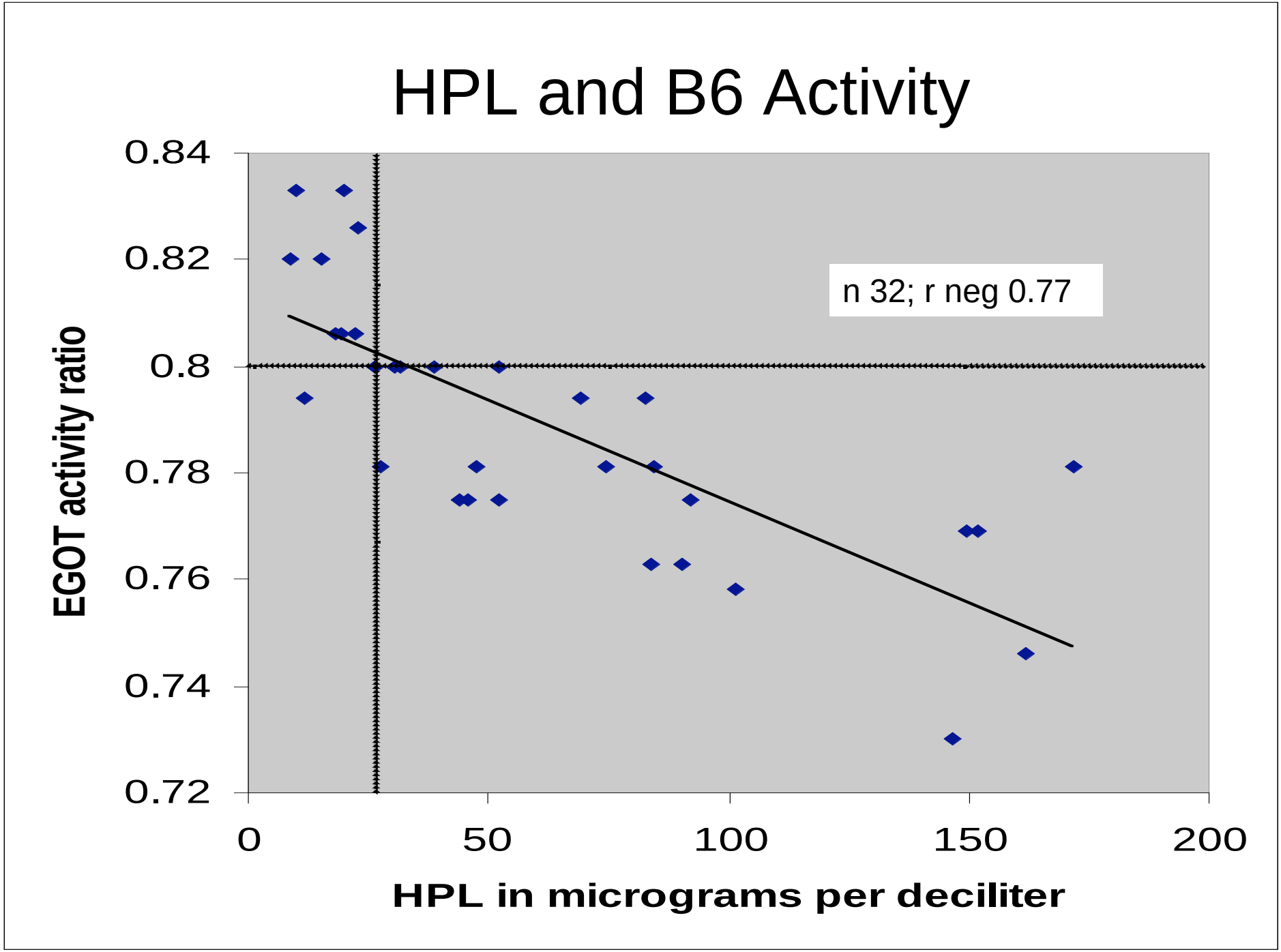
Validation of Colorimetric Assay



Mauve Testing

- Levels can fluctuate rapidly during the day, so 24-hour collection
- Variations in urine volume can affect levels appreciably, so normalize to SG or creatinine
- Light and temperature labile, so dark techniques, ascorbate preservative, freeze / overnight transport




HPL and B6 Activity
n 32; r neg 0.77
EGOT activity ratio
0.84
0.82
0.8
0.78
0.76
0.74
0.72
0
50
100
150
200
HPL in micrograms per deciliter

Mauve Associations

Poor dream recall

Poor breakfast appetite

Nail spots (leukodynia)

Stretch marks (striae)

Pale skin / poor tanning

Acne, allergy, obesity

Mauve Associations

Course eyebrows

Knee and joint pain

Cold hands or feet

Abdominal tenderness

Constipation

Eosinophilia

Mauve Associations

Light / sound / odor intolerance

Tremor / shaking / spasms

Hypoglycemia / glucose intolerance

Delayed Puberty / Impotence

Amenorrhea / irregular periods

B6-responsive anemia

Mauve Associations

Stress intolerance

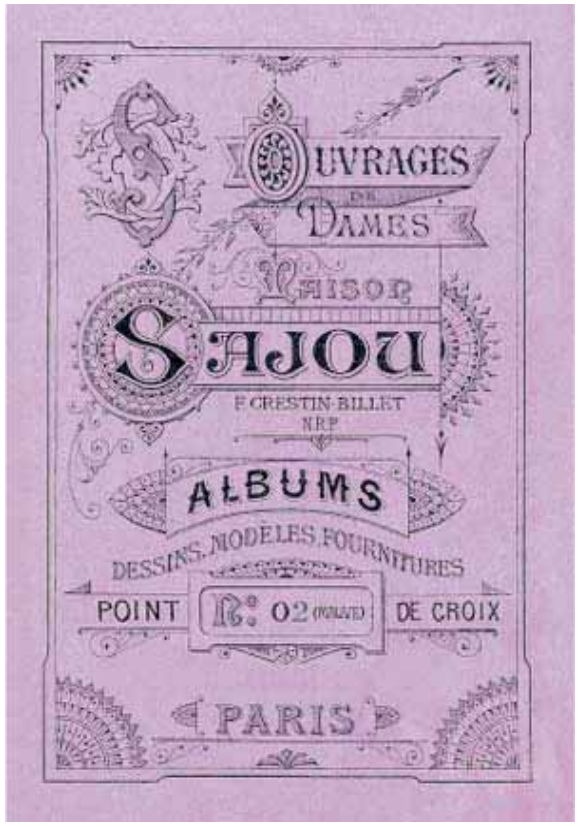
Emotional lability

Explosive anger

Anxiety / Withdrawal

Pessimism

Depression



Mauve Associations

Familial

Paranoia / Hallucinations

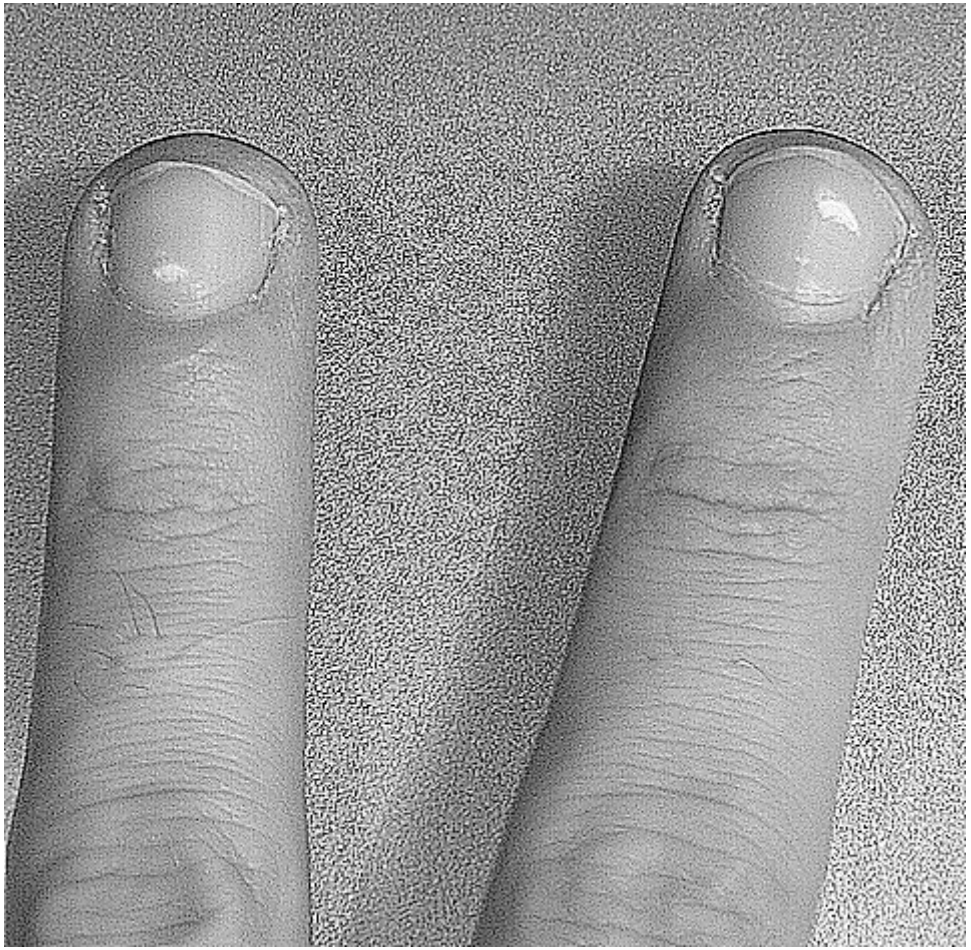
Perceptual disorganization

Crime and deliquency

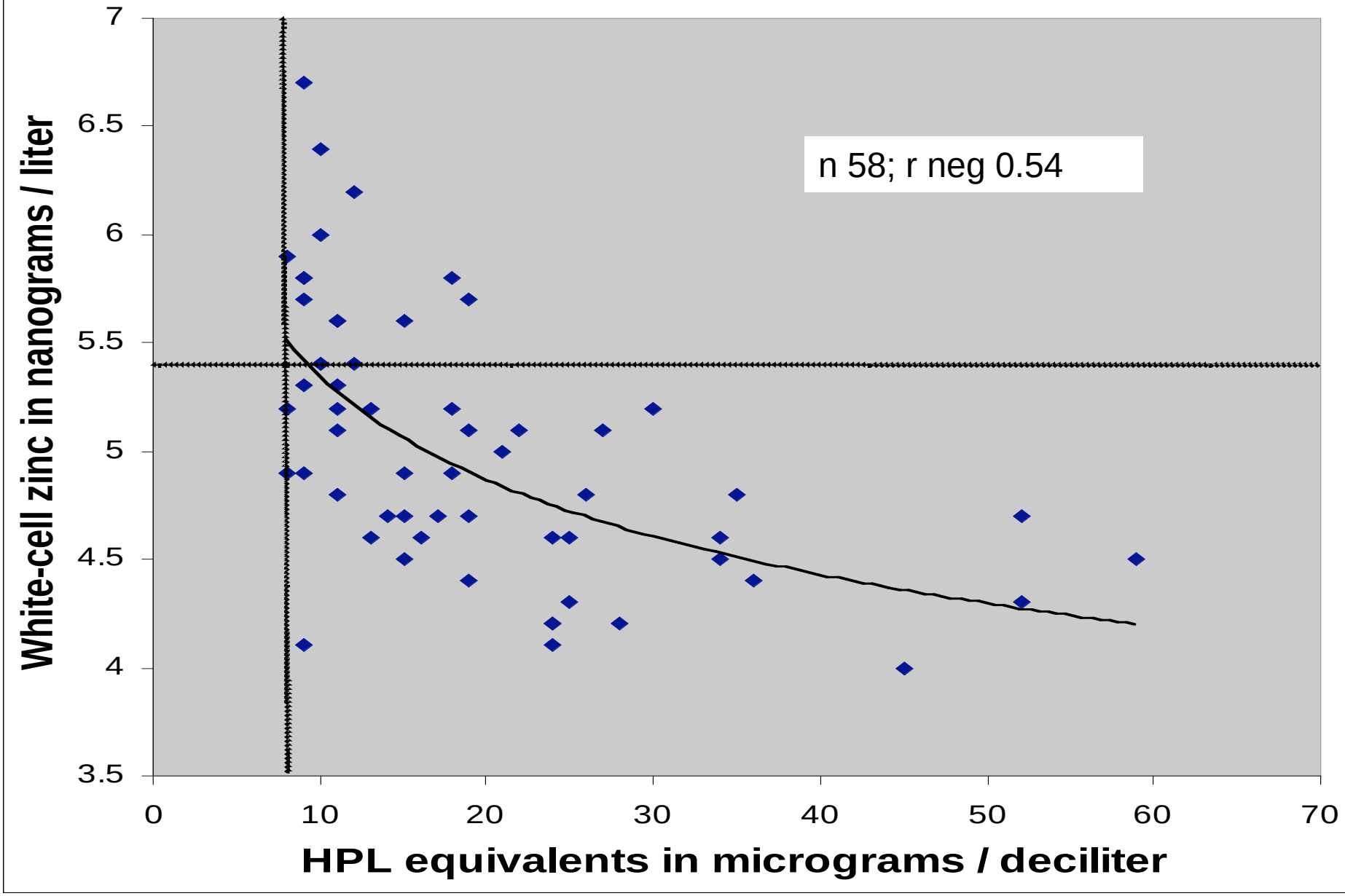
Substance abuse

Attention deficit / ADHD
Autism

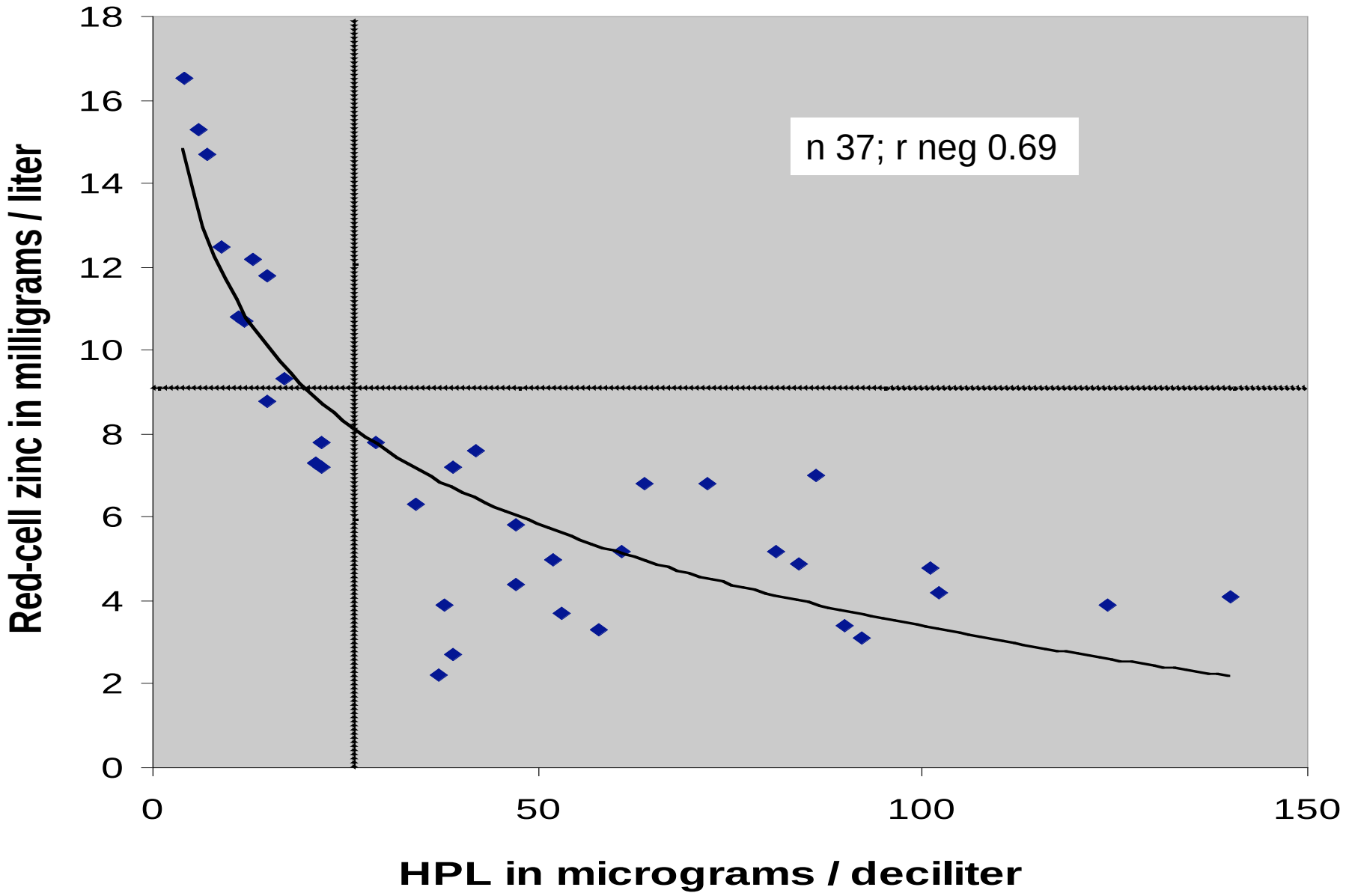
Leukodynia in Zinc Deficiency



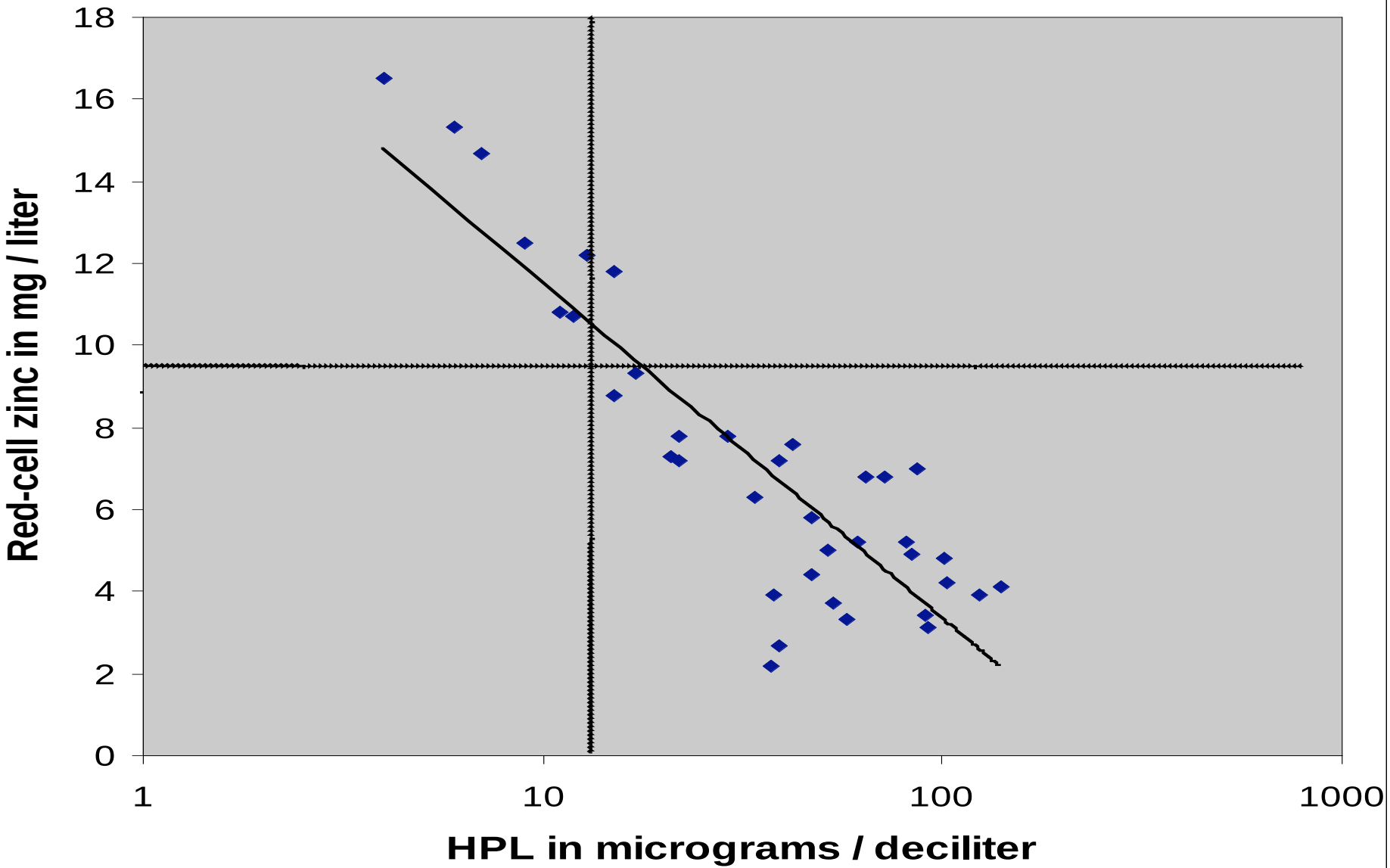
Colorimetric Mauve and WBC Zinc



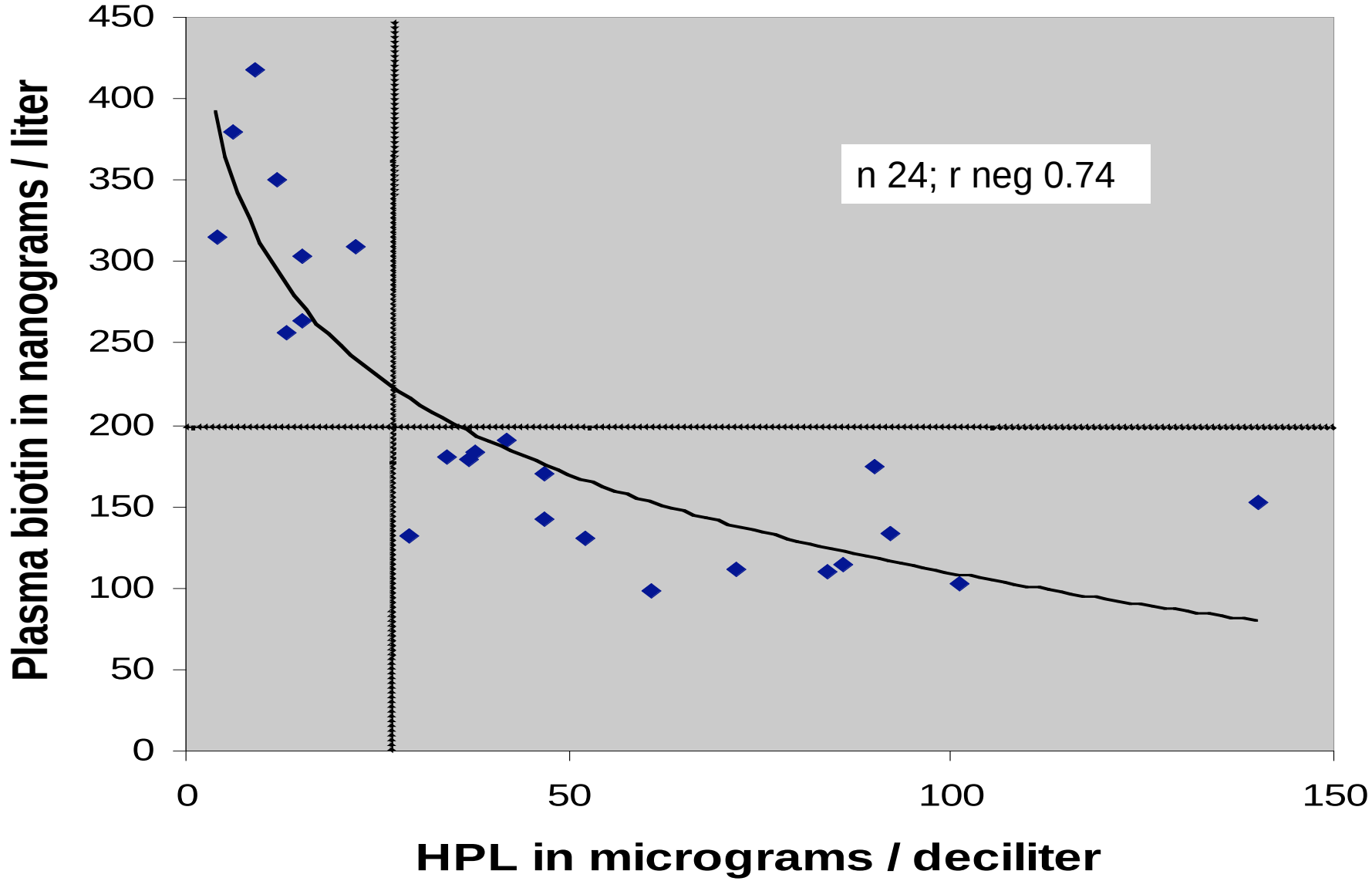
HPL and RBC Zinc

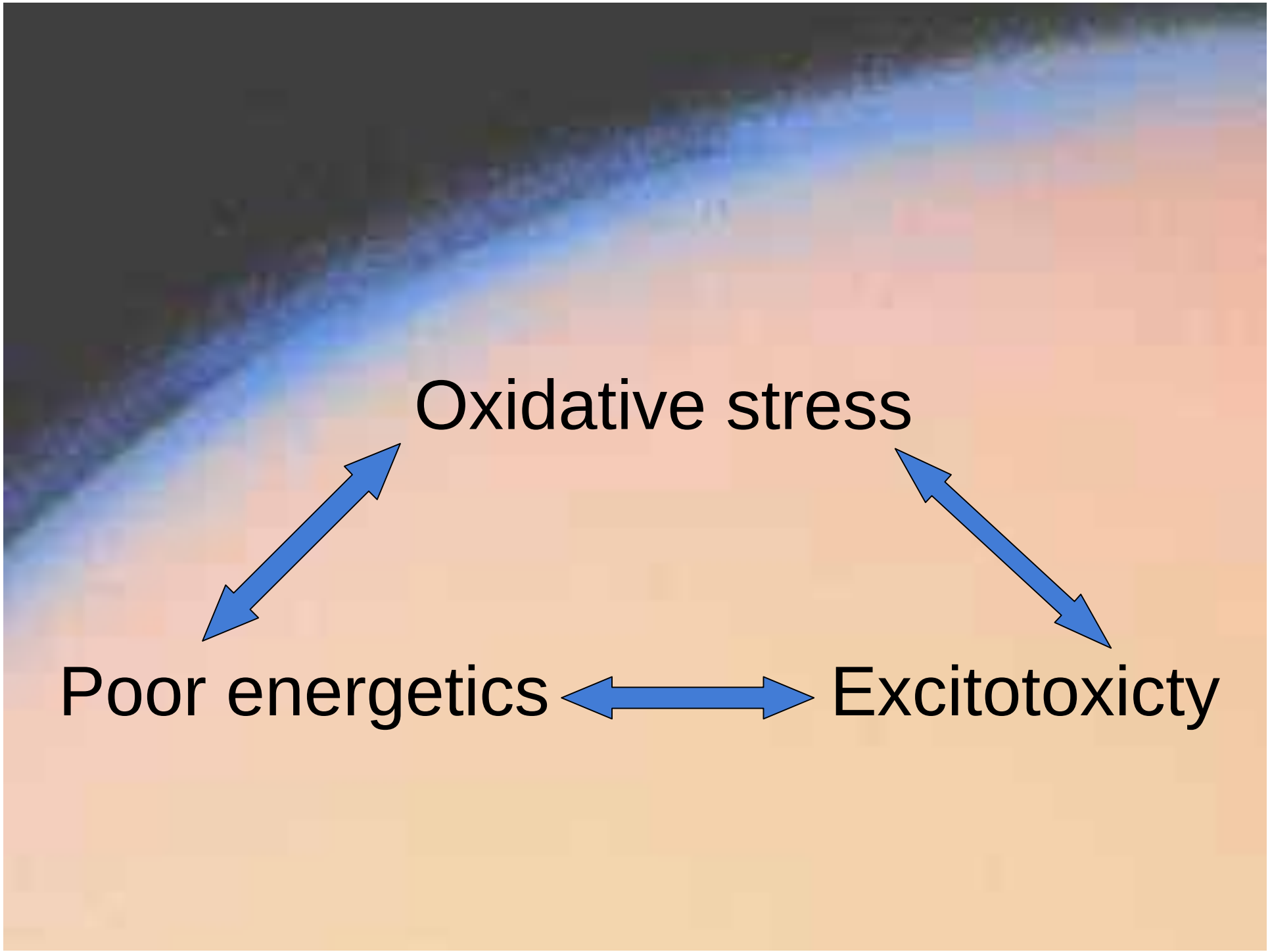


HPL and RBC Zinc



HPL and Plasma Biotin




Oxidative stress
Poor energetics
Excitotoxicty


Emotional Stress →
Oxidative Stress

Emotional stress→ Oxidative stress

Tension-anxiety scores correlate with oxidized DNA in blood

Meditation lowers blood lipid peroxides

Immobilization-stress

Increases free radicals and oxidized lipid, protein and DNA

Brain peroxidation prevented by antioxidants

Mauve and Stress

O’Reilly 1965: Hypothesized relationship

Ward 1973: Mauve proportionate to stress

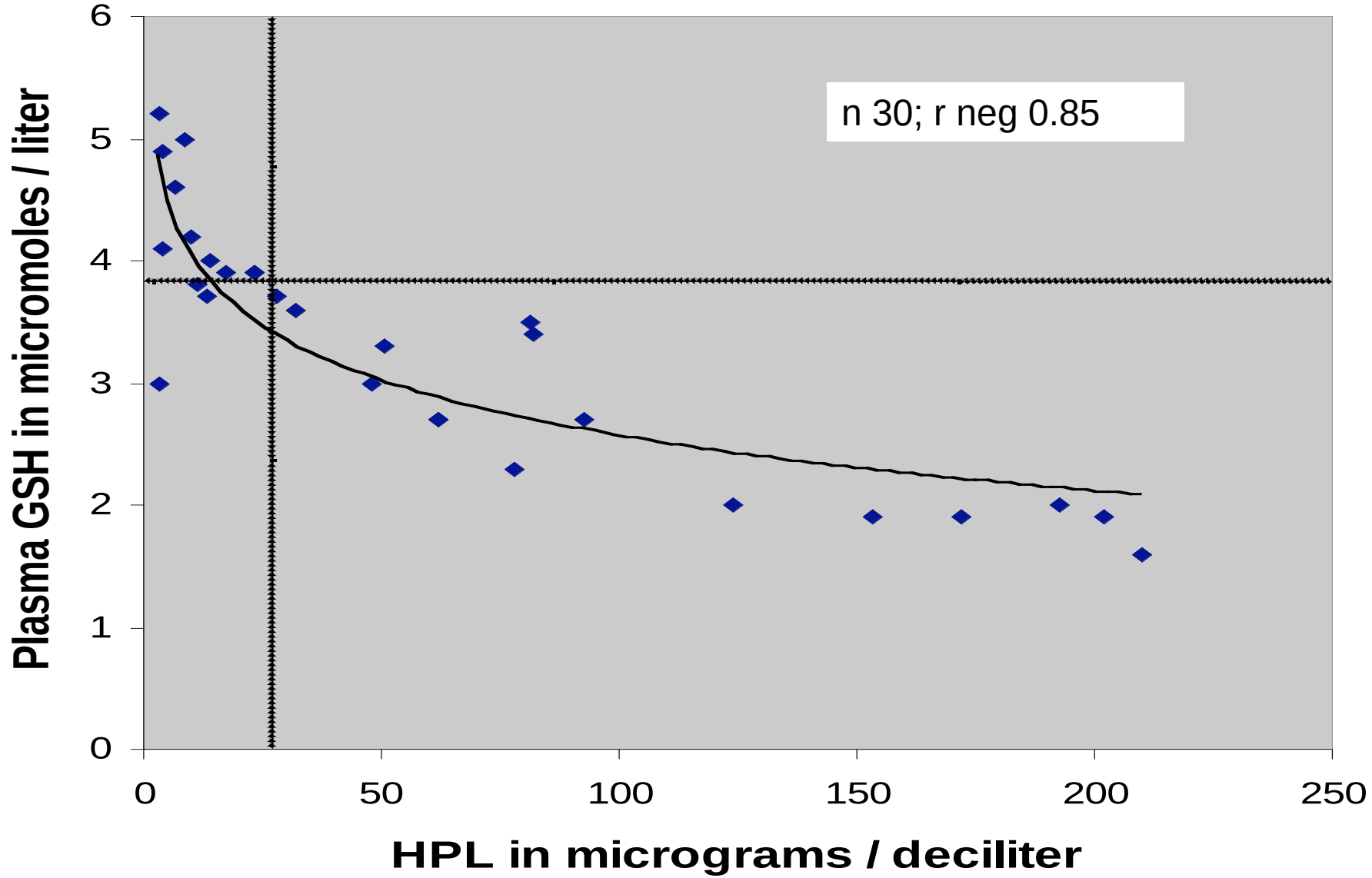
Pfeiffer 1976: Mauve “is induced by stress”

Sohler unpublished animals studies

McCabe 1983: B6 and zinc “stress doses”

Audya 1992: US Navy cold water stress

HPL and Plasma Reduced Glutathione



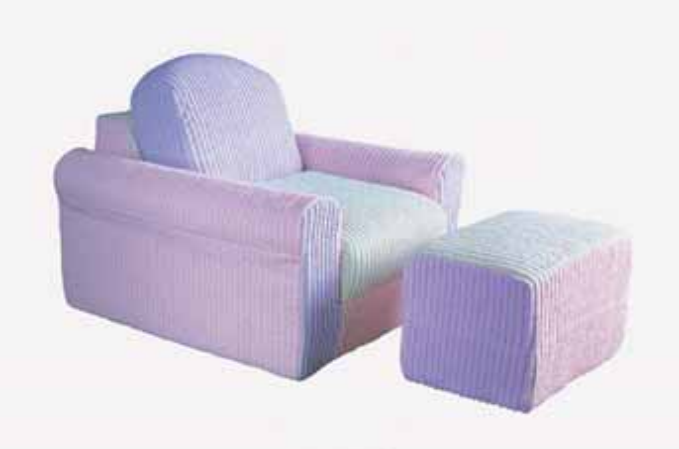
HPL and Heme

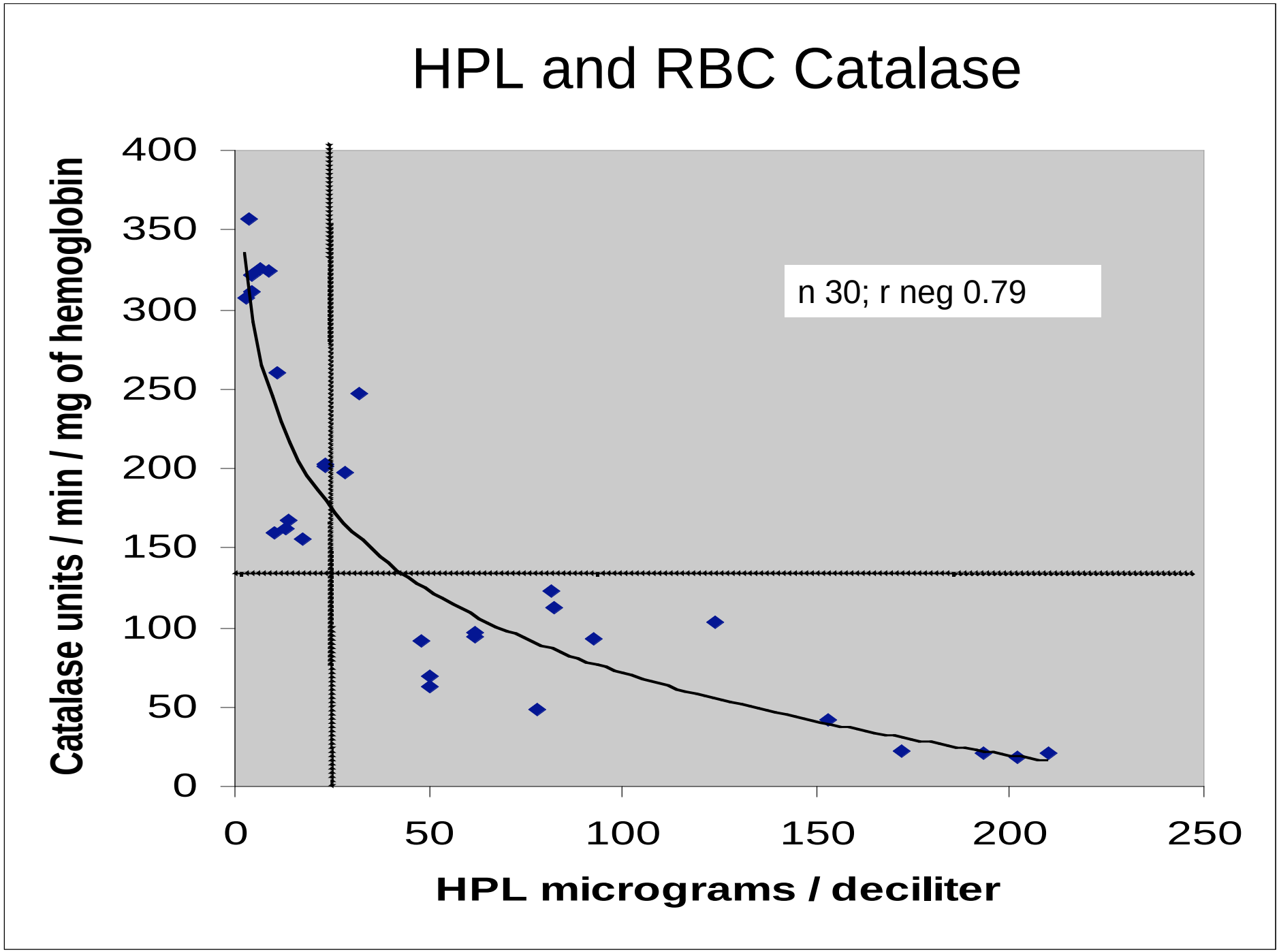
Graham 1979: HPL injection acutely depresses hepatic microsomal heme and p450 levels

Ames 2002: Experimental heme depression lowers intracellular zinc, induces NOS and increases oxidative stress

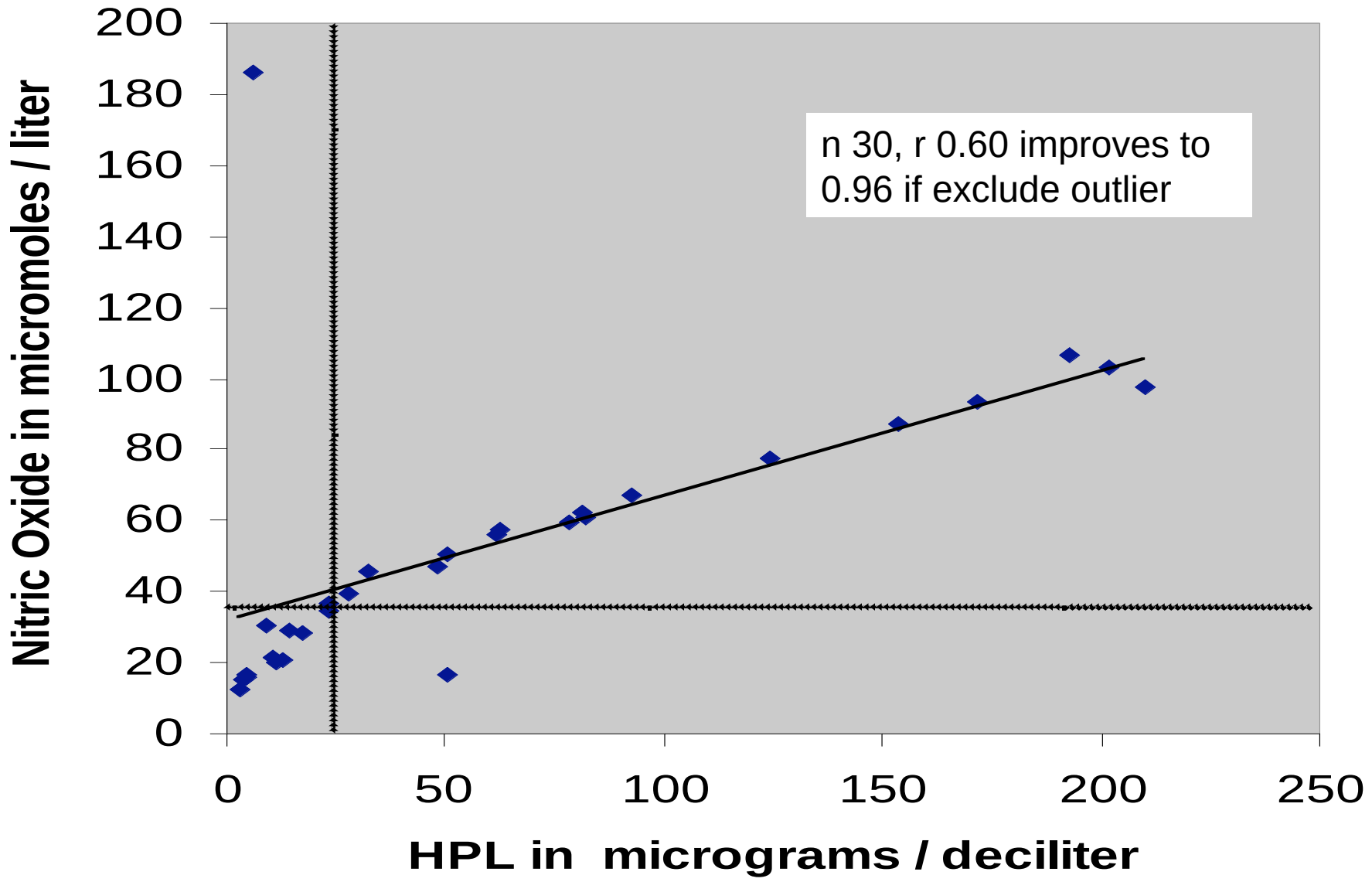
Require Heme

- Cystathionine synthase
- Catalase
- Heme-hemopexin for MT translation
- Guanylate cyclase
- Cytochromes
- Sulfite reductase
- NOS
- Pyrrolase




HPL and RBC Catalase
Catalase units / min / mg of hemoglobin
400
350
300
250
200
150
100
50
0
0
50
100
150
200
250
HPL micrograms / deciliter
n 30; r neg 0.79

HPL and Plasma Nitric Oxide



Mauve and Cortisol

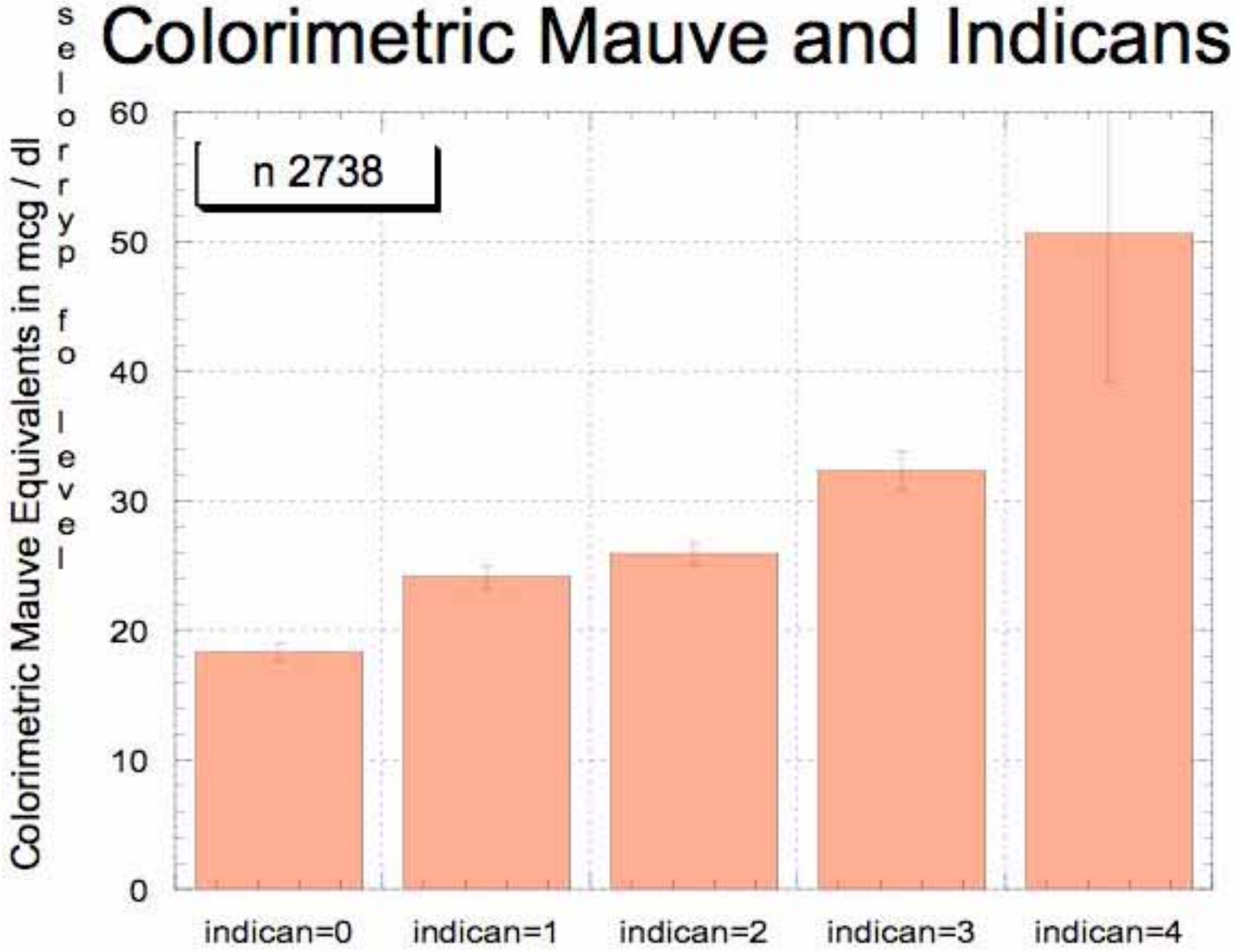
- Irvine 1972: corticosteroid administration to rats produced significant Mauve excretion.
- Increased intestinal permeability from psychological stress is mediated via endogenous glucocorticoids
- Administration of corticosteroids experimentally increases intestinal permeability

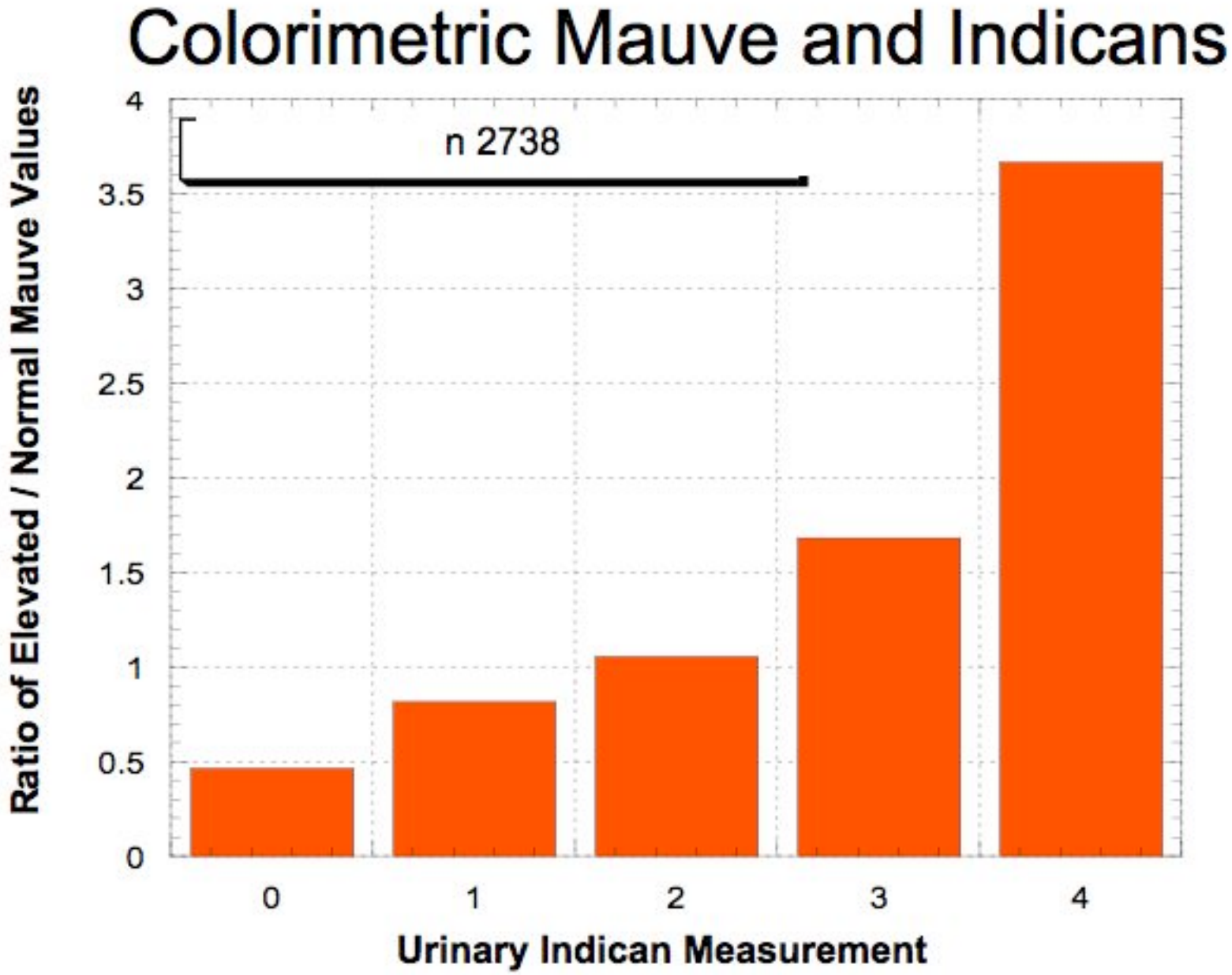
Mauve from Microbes?

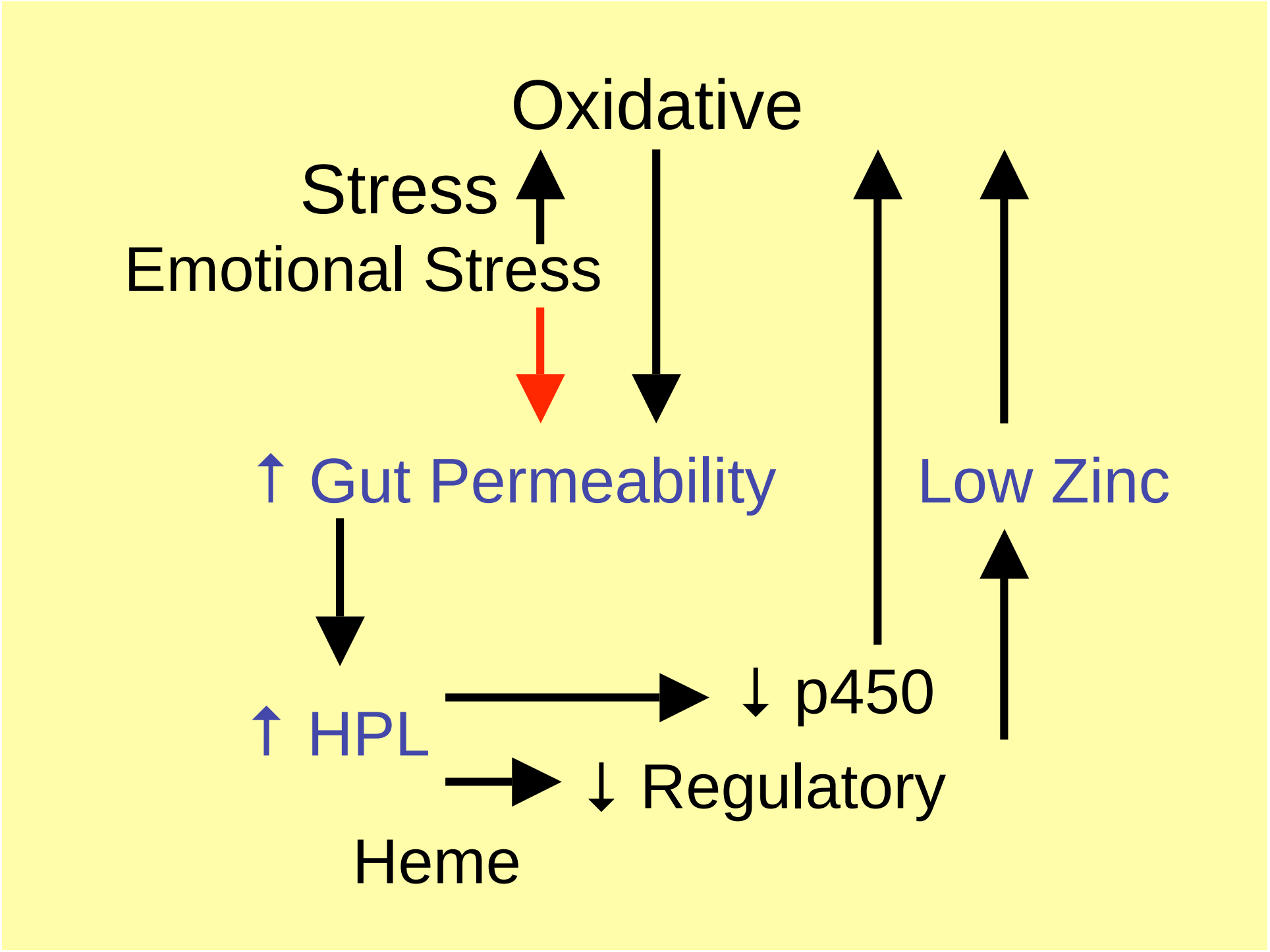
- Irvine 1973: Tetracycline reversibly abolished Mauve excretion in 4 subjects.

  Kanamycin abolished or significantly decreased Mauve in 9 subjects.

- Monopyrroles are generated by various bacteria, including pseudomonas spp.


Colorimetric Mauve and Indicans
Colorimetric Mauve Equivalents in mcg / dl
serotyp folie
n 2738
60
50
40
30
20
10
0
indican=0
indican=1
indican=2
indican=3
indican=4


Colorimetric Mauve and Indicans
n 2738
Ratio of Elevated / Normal Mauve Values
4
3.5
3
2.5
2
1.5
1
0.5
0
0
1
2
3
4
Urinary Indican Measurement


Oxidative
Stress
Emotional Stress
↑ Gut Permeability
Low Zinc
↑ HPL
↓ p450
↓ Regulatory
Heme

Summary

- Mauve levels predict proportionately lower functional B6 and zinc blood levels.
  - Strong relationship to stress.
- Emerging evidence that Mauve is a biomarker for oxidative stress.
  - Possible enteric origin of Mauve.
- Need for prospective laboratory studies and randomized clinical trials